Washington State Health Care Authority

Use of Stereotactic Body Radiation Therapy

Final Evidence Report

April 10, 2023

Health Technology Assessment Program (HTA)

Washington State Health Care Authority
PO Box 42712
Olympia, WA 98504-2712
(360) 725-5126
www.hca.wa.gov/hta
shtap@hca.wa.gov

Use of Stereotactic Body Radiation Therapy

Final Evidence Report

April 10, 2023

Prepared by:

Center for Evidence-based Policy
Oregon Health & Science University
3030 S Moody, Suite 250
Portland, OR 97201
Phone: 503.494.2182
Fax: 503.494.3807
http://centerforevidencebasedpolicy.org/

Authors:

Beth Shaw, MSc, Shannon Robalino MSc, Valerie J. King, MD, MPH.

The authors would like to acknowledge Veronique Johnstone, Jennifer Lyon, Jana Schellinger, and Sneha Yeddala from the Center for Evidence-based Policy for their contributions to this work.

This health technology assessment report is based on research conducted by the Center for Evidence-based Policy (Center) under contract to the Washington State Health Care Authority (HCA). This report is an independent assessment of the technology question(s) described based on accepted methodological principles. The findings and conclusions contained herein are those of the authors, who are responsible for the content. These findings and conclusions do not necessarily represent the views of the Washington HCA and thus, no statement in this report shall be construed as an official position or policy of the HCA.
The information in this assessment is intended to assist health care decision makers, clinicians, patients, and policy makers in making evidence-based decisions that may improve the quality and cost-effectiveness of health care services. Information in this report is not a substitute for sound clinical judgment. Those making decisions regarding the provision of health care services should consider this report in a manner similar to any other medical reference, integrating the information with all other pertinent information to make decisions within the context of individual patient circumstances and resource availability.

About the Center for Evidence-based Policy

The Center is recognized as a national leader in evidence-based decision making and policy design. The Center understands the needs of policymakers and supports public organizations by providing reliable information to guide decisions, maximize existing resources, improve health outcomes, and reduce unnecessary costs. The Center specializes in ensuring that diverse and relevant perspectives are considered and appropriate resources are leveraged to strategically address complex policy issues with high-quality evidence and collaboration. The Center is based at Oregon Health & Science University in Portland, Oregon.

Conflict of Interest Disclosures: No authors have conflicts of interest to disclose. All authors have completed and submitted the Oregon Health & Science University form for Disclosure of Potential Conflicts of Interest, and none were reported.

Table of Contents

List of Tables

List of Figures

List of Abbreviations

ADT	androgen deprivation therapy
aHR	adjusted hazard ratio
AS	active surveillance
BED	biologically-equivalent dose
BT	brachytherapy
CI	confidence interval
CMS	Centers for Medicare & Medicaid Services
CNS	central nervous system
CPT	Current Procedural Terminology
cRT	conventional radiation therapy
CT	chemotherapy
CTV	clinical target volume
EANM	European Association of Nuclear Medicine
EAU	European Association of Urologists
EBRT	external beam radiation therapy
ENRT	elective nodal radiation therapy
ESP	European Society of Pathology
ESTRO	European SocieTy for Radiotherapy and Oncology
ESUR	European Society of Urogenital Radiotherapy
EURACAN	European Reference Network for rare adult solid cancers
FDA	U.S. Food and Drug Administration
GENTURIS-ERN	European Reference Network for all patients with one of the rare genetic tumor risk syndromes
GI	gastrointestinal
GRADE	Grading of Recommendations, Assessment, Development, and Evaluation
GU	genitourinary
Gy	Gray
HCC	hepatocellular carcinoma
HDR	high-dose rate
HFRT	hypofractionated radiotherapy
HIFU	high-intensity focused ultrasound
HR	hazard ratio
ICD	International Classification of Diseases
ICER	incremental cost-effectiveness ratio
IHC	intrahepatic cholangiocarcinoma
IMRT	intensity-modulated radiation therapy
IQR	interquartile range
ISUP	International Society of Urological Pathology
IV	intravenous
KQ	key question
LCNEC	large-cell neuroendocrine carcinoma of the lung
MFRT	multifraction radiation therapy

MRI	magnetic resonance imaging
NCT	US National Clinical Trial
NSBM	nonspine bone metastases
NSCLC	non-small cell lung cancer
NR	not reported
NRS	nonrandomized study
OLT	orthotopic liver transplantation
OR	odds ratio
PFS	progression-free survival
PM	pulmonary metastasectomy
PN	partial nephrectomy
PS	performance status
PSA	prostate-specific antigen
PTV	planning target volume
QALY	quality-adjusted life year
RCC	renal cell carcinoma
RCT	randomized controlled trial
RFA	radiofrequency ablation
RT	radiation therapy
SABR	stereotactic ablative radiotherapy
SBRT	stereotactic body radiation therapy
SIOG	International Society of Geriatric Oncology
SRS	stereotactic radiosurgery
TA	thermal ablation
TACE	transarterial chemoembolization
UHRT	ultrahypofractionated radiation therapy
UN	United Nations
VMAT	volumetric-modulated arc therapy
WTP	willingness-to-pay

Executive Summary

Structured Abstract

Purpose

This updated evidence report reviews the effectiveness and cost-effectiveness of stereotactic body radiation therapy (SBRT) for the treatment of a range of cancers, specifically, those cancers not currently covered under the coverage determination made by the Washington Health Technology Clinical Committee in 2012.

Data Sources

For this update, we identified all included studies from the previous report, the 3 interim evidence updates, and all references suggested during the public comment period. We also conducted searches using multiple electronic databases.

Study and Guideline Selection

Using a priori criteria, we conducted dual independent title and abstract screening and full-text article review for English language randomized controlled trials (RCTs), nonrandomized studies (NRSs), and economic evaluations of SBRT in adults and children. A third reviewer settled discrepancies, as needed. We also selected relevant clinical practice guidelines using a similar process to select and assess them.

Data Extraction and Risk-of-bias Assessment

We used standardized procedures to extract relevant data from each of the included trials and a second researcher fully cross-checked a random sample (10%) of data for accuracy. We performed dual independent risk-of-bias assessment on the included studies and guidelines. A third reviewer settled discrepancies.

Data Synthesis and Analysis

We applied the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) Working Group system to rate the overall certainty of evidence on selected measures of outcomes.

Results

Based on the studies included in this review, we conclude that SBRT:

- May be similarly or more effective than other options for individuals with localized prostate cancer (very low to moderate certainty of evidence [CoE], based on 3 RCTs and 7 comparative NRSs);
- May be similarly or more effective than radiation therapy for inoperable stage II non-small cell lung cancer (NSCLC; low CoE, based on 1 comparative NRS) or in combination with pembrolizumab than pembrolizumab alone for advanced NSCLC (low to moderate CoE, based on 1 RCT). SBRT also appears to be similarly or more effective than conventional radiation therapy (cRT) for people with lung metastases (very low to low CoE, based on 4 comparative NRSs) or large cell neuroendocrine carcinoma (LCNEC) of the lung (low CoE, based on 2 comparative NRSs). In general, surgery appears to be more effective than SBRT for resectable lung cancer (very low to low CoE, based on 10 comparative NRSs);

- In combination with nivolumab and ipilimumab, may be as effective as nivolumab and ipilimumab for Merkel cell carcinoma (low CoE, based on 1 RCT);
- May be less effective than ablation (RFA, microwave, or cryoablation) or surgery for stage 1 renal cell carcinoma (low CoE, based on 1 comparative NRS);
- May be more effective than chemotherapy or intensity-modulated radiation therapy for unresected pancreatic cancer (low CoE, based on 1 comparative NRS);
- May be more effective than conventional RT for pancreatic cancer (low CoE, based on 1 comparative NRS);
- May be similarly effective to brachytherapy, when used as a boost treatment after cRT for early-stage oropharyngeal cancer (low CoE, based on 1 comparative NRS);
- May be less effective than charged particle RT for recurrent or metastatic head and neck cancer, but similar in effectiveness to intensity-modulated RT (IMRT) and conformal RT (low to moderate CoE, based on 1 RCT and 3 comparative NRSs);
- May be as effective as radiofrequency ablation (RFA) for early-stage liver cancer; however, results were mixed (very low to low CoE, based on 4 comparative NRSs);
- Alone, or in combination with transarterial chemoembolization (TACE), may be as effective as RFA or TACE alone for small liver cancers (very low to low CoE, based on 4 comparative NRSs) and for unresectable liver cancer (low CoE, based on 8 comparative NRSs);
- May be more effective than sorafenib for advanced liver cancer (very low to low CoE, based on 1 comparative NRS);
- May be similarly or more effective than other options (RFA, TACE, high-intensity focused ultrasound [HIFU]) when used as a bridging therapy for people on the waiting list for liver transplantation due to liver cancer (very low to low CoE, based on 2 comparative NRSs);
- May be more effective than sorafenib for advanced liver cancer (very low to low CoE, based on 1 comparative NRS);
- May be more effective than transarterial radioembolization (TARE) for unresectable intrahepatic cholangiocarcinoma (low CoE, based on 1 comparative NRS);
- Appears to be more effective than standard of care or observation for oligometastatic cancer (low to moderate CoE, based on 3 RCTs); however, for oligometastatic prostate cancer, elective nodal radiation therapy may be more effective than SBRT (very low to low CoE, based on 2 comparative NRSs); and
- May be as effective as multifraction RT for painful bone metastases (moderate CoE, based on 1 RCT).

No comparative studies were identified on the use of SBRT for adrenal cancer or large tumors. Few studies reported on clinical subgroups of interest, but there was some indication specific populations (by cancer site) may be more likely to benefit from SBRT compared with other populations. However, subgroups varied by cancer type and treatment site and were often only reported in single studies.

Overall, SBRT was not associated with significantly higher rates of toxicity than other treatment options. The types of toxicity varied by treatment site, and events classed as grade 4 and 5 toxicities were rare.

While the economic literature was sparse, SBRT appears to be:

- Possibly cost-effective for oligometastatic hormone-resistant prostate cancer (low CoE, based on 1 economic modeling study)
- Lower in costs than IMRT for prostate cancer (very low CoE, based on 1 comparative NRS);
- Cost-ineffective when compared with maintenance therapy for oligometastatic lung cancer (moderate CoE, based on 1 economic modeling study);
- Higher in costs than cRT or chemotherapy for pancreatic cancer (very low CoE, based on 1 comparative NRS);
- Cost-ineffective as reirradiation when compared with other salvage therapies, including IMRT with chemotherapy, for head and neck cancer (moderate CoE, based on 1 economic modeling study);
- Cost-ineffective when compared with RFA for liver cancer (low CoE, based on 1 economic modeling study);
- Cost-effective when compared with standard of care for oligometastatic cancer (moderate CoE, based on 2 economic modeling studies); and
- More expensive than EBRT and IMRT for bone cancer

Clinical Practice Guidelines and Payer Policies

Recommendations on the use of SBRT and payer policies varied in approach to the use of SBRT, with some guidelines or policies being more supportive of the use of SBRT depending on the cancer site. Guidelines and payer policies often noted the limited evidence base, but also highlighted that SBRT may be preferred by patients because of the fewer treatment fractions, and has a favorable safety profile.

Conclusions

The use of SBRT for many cancers remains unsupported with limited or no comparative evidence of effectiveness. However, for other cancer sites, evidence shows SBRT has the potential to be an effective option when compared with cRT. The results for SBRT are mixed, depending on the cancer site and the specific type of alternative RT when compared with other forms of RT. Some guidelines are more supportive of the use of SBRT, but most note the limited evidence base, highlighting it may be preferred by patients because of the fewer treatment fractions and the favorable safety profile of SBRT when compared with other treatment options.

Background

Radiation therapy is a cancer treatment that uses high-energy X-ray or other particles to destroy cancer cells.[1] A radiation therapy regimen or schedule usually consists of a specific number of treatments given over a set time period to treat different types of cancer.[1] Radiation therapy also can be used in combination with other cancer treatments, such as chemotherapy or surgery.[1]

Technology of Interest

Treatment by SBRT is defined as an extracranial stereotactic ablative treatment (which can include the spine) typically delivered in 1 to 5 fractions, and is also referred to as stereotactic ablative radiotherapy (SABR).[2] Clinical indications for SBRT can be as primary treatment for selected early-stage cancers, as treatment for discrete tumors in patients with oligometastatic disease, for selected benign neoplasms in or near the central nervous system (CNS), or in recurrent cancer within previously irradiated regions.[2]

Policy Context

The use of SBRT for various cancers is increasing in the US[3-5]; however, its effectiveness and safety in routine clinical practice for most cancers is unclear.

In 2012 the Washington State HTCC commissioned an evidence review on the effectiveness of stereotactic radiosurgery (SRS) and SBRT for treating various cancers.[6] On March 22, 2013, using that evidence review to guide decision making, the committee adopted the following coverage determination[7]:

- SRS for central nervous system (CNS) primary and metastatic tumors is a covered benefit for adults and children when the following criteria are met:
  - Patient functional status score (i.e., Karnofsky score) is greater than or equal to 50; **and**
  - Evaluation includes multidisciplinary team analysis (e.g., tumor board), including surgical input.
- SBRT is covered for adults and children for the following conditions when the following criteria are met:
  - For cancers of spine/paraspinal structures; **or**
  - For inoperable non-small cell lung cancer (NSCLC), stage 1; **and**
  - Evaluation includes multidisciplinary team analysis, including surgical input.
- All other indications are noncovered.

This topic was selected because of medium-level concerns about the safety and efficacy of SBRT and high-level concern about costs. This topic was selected for re-review based on new evidence from signal searches that could prompt potential coverage policy changes. This updated evidence review will help inform Washington's independent Health Technology Clinical Committee as the committee determines coverage regarding SBRT in adults and children for noncovered indications.

Methods

This evidence review is based on the final key questions (KQs) published on September 21, 2022.[8] The draft KQs were available for public comment from July 27 to August 12, 2022, and appropriate revisions were made to the KQs based on the comments and responses. All public comments received and a table of responses can be found on the Washington Health Technology Assessment website. The draft report was available for public comment between February 16 and March 16, 2023; no comments were received. The draft report was also peer-reviewed by subject matter experts, with appropriate revisions reflected in this final report. The PICO statement (population, intervention, comparator, outcome), along with the setting, study design, and publication factors that guided development of the KQs and study selection are presented in Table 5.

Key Questions

KQ1. What is the evidence of effectiveness for SBRT for patients with cancers not currently covered (CNS cancers and inoperable stage 1 NSCLC)?

KQ2. What are the harms of SBRT in patients with included cancers?

KQ3. What is the evidence that SBRT has differential efficacy or harms in subpopulations, including:

a. Sex
b. Age
c. Site and type of cancer
d. Stage and grade of cancer
e. Setting, provider characteristics, equipment, quality assurance standards and procedures

KQ4. What is the evidence of cost and cost-effectiveness of SBRT?

Data Sources and Searches

For this update, we identified all included studies from the previous report and the evidence updates,[6,9-11] and all references suggested during the public comment period. We excluded any studies in populations with covered indications and rescreened the remaining studies against our inclusion and exclusion criteria for this update report. We also conducted searches of the peer-reviewed published literature using multiple electronic databases. The time periods for searches were:

- Ovid MEDLINE All: from 1946 to October 21, 2022
- Cochrane Library databases (Cochrane Database of Systematic Reviews and Cochrane Central Register of Controlled Trials): from database inception to October 31, 2022

Study and Guideline Selection

We independently screened titles and abstracts and reached agreement on exclusion through discussion. We performed dual full-text review for any study not excluded by review of title and abstract (Appendix H lists the excluded studies at full-text review, with reasons). For studies on which we did not agree after initial full-text review, we discussed each study and came to consensus. Any remaining disagreements were settled by a third independent researcher.

Data Abstraction and Quality Assessment

We used standardized procedures to extract relevant data from each of the included trials and fully cross-checked all entered data for accuracy.

We evaluated each eligible study for methodological risk-of-bias (Appendix B) and held discussions to reach agreement on these assessments. Any remaining disagreement was settled by a third independent researcher. Each trial was assessed using Center instruments adapted from national and international standards and assessments for risk-of-bias.[12-16] A rating of high, moderate, or low risk-of-bias was assigned to each study based on adherence to recommended methods and the potential for internal and external biases. The risk-of-bias criteria for the included study types are shown in Appendix D.

We evaluated the methodological quality of eligible clinical practice guidelines. Any remaining disagreement among these assessments was settled by a third independent researcher. The methodological quality of clinical practice guidelines was rated as good, fair, or poor. The assessment criteria for the methodological quality of the clinical practice guidelines are shown in Appendix B.

Data Analysis and Synthesis

We assigned selected outcomes a summary judgment for the overall quality of evidence (Appendix E) using the system developed by the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) Working Group.[17,18] The outcomes of overall survival, progression, disease control, quality of life, and toxicity were selected from measures of effectiveness and safety. Specific measures from general domains of interest were selected in a post hoc manner based on the outcomes available from the included studies.

Results

Our searches and reference checking, including from public comments and peer review, returned a total of 3,982 records. We found no additional studies, beyond those identified in electronic databases and reference list checking, through Google and gray literature searches. After duplicate studies were removed, 2,536 records remained (Figure 2. PRISMA Flow Study Diagram). Of these, 644 required full-text review to determine eligibility. In total, 12 RCTs (in 21 publications) and 115 NRSs (in 131 publications) met the inclusion criteria for KQs 1, 2, 3, and 4. In addition, a further 6 economic- or cost-focused studies met the inclusion criteria for KQ 4.

Key Questions 1 and 2

Based on the studies included in this review, we conclude that SBRT:

- May be similarly or more effective than other options for individuals with localized prostate cancer (very low to moderate certainty of evidence [CoE], based on 3 RCTs and 7 comparative NRSs);
- May be similarly or more effective than radiation therapy for inoperable stage II non-small cell lung cancer (NSCLC; low CoE, based on 1 comparative NRS) or in combination with pembrolizumab than pembrolizumab alone for advanced NSCLC (low to moderate CoE, based on 1 RCT). SBRT also appears to be similarly or more effective than conventional radiation therapy (cRT) for people with lung metastases (very low to low CoE, based on 4 comparative NRSs) or large cell neuroendocrine carcinoma (LCNEC) of the lung (low CoE, based on 2 comparative NRSs). In general, surgery appears to be more effective than SBRT for resectable lung cancer (very low to low CoE, based on 10 comparative NRSs);
- In combination with nivolumab and ipilimumab, may be as effective as nivolumab and ipilimumab for Merkel cell carcinoma (low CoE, based on 1 RCT);
- May be less effective than ablation (radiofrequency ablation [RFA], microwave, or cryoablation) or surgery for stage 1 renal cell carcinoma (low CoE, based on 1 comparative NRS);
- May be more effective than chemotherapy or intensity-modulated radiation therapy for unresected pancreatic cancer (low CoE, based on 1 comparative NRS);
- May be more effective than conventional RT for pancreatic cancer (low CoE, based on 1 comparative NRS);
- May be similarly effective to brachytherapy, when used as a boost treatment after cRT for early-stage oropharyngeal cancer (low CoE, based on 1 comparative NRS);
- May be less effective than charged particle RT for recurrent or metastatic head and neck cancer, but similar in effectiveness to intensity-modulated RT (IMRT) and conformal RT (low to moderate CoE, based on 1 RCT and 3 comparative NRSs);

- May be as effective as RFA for early-stage liver cancer; however, results were mixed (very low to low CoE, based on 4 comparative NRSs);
- Alone, or in combination with transarterial chemoembolization (TACE), may be as effective as RFA or TACE alone for small liver cancers (very low to low CoE, based on 4 comparative NRSs) and for unresectable liver cancer (low CoE, based on 8 comparative NRSs);
- May be more effective than sorafenib for advanced liver cancer (very low to low CoE, based on 1 comparative NRS);
- May be similarly or more effective than other options (RFA, TACE, high-intensity focused ultrasound [HIFU]) when used as a bridging therapy for people on the waiting list for liver transplantation due to liver cancer (very low to low CoE, based on 2 comparative NRSs);
- May be more effective than sorafenib for advanced liver cancer (very low to low CoE, based on 1 comparative NRS);
- May be more effective than transarterial radioembolization (TARE) for unresectable intrahepatic cholangiocarcinoma (low CoE, based on 1 comparative NRS);
- Appears to be more effective than standard of care or observation for oligometastatic cancer (low to moderate CoE, based on 3 RCTs); however, for oligometastatic prostate cancer, elective nodal radiation therapy may be more effective than SBRT (very low to low CoE, based on 2 comparative NRSs); and
- May be as effective as multifraction RT for painful bone metastases (moderate CoE, based on 1 RCT).

No comparative studies were identified on the use of SBRT for adrenal cancer or large tumors. Few studies reported on clinical subgroups of interest, but there was some indication that specific populations (by cancer site) may be more likely to benefit from SBRT compared with other populations. However, subgroups varied by cancer type and treatment site and were often only reported in single studies.

Overall, SBRT was not associated with significantly higher rates of toxicity than other treatment options. The types of toxicity varied by treatment site and reports of grade 4 and 5 toxicities were rare.

FDA-reported Harms for Stereotactic Body Radiation Therapy

We also searched the U.S. FDA MAUDE database from the past 5 years and the Medical Device Recall reports (Appendix F). We found 618 entries in the MAUDE database, including voluntary, user facility, distributor, and manufacturer reports of adverse events relating to SBRT use in the past 5 years. We were not able to analyze the reports by cancer site, but the types of adverse events appeared similar to those reported in our eligible studies, as device failures and process errors.

Key Question 3

We did not identify any additional studies reporting on the effectiveness or harms of SBRT by subgroup, but do report on relevant subgroup findings by cancer site in the main body of the report. Because of the heterogeneity across the cancer sites and relevant groups, we were not able to identify any specific groups who were more likely to benefit from SBRT in general.

Key Question 4

While the economic literature was sparse, SBRT appears to be:

- Possibly cost-effective for oligometastatic hormone-resistant prostate cancer (low CoE, based on 1 economic modeling study)
- Lower in costs than IMRT for prostate cancer (very low CoE, based on 1 comparative NRS);
- Cost-ineffective when compared with maintenance therapy for oligometastatic lung cancer (moderate CoE, based on 1 economic modeling study);
- Higher in costs than cRT or chemotherapy for pancreatic cancer (very low CoE, based on 1 comparative NRS);
- Cost-ineffective as reirradiation when compared with other salvage therapies, including IMRT with chemotherapy, for head and neck cancer (moderate CoE, based on 1 economic modeling study);
- Cost-ineffective when compared with RFA for liver cancer (low CoE, based on 1 economic modeling study);
- Cost-effective when compared with standard of care for oligometastatic cancer (moderate CoE, based on 2 economic modeling studies); and
- More expensive than EBRT and IMRT for bone cancer.

Summary

The use of SBRT for many cancers remains unsupported with limited or no comparative evidence of effectiveness. However, evidence shows SBRT has the potential to be an effective option when compared with cRT for other cancer sites. When compared with other forms of RT, the results for SBRT are mixed, depending on the cancer site and the specific type of RT. For some cancers, such as oligometastatic cancer, SBRT may also have the potential to be cost-effective when compared with other options.

Clinical Practice Guidelines

Recommendations on the use of SBRT varied in the approach, with some guidelines being more supportive depending on the cancer site. Guidelines often noted the limited evidence base, but also highlighted that SBRT may be preferred by patients because of fewer treatment fractions and its favorable safety profile.

Selected Payer Coverage Determinations

Payer policies varied in coverage decisions for SBRT.

Ongoing Studies

We identified 47 ongoing studies, including studies in populations such as people with breast cancer, in which we did not identify any eligible studies for this updated review.

Conclusions

Findings

The use of SBRT for many cancers remains unsupported with limited or no comparative evidence of effectiveness. However, evidence shows SBRT has the potential to be an effective option when compared with cRT for other cancer sites. When compared with other forms of RT, the results for SBRT are mixed, depending on the cancer site and specific type of RT. Some

guidelines are more supportive of the use of SBRT, but most note the limited evidence base, and highlight it may be preferred by patients because of fewer treatment fractions with a favorable safety profile.

FDA-reported Harms

SBRT appears to be a safe form of RT and adverse events reflect those reported in published studies, but also include device failures and process issues, such as placement errors.

Clinical Practice Guidelines and Coverage Policies

Recommendations on the use of SBRT and payer policies varied in approach, with some guidelines or policies being more supportive of the use of SBRT depending on the cancer site. Guidelines and payer policies often noted the limited evidence base, but also highlight that SBRT may be preferred by patients because of fewer treatment fractions and its favorable safety profile.

Summary

The use of SBRT for many cancers remains unsupported with limited or no comparative evidence of effectiveness. However, evidence shows SBRT has the potential to be an effective option when compared with cRT for other cancer sites. When compared with other forms of RT, the results for SBRT are mixed, depending on the cancer site and the specific type of RT. Some guidelines are more supportive of the use of SBRT, but most note the limited evidence base, and highlight it may be preferred by patients because of fewer treatment fractions and the favorable safety profile of SBRT when compared with other treatment options.

Technical Report

Background

Technology of Interest

Radiation therapy is a cancer treatment that uses high-energy X-ray or other particles to destroy cancer cells.[1] A radiation therapy regimen, or schedule, usually consists of a specific number of treatments given over a set time period, and can be used to treat different types of cancer.[1] Radiation therapy also can be used in combination with other cancer treatments, such as chemotherapy or surgery.[1]

The most common type of radiation therapy is external-beam radiation therapy (EBRT), which delivers radiation from outside the body.[1] The different types of external-beam radiation therapy are[1]:

- 3-dimensional conformal radiation therapy (3D-CRT)
- Intensity modulated radiation therapy (IMRT)
- Proton beam therapy
- Image-guided radiation therapy (IGRT
- Stereotactic body radiation therapy (SBRT)

Treatment by SBRT is defined as an extracranial stereotactic ablative treatment (which can include the spine) typically delivered in 1 to 5 fractions, and is also referred to as stereotactic ablative radiotherapy (SABR).[2] Clinical indications for SBRT can be as primary treatment for selected early-stage cancers, as treatment for discrete tumors in patients with oligometastatic disease, for selected benign neoplasms in or near the central nervous system (CNS), or in recurrent cancer within previously irradiated regions.[2]

Other radiation-based therapies include implanted internal radiation therapy (or brachytherapy), intraoperative radiation therapy (IORT), systemic radiation therapy, radioimmunotherapy, and the use of radiosensitizers or radioprotectors.[1]

Clinical Need and Target Populations

In 2019, a total of 1,752,735 new invasive cancer cases were reported in the US: 863,830 among females and 888,905 among males.[19] For all cancers combined, the incidence rate was 439 per 100,000 standard population overall.[19] While cancer affects people of all ages, races, ethnicities, and sexes, it does not affect all groups equally.[19] Differences in genetics, healthy choices, environmental exposures, and other factors can lead to differences in risk among groups of people.[19] For most cancers, increasing age is the most important risk factor, with around 58% of cancers occurring in adults aged 65 years or older.[19]

Policy Context

The use of SBRT for various cancers is increasing in the US[3-5]; however, its effectiveness and safety in routine clinical practice for most cancers are unclear.

In 2012 the Washington State HTCC commissioned an evidence review on the effectiveness of stereotactic radiosurgery (SRS) and SBRT for treating various cancers.[6] On March 22, 2013, using

that evidence review to guide decision making, the committee adopted the following coverage determination[7]:

- SRS for central nervous system (CNS) primary and metastatic tumors is a covered benefit for adults and children when the following criteria are met:
  - Patient functional status score (i.e., Karnofsky score) is greater than or equal to 50; **and**
  - Evaluation includes multidisciplinary team analysis (e.g., tumor board), including surgical input.
- SBRT is covered for adults and children for the following conditions when the following criteria are met:
  - For cancers of spine/paraspinal structures; **or**
  - For inoperable non-small cell lung cancer (NSCLC), stage 1; **and**
  - Evaluation includes multidisciplinary team analysis, including surgical input.
- All other indications are noncovered.

The Washington (WA) Health Technology Assessment (HTA) program contracted with the Center for Evidence-based Policy (Center) in 2016 and 2018 to conduct updated evidence searches on this topic and produce briefs on the included eligible studies to help determine whether the previous coverage policy decision should be reviewed. The Center completed these evidence updates in January 2017[9] and January 2019.[10] Based on the evidence updates, Washington State Health Care Authority did not find sufficient evidence to commission an updated full review on the topic at either time point. A third evidence update was commissioned in October 2021, and was based on a search for studies published since the 2019 evidence update report.[11] The evidence update summarizes the findings of all relevant studies published since the 2012 full evidence review.[11]

This topic was selected because of medium-level concerns about the safety and efficacy of SBRT and high-level concern about costs. This topic was selected for re-review based on new evidence that could prompt potential coverage policy changes. This updated evidence review will help inform Washington's independent Health Technology Clinical Committee as the committee determines coverage regarding SBRT in adults and children for noncovered indications.

Washington State Utilization and Cost Data

Population

Administrative claims and encounter data for stereotactic body radiation therapy (SBRT) from the following Washington State health programs were assessed: Public Employees Benefit Board (PEBB) and School Employees Benefit Board (SEBB) Uniform Medical Plan (UMP), Medicaid managed care (MC) and fee-for-service (FFS), and the Department of Labor and Industries (L&I) Workers' Compensation Plan.

The assessment includes final paid and adjudicated claims and encounters for all ages. Denied claims or rejected encounters are excluded. Individuals dually eligible for Medicare and Medicaid are excluded from the Medicaid program analysis. The PEBB/SEBB UMP experience includes claims for non-Medicare services.

SBRT Procedures

The assessment includes only procedures and services specific to SBRT with a date of service between January 1, 2018, and December 31, 2021.

Claims and encounters with qualifying procedures or services according to current procedural terminology (CPT) codes during the period were extracted for analysis. Qualifying CPT codes included 77373 and 77435.

Copyright Notice

CPT codes, descriptions and other data only are copyright 2020 American Medical Association. All Rights Reserved. Applicable FARS/HHSARS apply.

Disclaimer

Fee schedules, relative value units, conversion factors and/or related components aren't assigned by the AMA, aren't part of CPT, and the AMA isn't recommending their use. The AMA doesn't directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein.

Table 1. Utilization of SBRT and related procedures and services, by state health program (2018-2021)

Medicaid	2018	2019	2020	2021	Total (unique)
Fee for service (FFS)					
Individuals with at least 1 SBRT-related procedure/service	NR	NR	NR	NR	NR
Managed care (MC)					
Individuals with at least 1 SBRT-related procedure/service	114	143	120	142	487
Female, count	60	75	58	90	263
Male, count	52	65	62	50	217
Number of encounters with SBRT	601	830	624	716	2,771
Average encounters with SBRT/individual	5	6	5	5	6
Amount paid, SBRT	$429,007	$647,794	$463,278	$473,480	$2,013,559
Average payments per individual	$3,865	$4,594	$3,893	$3,788	$4,321
Amount paid, SBRT and related procedures	$692,542	$1,009,275	$705,186	$807,368	$3,214,371
Public Employees Benefit Board/School Employees Benefit Board Uniform Medical Plan (PEBB/SEBB UMP)					
Individuals with at least one SBRT-	68	91	97	83	300

Medicaid	2018	2019	2020	2021	Total (unique)
related procedure/service					
Female, count	32	41	56	45	158
Male, count	36	50	41	38	142
Number of encounters with SBRT	374	513	550	490	1,927
Average encounters with SBRT/individual	6	6	6	6	6
Amount paid, SBRT	$371,059	$575,652	$733,264	$434,717	$2,114,691
Average payments per individual	$5,457	$6,468	$8,058	$5,573	$7,343
Amount paid, SBRT and related procedures	$471,609	$673,126	$952,727	$568,125	$2,665,587
Washington State Department of Labor and Industries (L&I)					
Individuals with at least 1 SBRT-related procedure/service	NR	NR	NR	NR	NR
Female, count	NR	NR	NR	NR	NR
Male, count	NR	NR	NR	NR	NR
Number of encounters with SBRT	NR	12	10	NR	30
Average encounters with SBRT/individual	NR	NR	NR	NR	NR
Amount paid, SBRT	$12,220	$14,621	$19,560	$6,030	$52,431
Average payments per individual	NR	NR	NR	NR	NR
Amount paid, SBRT and related procedures	$53,367	$49,802	$175,177	$12,061	$290,407
Washington State – Combined Medicaid & PEBB/SEBB UMP					
Individuals with at least 1 SBRT-related procedure/service	182	234	217	225	787
Female, count	92	116	114	135	421
Male, count	88	115	103	88	359
Number of encounters with SBRT	975	1,343	1,174	1,206	4,698
Amount paid, SBRT	$800,066	$1,223,446	$1,196,542	$908,197	$4,128,250
Amount paid, SBRT and related procedures	$1,164,151	$1,682,401	$1,657,914	$1,375,493	$5,879,959

Note. Claimant sex was not always reported. Annual members for Medicaid excludes members who are dually eligible for Medicaid and Medicare. Amount paid reflects all claims submitted with the procedure code for the same date of service, and includes professional, facility, and ancillary claims (such as durable medical equipment). Managed care amount paid reflects an estimate of the amount paid for the procedure. UMP data does not reflect patient cost share. Individuals who had a procedure in more than 1 year are only counted once in the "Total" summary. Amounts paid of $0 were excluded from amount paid table value calculations. Abbreviations. NR = not reported; small numbers suppressed to protect patient privacy.

Table 2. Demographics of Medicaid & UMP beneficiaries with at least 1 SBRT procedure, SFY 2018-2021

Age	Total individuals (count)
18-64 years	539
65 years and above	247
Total	**786**

Table 3. SBRT breakdown by cancer type

Cancer	Total individuals/encounters
Breast	23/67
Prostate	50/206
Lung	225/804
Melanoma	NR/12
Renal	15/63
Pancreatic	11/37
Head and neck	NR
Liver	35/113
Oligometastatic	255/771
Adrenal	NR
Bone	NR

Data notes: NR = not reported; small numbers suppressed to protect patient privacy. ICD-10 category codes included: Breast – C50; Prostate – C61; Lung – C34; Melanoma – C43; Renal – C64; Pancreatic – C25; Head and neck – C76; Liver – C22; Oligometastatic – C79 & C80; Adrenal – C74; Bone – C40 & C41.

Table 4. Codes and cost by HCPCS/CPT code (maximum allowable), by state health program and setting

Code	Description	Medicaid FFS		L&I	
CPT		Nonfacility	Facility	Nonfacility	Facility
77373	Stereotactic body radiation therapy, treatment delivery, per fraction to 1 or more lesions, including image guidance, entire course not to exceed 5 fractions	$692.98	$692.98	$2,102.93	$2,102.93
77435	Stereotactic body radiation therapy, treatment management, per treatment course, to 1 or more lesions, w/ image guidance, max 5 fractions	$367.87	$367.87	$1,082.15	$1,082.15

Notes. Medicaid FFS from October 1, 2021, Physician-Related Services Fee Schedule (accessed January 18, 2023; web page). L&I from 2021 provider fee schedule (accessed January 18, 2023). PEBB/UMP fees are

confidential and not publicly available (proprietary).

Methods

This evidence review is based on the final key questions (KQs) published on September 21, 2022.[8] The draft KQs were available for public comment from July 27 to August 12, 2022, and appropriate revisions were made to the KQs based on the comments and responses. The draft report was available for public comment between February 16 and March 16, 2023; no comments were received. The draft report was also peer-reviewed by subject matter experts, with appropriate revisions reflected in this final report. The PICO statement (population, intervention, comparator, outcome), along with the setting, study design, and publication factors that guided development of the KQs and study selection are presented in Table 5.

Key Questions

KQ1. What is the evidence of effectiveness for SBRT for patients with cancers not currently covered (CNS cancers and inoperable stage 1 NSCLC)?

KQ2. What are the harms of SBRT in patients with included cancers?

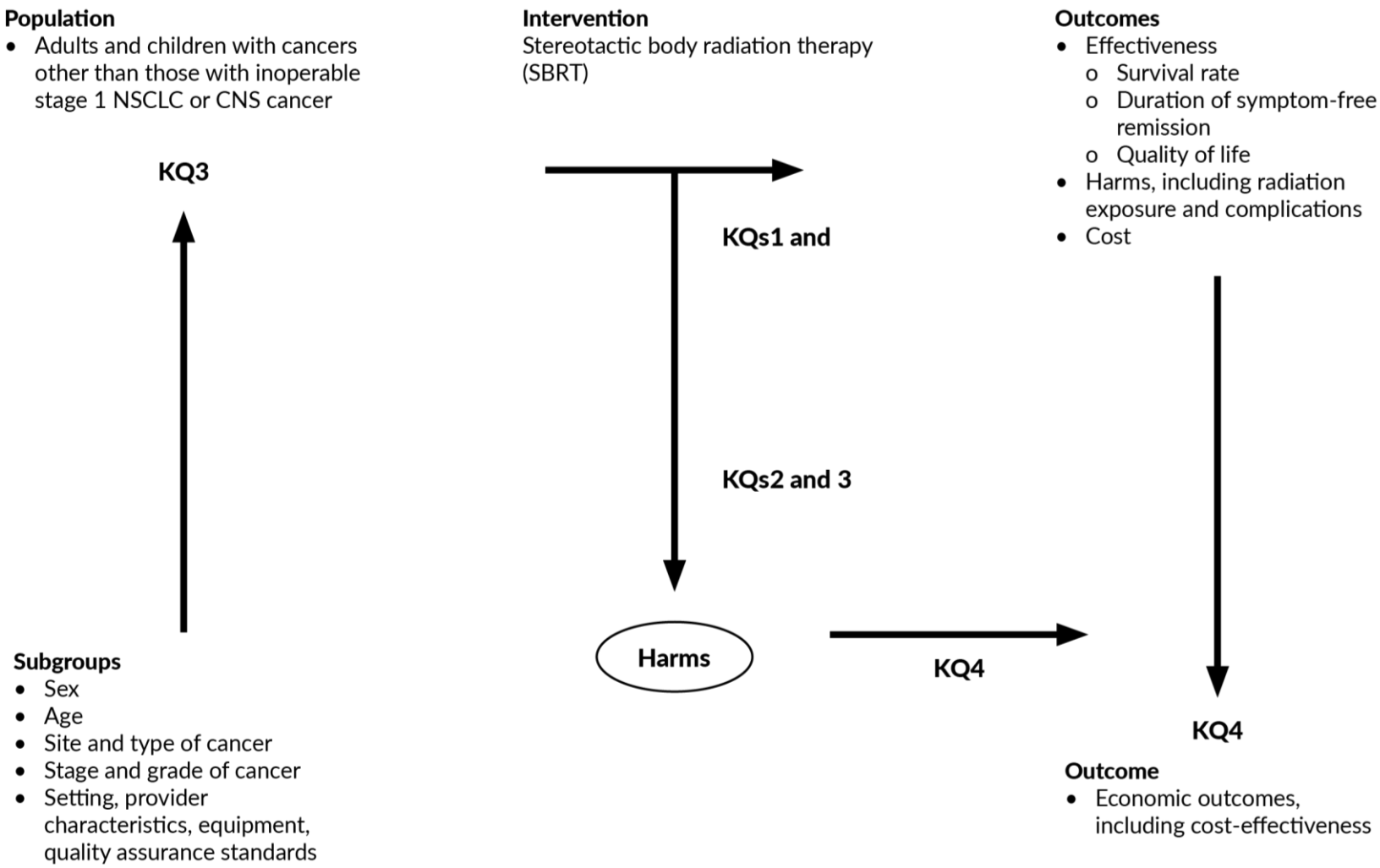
KQ3. What is the evidence that SBRT have differential efficacy or harms in subpopulations, including:

a. Sex
b. Age
c. Site and type of cancer
d. Stage and grade of cancer
e. Setting, provider characteristics, equipment, quality assurance standards and procedures

KQ4. What is the evidence of cost and cost-effectiveness of SBRT?

Analytic Framework

Figure 1. Analytic Framework



Eligible Studies

Table 5 summarizes the study inclusion and exclusion criteria.

Table 5. Key Study Inclusion and Exclusion Criteria for Stereotactic Body Radiation Therapy

Study Component	Inclusion	Exclusion
Populations	• Adults and children with non-CNS and NSCLC (inoperable, stage 1) malignancies where treatment by radiation therapy is appropriate	• Studies in people with noncancer conditions (e.g., trigeminal neuralgia)
Interventions	• SBRT, with devices such as Gamma Knife, CyberKnife, TomoTherapy, delivered in 10 or fewer fractions	• Treatments delivered in 11 or more fractions • Interventions used for treatment planning or treatment delivery assessment only
Comparators	• Conventional (conformal) EBRT • Other forms of radiation (e.g., brachytherapy) • Chemotherapy • Surgery • No treatment	• Comparators other than those stated
Outcomes	• Effectiveness ○ Survival rate ○ Duration of symptom-free remission ○ Quality of life • Harms, including radiation exposure and complications • Cost • Cost-effectiveness	• Studies that do not report outcomes of interest • Data for treatment planning (e.g., dosing) or treatment delivery (e.g., accuracy) • Economic outcomes from studies performed in non-US countries • Economic outcomes from studies performed in the US and published more than 5 years ago
Timing	• Any point in the treatment pathway	• None stated
Setting	• Any outpatient or inpatient clinical setting in countries categorized as very high on the UN Human Development Index[20]	• Emergency use settings • Nonclinical settings (e.g., studies in healthy volunteers, animal models of disease) • Countries categorized other than very high on the UN Human Development Index[20]
Study Design	• For KQ1, KQ2, and KQ3 ○ Comparative study designs (prospective, retrospective, and randomized or controlled clinical trials) • For KQ2 ○ Comparative study designs ○ Noncomparative study designs (≥ 100 participants) • For KQ4 ○ Comparative cost data and relevant economic evaluations ○ Cost-effectiveness analyses ○ Economic simulation modeling studies	• Abstracts, conference proceedings, posters, editorials, letters • Studies without a comparator (unless for harms only) • Proof-of-principle studies (e.g., technology development or technique modification) • Studies without extractable data

Study Component	Inclusion	Exclusion
Sample Size	• Minimum sample size of 50 participants for comparative study designs • Minimum sample size of 100 participants for noncomparative study designs	• Studies that do not meet the minimum sample size
Publication	• Published, peer-reviewed, English-language articles	• Studies reported only as abstracts that do not allow study characteristics to be determined • Studies that cannot be located • Duplicate publications of the same study that do not report different outcomes or follow-up times, or single site reports from published multicenter studies • Studies published in languages other than English

Abbreviations. CNS: central nervous system; EBRT: external beam radiation therapy; KQ: key question; NSCLC: non-small cell lung cancer; SBRT: stereotactic body radiation therapy; UN: United Nations.

Data Sources and Searches

For this update, we identified all included studies from the previous report and the evidence updates,[6,9-11] and all references suggested during the public comment period. We excluded any studies in populations with covered indications and re-screened the remaining studies against our inclusion and exclusion criteria for this update. We also conducted searches of the peer-reviewed published literature using multiple electronic databases. The time periods for searches were:

- Ovid MEDLINE All: from 1946 to October 21, 2022
- Cochrane Library databases (Cochrane Database of Systematic Reviews and Cochrane Central Register of Controlled Trials): from database inception to October 31, 2022

Because of the size of the evidence base, we prioritized studies meeting indexing criteria for RCTs and comparative studies. Randomized controlled trials (RCTs) and systematic reviews (with and without meta-analyses) and health technology assessments that included RCTs were considered for KQs 1 to 4. Nonrandomized comparative studies and nonrandomized studies without a comparator from large, multicenter, national, and international registries were considered for KQs 1 and 3 and for the harm-related aspects of KQs 2 and 3 if evidence for the intervention was included in KQ 1. For KQ 4, we also considered cost-effectiveness studies and other comparative economic evaluations reporting economic outcomes.

We also screened reference lists of relevant studies and used lateral search functions, such as *related articles* and *cited by*. We searched a range of sources, including guideline repositories and organizational websites for systematic reviews and clinical practice guidelines using the same search terms outlined for the evidence search. The database search strategies and list of guideline sources is shown in Appendix A.

Using Google, we conducted a general internet search for appropriate published studies and relevant gray literature. Because of the limited reporting of harms in published studies, we also

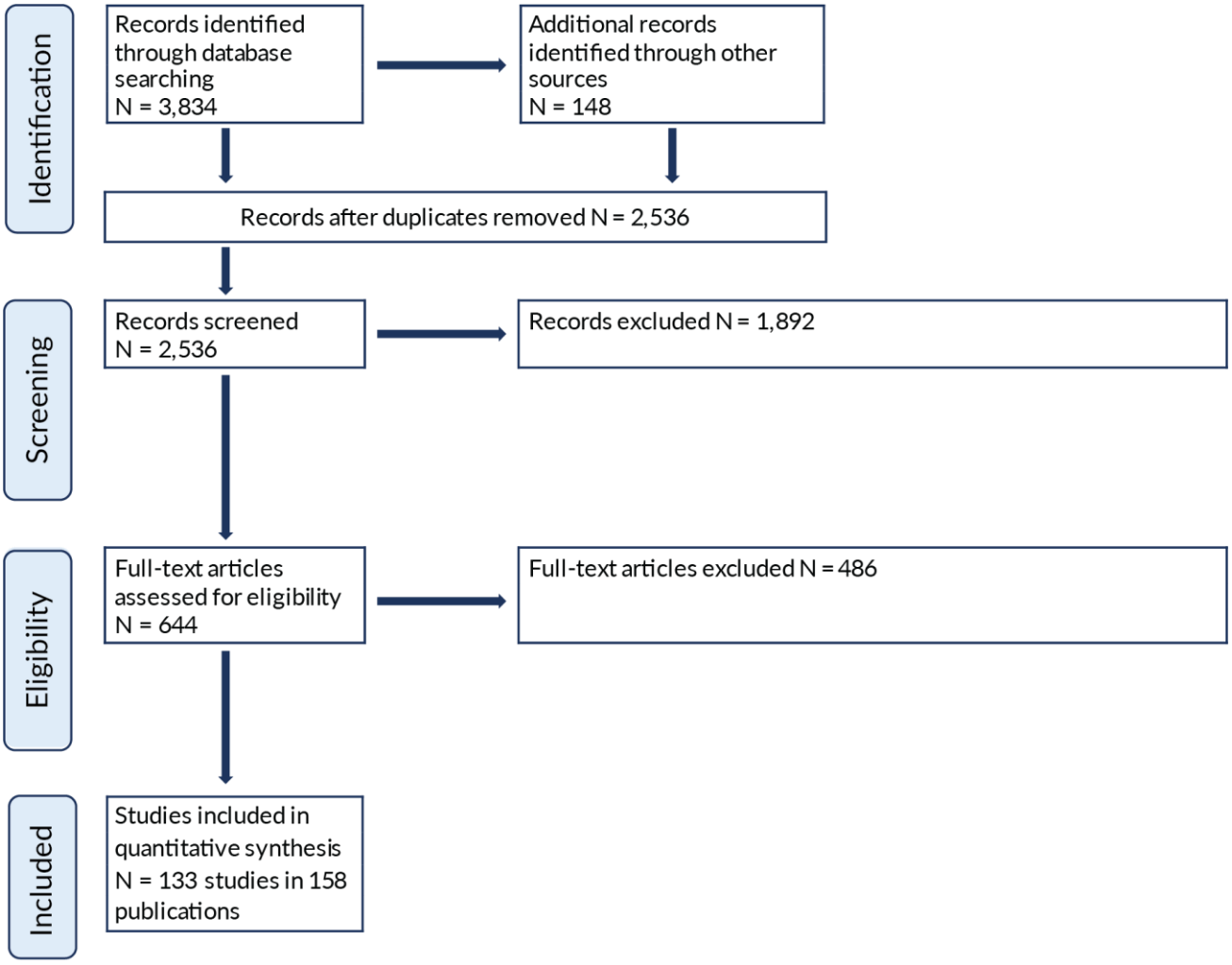
conducted a search of the US FDA Manufacturer and User Facility Device Experience database (MAUDE) for SBRT. We searched for reports posted through December 2022 and the searchable database contains reports from the past 5 years. A search was also conducted of the FDA database of Medical Device Recalls, from its inception in 2002 through January 20, 2022. Findings from these searches are described in the relevant sections, and a detailed table of database reports is in Appendix F. We also searched the Medicare Coverage Database for National Coverage Determinations and Local Coverage Determinations located on the CMS's website for literature relevant to the state of Washington. We searched the Aetna, Cigna, and Regence websites for private payer coverage policies. We also searched key sources for relevant clinical practice guidelines published in the past 5 years.

To identify relevant ongoing clinical trials, in December 2022 we searched the online database of ClinicalTrials.gov maintained by the National Library of Medicine at the National Institutes of Health for terms related to stereotactic. The information in this database was listed by the sponsor or principal investigator of each study. Studies are generally registered in the database when started and information is updated as the study progresses.

Screening

We independently screened titles and abstracts and reached agreement on exclusion through discussions. We performed dual full-text review for any study not excluded by review of title and abstract (Appendix H lists the excluded studies at full-text review, with reasons). For studies on which we did not agree after initial full-text review, we discussed each study and came to consensus. Any remaining disagreements were settled by a third independent researcher.

Figure 2. PRISMA Flow Study Diagram



Data Abstraction and Quality Assessment

We used standardized procedures to extract relevant data from each of the included trials and fully cross-checked all entered data for accuracy.

We evaluated each eligible study for methodological risk-of-bias (Appendix D) and held discussions to reach agreement on these assessments. Any remaining disagreement was settled by a third independent researcher. Each trial was assessed using Center instruments adapted from national and international standards and assessments for risk-of-bias.[12-16] A rating of high, moderate, or low risk-of-bias was assigned to each study based on adherence to recommended methods and the potential for internal and external biases. The risk-of-bias criteria for the study types are shown in Appendix B.

We evaluated the methodological quality of eligible clinical practice guidelines. Any remaining disagreement among these assessments was settled by a third independent researcher. The

methodological quality of clinical practice guidelines was rated as good, fair, or poor. The assessment criteria for the methodological quality of the clinical practice guidelines are shown in Appendix B.

Data Analysis and Synthesis

We assigned selected outcomes a summary judgment for the overall quality of evidence (Appendix E) using the system developed by the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) Working Group.[17,18] The outcomes of overall survival, progression, disease control, quality of life, and toxicity were selected from measures of effectiveness and safety. Specific measures from general domains of interest were selected in a post-hoc manner based on the outcomes available from the included studies.

The GRADE system[18] defines the overall quality of a body of evidence for an outcome in the following manner:

- **High**: Raters are very confident that the estimate of the effect of the intervention on the outcome lies close to the true effect. Typical sets of studies are RCTs with few or no limitations, and the effect estimate is likely stable.
- **Moderate**: Raters are moderately confident in the estimate of the effect of the intervention on the outcome. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is different. Typical sets of studies include RCTs with some limitations or well-performed nonrandomized studies (NRSs) with additional strengths that guard against potential bias and have large estimates of effects.
- **Low**: Raters have little confidence in the estimate of the effect of the intervention on the outcome. The true effect may be substantially different from the estimate of the effect. Typical sets of studies include RCTs with serious limitations or nonrandomized studies without special strengths.
- **Very low**: Raters have no confidence in the estimate of the effect of the intervention on the outcome. The true effect is likely to be substantially different from the estimate of the effect. Typical sets of studies include NRSs with serious limitations or inconsistent results across studies.
- **Not applicable**: Researchers did not identify any eligible articles.

Common Outcome Measures Reported in the Included Studies

In 2018, the US Food and Drug Administration (FDA) issued guidance on clinical trial endpoints for the approval and cancer drugs and biologics.[21] As part of the guidance, the FDA outlined the advantages and disadvantages of the key cancer outcomes measures (Table 6). The advantages and disadvantages of each outcome measure should be considered when assessing the impact of new studies on the existing coverage decision.

Table 6. Advantages and Disadvantages of Key Cancer Outcome Measures[21]

Outcome Measure	Advantages	Disadvantages
Overall survival (OS)	• Easily and precisely measured • Generally based on objective and quantitative assessment	• May be affected by switch-over of control to treatment or subsequent therapies • Needs longer follow-up • Includes noncancer deaths

Outcome Measure	Advantages	Disadvantages
Disease-free survival, event-free survival	• Generally assessed earlier and with smaller sample size compared with survival studies • Generally based on objective and quantitative assessment	• Potentially subject to assessment bias, particularly in open-label studies • Definitions vary among studies • Balanced timing of assessments among treatment arms is critical • Includes noncancer deaths
Progression-free survival (PFS), time to progression	• Generally assessed earlier and with smaller sample size compared with survival studies • Measurement of stable disease included • Generally based on objective and quantitative assessment	• Potentially subject to assessment bias, particularly in open-label studies • Definitions vary among studies • Frequent radiological or other assessments • Balanced timing of assessments among treatment arms is critical • May not always correlate with survival
Objective response rate (ORR)	• Generally assessed earlier and with smaller sample size compared with survival studies • Effect on tumor attributable to drug(s) or other treatment, not natural history • Generally based on objective and quantitative assessment	• Definitions vary among studies • Frequent radiological or other assessments • May not always correlate with survival
Complete response rate (CRR)	• Generally assessed earlier and with smaller sample size compared with survival studies • Effect on tumor attributable to drug(s) or other treatment, not natural history • Generally based on objective and quantitative assessment	• Definitions vary among studies • Frequent radiological or other assessments • May not always correlate with survival

Source. Adapted from the US FDA guidance for industry on cancer approval endpoints.[21]

Evidence Summary

Our searches returned a total of 3,834 records. We also checked the reference lists of relevant systematic reviews and checked references submitted during the public comment period on the key questions and peer review.

We found 148 additional studies, beyond those identified in electronic databases, through Google and gray literature searches and reference checking. After duplicate studies were removed, 2,536 records remained (Figure 2. PRISMA Flow Study Diagram). Of these, 644 required full-text review to determine eligibility. In total, 12 RCTs (in 21 publications) and 115 NRSs (in 131 publications) met the inclusion criteria for KQs 1, 2, 3, and 4. In addition, a further 7 economic- or cost-focused studies met the inclusion criteria for KQ 4.

We also searched relevant systematic reviews and other structured reviews to identify any further studies.[22-72]

Key Questions 1 and 2

Breast Cancer

History

No eligible studies on the use of SBRT in breast cancer were included in the 2012 report.[6]

Study Characteristics

We did not identify any eligible studies for the use of SBRT in breast cancer in this updated evidence review.

Prostate Cancer

History

In the 2012 report presented to the HTCC,[6] the overall strength of evidence was assessed as very low for harms, based on 4 case series.[73-76] No comparative studies on the effectiveness of SBRT in this population were identified.[6]

Study Characteristics

We identified 4 RCTs, reported in 6 publications, evaluating the use of SBRT for localized prostate cancer (Table 7).[77-82] Each of the RCTs included men with localized prostate cancer at different levels of risk.[77-80] All of the RCTs included men with localized prostate cancer at different levels of risk.[77-80] We assessed each of the 4 RCTs as being at moderate risk-of-bias because of a lack of blinding and in some studies, methods of analysis, including per protocol analyses.[77-80]

We also identified another 14 comparative studies, reported in 16 publications, on the use of SBRT for prostate cancer (Table 7).[83-98] The majority of the studies included men with localized cancer, with only 2 not reporting any specific limitations on the stage or risk group of the prostate cancer as inclusion criteria.[83-98] We assessed 5 of the studies to be at low risk-of-bias as these were complex analytic studies using data from large, national databases,[83,92-94,98] 5 at high risk-of-bias because of the potential for confounding,[85-88,97] and the remaining studies were at moderate risk-of-bias because although confounding had been addressed, there remained the possibility of differences between the patient populations.[89-91,96]

Table 7. Summary Study Characteristics of RCTs and Comparative Studies in Prostate Cancer

Citation Setting NCT or Other Trial ID or Study Name	Duration Risk-of-bias	Patient Characteristics	Intervention	Comparator(s)
Randomized controlled trials				
Brand et al, 2019[77,81] 37 centers in the UK, Ireland, and Canada NCT01584258 PACE-B	Followed up to 24 months Moderate risk-of-bias	Total N = 874 men with low- to intermediate-risk localized prostate cancer, comprising 433 in the SBRT group and 441 in the control group	• SBRT ○ 36.25 Gy in 5 fractions over 1 to 2 weeks (i.e., daily or alternate days, at center discretion), with an additional secondary CTV dose target of 40 Gy	• cRT or moderately hypofractionated radiotherapy ○ PTV dose was 78 Gy in 39 daily fractions or, following an approved protocol amendment, 62 Gy in 20 daily fractions
Kwan et al., 2022[80] 2 sites in Canada NCT02594072 ASSERT	At least 6 months Moderate risk-of-bias	Total N = 80 men with intermediate- to high-risk localized prostate cancer, comprising 42 in the SBRT group and 36 in the control group	• SBRT ○ 36.25 Gy in 5 fractions weekly ○ ADT (6 months in intermediate risk and 18 months in high-risk) by either luteinizing hormone-releasing hormone agonists or antagonists	• Moderate hypofractionation RT ○ 70 Gy in 28 fractions 5 times a week ○ ADT (6 months in intermediate risk and 18 months in high-risk) by either luteinizing hormone-releasing hormone agonists or antagonists
Lukka et al., 2018[78] 37 sites, including academic centers, in the US and Canada NCT01434290	Median follow-up of 3.8 years Moderate risk-of-bias	Total N = 255 men with localized T1 to T2 stage prostate cancer, comprising 127 in the SBRT in the group and 128 in the UHRT group	• SBRT ○ 36.25 Gy in 5 fractions of 7.25 Gy ○ More than 2 weeks	• UHRT ○ 51.6 Gy in 12 fractions of 4.3 Gy ○ More than 2.5 weeks
Widmark et al., 2019[79,82]	Followed up to 10 years	Total N = 1,200 men with intermediate-to-high-risk localized prostate cancer,	• SBRT ○ 42.7 Gy in 7 fractions ○ 3 days over 2.4 weeks	• cRT ○ 78.0 Gy in 39 fractions ○ 5 days per week for 8 weeks

Citation Setting NCT or Other Trial ID or Study Name	Duration Risk-of-bias	Patient Characteristics	Intervention	Comparator(s)
12 centers in Sweden and Denmark ISRCTN45905321 HYPO-RT-PC	Moderate risk-of-bias	comprising 598 in the SBRT group and 602 in the cRT group		
Comparative nonrandomized studies				
Andruska et al., 2022[83] National Cancer Database (2004 to 2015) NR	Retrospective, database analysis (propensity-matched) Median follow-up of 60 months Low risk-of-bias	Total N = 28,028 men with unfavorable intermediate-risk prostate cancer, comprising 1,428 in the SBRT group, 532 in the moderately fractionated RT group, and 25,856 in the cRT	• SBRT ○ 35 to 40 Gy in 5 or fewer fractions	• Moderately fractionated RT ○ 60 Gy or higher in 2.4 to 3.2Gy per fraction ○ Biologically effective doses of 120 and higher • cRT ○ 72 to 86.4 Gy in 1.8 to 2.0 Gy per fraction
Glowacki et al, 2017[85] Single center in Poland NR	Prospective study Median follow-up NR High risk-of-bias	Total N = 216 men with prostate cancer (no further details), comprising 109 in the SBRT group and 107 in the cRT group	• SBRT ○ 36.25 Gy in 5 fractions in 2 weeks	• cRT ○ Total dose of 76 Gy in 2 Gy fractions
Halpern et al., 2016[86] Surveillance, Epidemiology, and End Results Program (SEER)-	Retrospective analysis Followed-up for at least 1 year	Total N = 17,889 men with localized prostate cancer for 1 year and 15,678 for 2-year outcomes; 237 in the SBRT group, 4,136 in the BT group, 10,715 in the IMRT group, 363 in the proton beam therapy group,	• SBRT ○ Based on ICD-9 and CPT-4 codes	• BT • IMRT • Proton beam • Combination ○ All based on ICD-9 and CPT-4 codes

Citation Setting NCT or Other Trial ID or Study Name	Duration Risk-of-bias	Patient Characteristics	Intervention	Comparator(s)
Medicare (2004 to 2011) NR	High risk-of-bias	and 2,438 in the combination group		
Katz et al., 2012[87] Single academic center in the US and 10 hospitals in Spain NR	Retrospective study Followed up to 36 months High risk-of-bias	Total N = 339 men with localized prostate cancer, comprising 216 in the SBRT group and 123 in the surgery group	• SBRT ○ 35 or 36.25 Gy in 5 daily fractions	• Surgery ○ Radical retropubic prostatectomy with nerve-sparing at the surgeon's discretion
Lee et al., 2016[88] Single academic center in Korea NR	Prospective study Median follow-up of 53.6 months High risk-of-bias	Total N = 69 men with low- and intermediate-risk prostate cancer, comprising 34 in the SBRT group and 35 in the cRT group	• SBRT ○ 36.25 Gy, delivered in 5 fractions	• cRT ○ 70.2 to 75.6 Gy in 39 to 42 fractions
Loblaw et al., 2017[89] 4 centers in Canada NR	Retrospective database analysis (propensity-matched) Median follow-up of 5.07 years for SBRT, 5.70 for low dose BT, and 6.97 for EBRT	Total N = 673 men with low risk localized prostate cancer, comprising 151 in the SBRT group, 458 in the BT group, and 64 in the EBRT group (364 included in the matched group)	• SBRT ○ 35 Gy in 5 fractions	• Low dose BT ○ I-125 ○ monotherapy in 144 to 145 Gy • EBRT ○ 74 to 79.8 Gy in 37 to 42 fractions

Citation Setting NCT or Other Trial ID or Study Name	Duration Risk-of-bias	Patient Characteristics	Intervention	Comparator(s)
	Moderate risk-of-bias			
Monaco et al., 2022[90] Single center in the US NR	Retrospective analysis Followed-up for up to 48 months Moderate risk-of-bias	Total N = 309 men with low- to intermediate-risk prostate can, comprising 161 in the SBRT group and 148 in the AS group	• SBRT ○ 35 to 36.25 Gy fractions delivered in 5 consecutive treatments over 5 days	• AS ○ PSA testing every 3 months ○ Annual multiparametric MRI ○ Biopsy if PSA rise, unfavorable genomics, or disease progression on imaging ○ Treatment based on patient preference, Gleason score increases, or increased tumor volume
Oliai et al., 2016[84,91,95] 1 community hospital and 1 academic center in the US NR	Retrospective propensity-matched analysis Median follow-up of 34 months (SBRT) and 51 months (IMRT) Moderate risk-of-bias	Total N = 263 men with localized prostate cancer, comprising 142 in the SBRT group and 121 in the IMRT group	• SBRT ○ 36.25 Gy in 5 fractions for most patients	• IMRT ○ 75.6 Gy in 42 fractions for most patients
Pan et al., 2018[92] MarketScan Commercial Claims and Encounters database (2008 to 2015)	Retrospective (propensity-matched) database analysis Median follow-up of	Total N = 12,128 men with localized prostate cancer, comprising 312 in the SBRT group, 693 in the proton therapy group, and 11,123 in the IMRT group	• SBRT ○ Median treatment fractions, 5 (IQR, 5 to 5)	• Proton therapy ○ Median treatment fractions, 39 (IQR, 39 to 44) • IMRT ○ Median treatment fractions, 42 (IQR, 38 to 44)

Citation Setting NCT or Other Trial ID or Study Name	Duration Risk-of-bias	Patient Characteristics	Intervention	Comparator(s)
NR	18 months for SBRT, 23 months for proton therapy, and 23 months for IMRT Low risk-of-bias			
Patel et al., 2020[93] National Cancer Database (2004 to 2016) NR	Retrospective database analysis Median follow-up of 74 months Low risk-of-bias	Total N = 41,355 men with unfavorable risk prostate cancer, comprising 558 in the SBRT group and 40,797 in the EBRT group	• SBRT ○ At least 5 Gy in 5 fractions	• cRT or moderate fractionation ○ At least 3 Gy per fraction with a total dose of at least 60 Gy
Ricco et al., 2017[94] National Cancer Database (2004 to 2013) NR	Retrospective database analysis (propensity-matched) Low risk-of-bias	Total N = 5,430 men with localized prostate cancer, comprising 2,715 in the SBRT group and 2,715 in the IMRT group	• SBRT ○ 35 to 50 Gy	• IMRT ○ 72 to 86.4 Gy
Tsang et al., 2021[96] Multicenter study in the UK NR	Retrospective study Median follow-up of 60.1 months	Total N = 185 men with low- and intermediate risk prostate cancer, comprising 43 in the SBRT group and 142 in the BT group	• SBRT ○ 36.25 Gy in 5 fractions ○ ADT for 6 months, commencing 1–3 months before RT, if T2c stage	• BT ○ 19 Gy in single dose or 26 Gy in 2 fractions ○ ADT for 6 months, commencing 1–3 months before RT, if T2c stage

Citation Setting NCT or Other Trial ID or Study Name	Duration Risk-of-bias	Patient Characteristics	Intervention	Comparator(s)
	Moderate risk-of-bias		disease and either PSA > 10 or Gleason score of 7	disease and either PSA > 10 or Gleason score of 7
Werneburg et al., 2018[97] Single academic center in the US NR	Retrospective, analysis Followed-up for 4 years High risk-of-bias	Total N = 279 men with prostate cancer (no further details), comprising 82 in the SBRT group, 129 in the cryotherapy group, and 68 in the AS group	• SBRT ○ 5 consecutive treatments of 35 to 36.25 Gy fractions ○ Delivered in a period of 5 days	• Cryotherapy • AS
Yu et al., 2014[98] Chronic Conditions Warehouse (2008 to 2011) NR	Retrospective, comparative database analysis, with matching Followed up to 24 months Low risk-of-bias	Total N = 55,176 men with early-stage prostate cancer, comprising 1,335 in the SBRT group and 53,841 in the IMRT group	• SBRT ○ Based on claim codes	• IMRT ○ Based on claim codes

Abbreviations. ADT: androgen deprivation therapy; AS: active surveillance; BT: brachytherapy; CPT: Current Procedural Terminology; cRT: conventional radiation therapy; CTV: clinical target volume; EBRT: external beam radiation therapy; Gy: Gray; ICD: International Classification of Diseases; IMRT; intensity-modulated radiation therapy; MRI: magnetic resonance imaging; NCT: US National Clinical Trial; NR: not reported; PSA: prostate-specific antigen; PTV: planning target volume; RCT: randomized controlled trial; RT: radiation therapy; SABR: stereotactic ablative radiotherapy; SBRT: stereotactic body radiation therapy; UHRT: ultrahypofractionated radiation therapy.

In addition, we identified a further 18 noncomparative studies, reported in 26 publications, describing the toxicities and adverse events associated with the use of SBRT for prostate cancer (Table 8).[99-124] All of the studies included men with localized prostate cancer.[99-102,104,105,108,109,111,114-118,120-123] We assessed each of the noncomparative studies at being at high risk-of-bias because of the lack of a comparator.

Table 8. Summary Study Characteristics of Noncomparative Studies in Prostate Cancer

Citation Setting NCT or Other Trial ID	Study Design and Duration Risk-of-bias	Patient Characteristics	Description of Intervention
Bolzicco et al, 2013[99] 1 academic center in Italy NR	Prospective study Median follow-up of 36 months High risk-of-bias	Total N = 100 men with localized prostate cancer	• SBRT ○ 35 Gy in 5 fractions of 7 Gy over consecutive days
Davis et al., 2015[101] RSSearch registry, including 27 sites and academic centers in the US, Australia, and Turkey (2006 to 2015) NCT01885299	Retrospective registry analysis Median follow-up of 20 months High risk-of-bias	Total N = 437 men with localized prostate cancer	• SBRT ○ 19.5 to 29 Gy in 2 to 3 fractions ○ 35 Gy in 5 fractions ○ 36.25 Gy in 5 fractions ○ 37 Gy in 5 fractions ○ 38 Gy in 4 fractions
Flushing Radiation 2006 to 2009[109,110] Single center in the US NR	Retrospective (assumed) study Up to 10 years High risk-of-bias	Total N = 230 men with early low-risk prostate cancer	• SBRT ○ 35 to 36.25 Gy in 5 daily fractions
Flushing Radiation Winthrop 2006 to 2010 [111-113] Single academic center in the US NR	Prospective study Median follow-up of 72 months High risk-of-bias	Total N = 477 men with localized low- and intermediate-risk prostate cancer	• SBRT ○ 35 or 36.25 Gy over 5 fractions, daily
Freeman et al., 2015[102] Registry for Prostate Cancer Radiosurgery (RPCR; 2010 to 2013) NR	Prospective analysis of a patient registry Followed up to 3 years High risk-of-bias	Total N = 1,743 men with localized prostate cancer	• SBRT ○ 35 to 40 Gy in 4 to 5 fractions ○ Boost following 45 to 50 Gy of EBRT
Fuller et al, 2018[103,104] 18 centers, including academic and community centers, in the US NCT00643617	Prospective study Median follow-up of 5 years High risk-of-bias	Total N = 259 men with low- or intermediate-risk prostate cancer	• SBRT ○ 38 Gy in 4 daily fractions of 9.5 Gy per fraction ○ ADT not allowed

Citation Setting NCT or Other Trial ID	Study Design and Duration Risk-of-bias	Patient Characteristics	Description of Intervention
Georgetown 2008 to 2011[100,106,107,124] Single academic center in the US NR	Retrospective study Median follow-up of 2.3 years High risk-of-bias	Total N = 100 men with localized prostate cancer	• SBRT ○ 35 or 36.25 Gy in 5 fractions ○ Every other day
Glowacki et al, 2015[105] Single center in Poland NR	Prospective study Median follow-up of 8.5 months High risk-of-bias	Total N = 132 men with low- or intermediate-risk prostate cancer	• SBRT ○ 36.25 Gy in 5 fractions
Johansson et al., 2019 [108] Single center in Sweden NR	Retrospective study Up to 10 years, with a median follow-up of 108 months High risk-of-bias	Total N = 531 men with localized prostate cancer	• SBRT ○ Boost of 20 Gy in 4 daily fractions ○ Followed by photon therapy (50 Gy in 2 Gy fractions)
Koskela et al., 2017[114] Not clear (assumed a single center), based in Finland NR	Retrospective study Median follow-up of 23 months High risk-of-bias	Total N = 218 men with localized prostate cancer	• SBRT ○ 35 or 36.25 Gy in 5 fractions of 7 or 7.25 Gy, respectively, delivered on every other day
Ma et al., 2022[115] 2 academic centers in the US NCT03541850 SCIMITAR	Prospective study Up to 6 months (safety) High risk-of-bias	Total N = 100 men with localized prostate cancer after radical prostatectomy	• SBRT ○ Median prostate bed dose, 32 Gy (range, 30 to 34) ○ Median prostate bed boost dose, 40 Gy (range, 36 to 40)
Mantz, 2014[116] Single center (assumed) in the US NR	Retrospective (assumed) study Followed up for a minimum of 5 years High risk-of-bias	Total N = 102 men with low-risk prostate cancer	• SBRT ○ 40Gy in 5 fractions, delivered every other day
Meier et al., 2018[117] 21 centers in the US, including 1 academic center NCT00643994	Prospective study Median follow-up of 61 months High risk-of-bias	Total N = 309 men with low- and intermediate-risk prostate cancer	• SBRT ○ 40 Gy in 5 fractions of 8 Gy

Citation Setting NCT or Other Trial ID	Study Design and Duration Risk-of-bias	Patient Characteristics	Description of Intervention
Miszczyk et al., 2017[118,119] Single center in Poland NR	Retrospective (assumed) study Median follow-up of 15 months High risk-of-bias	Total N = 400 men with low- and intermediate-risk prostate cancer	• SBRT ○ 7.25 Gy to a total of 36.25 Gy on every other day over a period of 9 days
Pasquier et al., 2019[120] 7 centers in France and Italy, including academic centers NR	Retrospective study Median follow-up of 29.2 months High risk-of-bias	Total N = 100 men with local prostate cancer recurrence after RT	• SBRT ○ 36 Gy in 6 fractions administered every other day in most patients
Paydar et al., 2016[121] Single academic center in the US NR	Prospective study Followed up to 3 months High risk-of-bias	Total N = 103 men with localized prostate cancer	• SBRT ○ 35 or 36.25 Gy delivered in 5 fractions (7 to 7.25 Gy per fraction)
Pryor et al., 2019[122] 5 centers in Australia, including academic centers ACTRN12615000223538 PROMETHEUS	Prospective study Median follow-up of 24 months High risk-of-bias	Total N = 135 men with low- and high-risk prostate cancer	• SBRT ○ 19 to 20Gy in 2 fractions delivered 1 week apart, followed by conventionally fractionated IMRT (46Gy in 23 fractions)
Rana et al., 2015[123] Single center in the US NR	Retrospective study Median follow-up of 4.3 years High risk-of-bias	Total N = 101 men with localized prostate cancer	• SBRT ○ 36.25 Gy (range 35 to 40 Gy) over 5 daily fractions

Abbreviations. Gy: Gray; NCT: US National Clinical Trial; NR: not reported; RT: radiation therapy; SBRT: stereotactic body radiation therapy.

GRADE Summary of Findings

Table 9. GRADE Summary of Evidence: Effectiveness of SBRT for Prostate Cancer

Number of Participants (N) Number of Studies	Findings	Certainty of Evidence	Rationale
SBRT vs. cRT for intermediate-to-high-risk localized prostate cancer			
Overall survival			
N = 1,200 1 RCT[79]	In intermediate-to-high-risk localized prostate cancer: • 5-year overall survival: HR, 1.11; 95% CI, 0.73 to 1.69	⨁⨁◯◯ LOW	Downgraded 2 levels for imprecision (i.e., very wide CIs)[a]
Progression-free survival			
N = 1,200 1 RCT[79]	In intermediate-to-high-risk localized prostate cancer: • 5-year failure-free survival (biochemical or clinical failure: aHR, 1.00 (95% CI, 0.76 to 1.33)	⨁⨁⨁◯ MODERATE	Downgraded 1 level for imprecision (i.e., wide CIs)[a]
Disease-control			
N = 1,200 1 RCT[79]	In intermediate-to-high-risk localized prostate cancer: • Local failure: HR, 0.94; 95% CI, 0.40 to 2.22 • Distant failure: HR, 0.99; 95% CI, 0.63 to 1.54 • Use of ADT at 5 years: HR, 1.12; 95% CI, 0.79 to 1.59	⨁◯◯◯ VERY LOW	Downgraded 1 level for risk of bias and 2 levels for imprecision (i.e., very wide CIs)[a]
Quality of life			
Not reported			
SBRT vs. other forms of RT for localized prostate cancer (all risk groups)			
Overall survival			
N = 75,749 5 comparative NRSs[83,89,91,93,94]	Men with localized prostate cancer (all risk groups) treated with SBRT had similar or improved overall survival when compared with other treatment options, including cRT, IMRT and brachytherapy; studies reported at different times using different statistics, precluding any summary statistics (see detailed findings below).	⨁⨁◯◯ LOW	Not downgraded
Progression-free survival			
Not reported			
Disease-control			
N = 1,190 4 comparative NRSs[88,89,91,96]	Men with localized prostate cancer (all risk groups) treated with SBRT had similar or improved disease control when compared with other treatment options, including cRT, IMRT and brachytherapy, with biochemical control rates of around 89% to 100% at 5 years.	⨁⨁◯◯ LOW	Not downgraded

Number of Participants (N) Number of Studies	Findings	Certainty of Evidence	Rationale
Quality of life			
N = 2,154 3 RCTs[77,79,80]	Men with localized prostate cancer (all risk groups) treated with SBRT had a similar quality of life to men treated with other forms of RT; however, specific symptoms affecting quality of life may vary between treatments.	⊕⊕◯◯ LOW	Downgraded 1 level each for risk-of-bias and imprecision (i.e., not assessable)
SBRT vs. other forms of RT for localized prostate cancer (all risk groups)			
Toxicity			
N = 2,409 4 RCTs[77-80]	Rates of toxicities of grade 3 or higher were relatively infrequent in SBRT for localized prostate cancer (around 1% to 2%), and were similar to those of other RTs.	⊕⊕⊕◯ MODERATE	Downgraded 1 level for risk-of-bias
N = 67,968 5 comparative NRSs[85,91,92,96,98]	Overall, grade 3 toxicities were rare (up to 6% depending on the specific toxicity and the time point) and no grade 4 or 5 events were reported when SBRT was used for localized prostate cancer (all risk groups). There may be some evidence SBRT is associated with increased urinary retention or obstruction, urinary fistula, and more GI and GU toxicity than IMRT, and greater GI toxicity than brachytherapy.	⊕⊕◯◯ LOW	Not downgraded

Notes. [a] *Inconsistency not assessable due to only 1 study.*
Abbreviations. ADT: androgen deprivation therapy; aHR: adjusted hazard ratio; CI; confidence interval; cRT: conventional radiation therapy; GI; gastrointestinal; GU: genitourinary; HR: hazard ratio; IMRT: intensity-modulated radiation therapy; NRS: nonrandomized study; RCT: randomized controlled trial; SBRT: stereotactic body radiation therapy.

Overall and Progression-free Survival

Only 1 of the RCTs reported overall survival and progression-free survival (PFS).[79] In the HYPO-RT-PC trial, men with intermediate-to-high-risk localized prostate cancer treated with SBRT and with conventional radiotherapy (cRT) had similar overall 5-year survival rates (94% SBRT vs. 96% cRT; hazard ratio [HR], 1.11; 95% confidence interval [CI], 0.73 to 1.69) and similar prostate cancer-specific 5-year survival rates (98.0% SBRT vs. 99.8%), cRT; HR, 1.40; 95% CI, 0.56 to 3.49).[79] Men with intermediate-to-high-risk localized prostate cancer treated with SBRT and cRT also had similar rates of failure-free (biochemical or clinical failure; adjusted HR [aHR], 1.00 (95% CI, 0.76 to 1.33) survival at 5 years.[79]

Of the 14 eligible comparative studies, 5 reported on overall survival or PFS.[83,89,91,93,94] Overall, men with localized prostate cancer treated with SBRT had similar or improved overall survival when compared with other treatment options, including cRT, IMRT and brachytherapy.[83,89,91,93,94]

- In an analysis of the National Cancer Database (NCDB), men with unfavorable intermediate-risk prostate cancer treated with SBRT lived significantly longer than men treated with cRT

regardless of androgen deprivation therapy (ADT) status (HR, 0.80; 95% CI, 0.65 to 0.98).[83] When analyzed by age, younger men had similar overall survival if treated with SBRT without ADT or cRT with ADT (HR, 1.04; 95% CI, 0.65 to 1.69) but older men lived significantly longer if treated with SBRT (HR, 0.77; 95% CI: 0.62 to 0.96).[83] There was no difference in survival between SBRT and moderately-fractionated RT.[83]

- In a study from 4 centers in Canada, men low risk localized prostate cancer treated with SBRT had similar 6-year overall survival rates to men treated with low-dose brachytherapy (97.1% SBRT vs. 95.2% BT; *P* = .46) or with cRT (95.0% SBRT; 97.1% EBRT; *P* = .65).[89]
- In a study from 2 centers in the US, men with localized prostate cancer treated with SBRT had a similar 5-year survival to men treated with intensity-modulated radiation therapy (IMRT; 90.8% SBRT vs. 88.1% IMRT; *P* = .73, when matched by treatment year, clinical T-stage, age, Gleason score, pretreatment prostate-specific antigen [PSA], and ADT use).[91]
- In another analysis of the NCDC, men older than age 40 with unfavorable risk localized prostate cancer had a similar 6-year overall survival rate when treated with SBRT or with cRT, regardless of risk status (adjusted HR [aHR] for unfavorable intermediate risk, 1.09; 95% CI, 0.68 to 1.74; aHR for high risk, 0.93; 95% CI, 0.76 to 1.14).[93] Sensitivity analyses showed similar results for men treated with preferred dose fractionations, with no comorbidities, or aged 65 years old or younger.[93]
- Men treated with SBRT or IMRT for localized prostate cancer had a similar 8-year survival rate (77.23% SBRT vs. 79.38%; *P* = .65).[94] The analysis of the NCDB also found no difference in overall survival between treatments when limited to patients with PSA higher than 10 ng/ml or a Gleason score greater than 7.[94]

Disease Control

Only 1 of the RCTs reported on the impact of treatment on disease control.[79] Men with intermediate-to-high-risk localized prostate cancer treated with SBRT and cRT also had similar rates of local (99% SBRT vs. 98% cRT; HR, 0.94; 95% CI, 0.40 to 2.22) and distant failure (94% SBRT vs. 95% cRT; HR, 0.99; 95% CI, 0.63 to 1.54), and use of ADT at 5 years (89% SBRT vs. 92% cRT; HR, 1.12; 95% CI, 0.79 to 1.59).[79]

Of the 14 eligible comparative studies, 4 reported on some measure of disease control.[88,89,91,96] Overall, men with localized prostate cancer treated with SBRT had similar or improved disease control when compared with other treatment options, including cRT, IMRT and brachytherapy.[88,89,91,96]

- In a study from a single academic center in South Korea, when compared with cRT, men treated for low- and intermediate-risk prostate cancer had significantly higher rates of biochemical-free survival at 5 years (100% SBRT vs. 80.8% cRT; *P* = .03).[88]
- In a study from 4 centers in Canada, men with low risk localized prostate cancer treated with SBRT had similar 6-year biochemical-free survival rates to men treated with low-dose brachytherapy (97.1% SBRT vs. 93.4% BT; *P* = .23), but significantly better biochemical-free survival than those treated with cRT (100% SBRT vs. 85.9% EBRT; *P* = .04).[89]
- In a study from 2 centers in the US, men with localized prostate cancer treated with SBRT had a similar 5-year biochemical-free survival compared with men treated with intensity-modulated radiation therapy (IMRT) (88.7% SBRT vs. 95.5% IMRT; *P* = .17, when matched by treatment year, clinical T-stage, age, Gleason score, pretreatment PSA, and ADT use).[91]

- A multicenter study from the UK found that men with low- and intermediate risk prostate cancer treated with SBRT had similar rates of biochemical control at 3 years (95% SBRT vs. 90% and 100%, depending on the brachytherapy dose) and at 5 years (92% SBRT vs. 69% and 95%, depending on the brachytherapy dose; *P* = .37 across 3 and 5 years) to men treated with brachytherapy.[96] When analyzed by dose, treatment with single fraction brachytherapy was associated with significantly worse biochemical control than SBRT (HR, 3.47; 95% CI, 1.08 to 11.13).[96]

Quality of Life

Of the 4 RCTs, 3 compared the quality of life in men with localized prostate cancer by treatment.[77,79,80] Overall, men treated with SBRT had a similar quality of life to men treated with other forms of RT; however, specific symptoms affecting quality of life may vary between treatments.

- In the PACE-B RCT, men with low- to intermediate-risk localized prostate cancer treated with SBRT or cRT, including moderately-fractionated RT, had a similar quality of life, when assessed at 12 weeks after treatment.[77]
- In the ASSERT RCT, men with intermediate- to high-risk localized prostate cancer treated with SBRT or moderately-fractionated RT had a similar quality of life, when assessed at up to 6 months after treatment.[80]
- In the HYPO-RT-PC RCT, men with intermediate-to-high-risk localized prostate cancer treated with SBRT and cRT reported on their quality of life up to 6 years after treatment in the HYPO-RT-PC trial.[79,82] More men treated with SBRT reported clinically relevant deteriorations in bowel symptoms or problems at the end of RT when compared with cRT (stool frequency, rush to the toilet, flatulence, bowel cramp, mucus, blood in stool, and limitation in daily activity; all *P* < 002).[82] There were no differences between groups for acute urinary symptoms and problems, or sexual functioning at the end of RT.[82] At 6 years, men in both groups had similar rates of clinically relevant deterioration for overall urinary bother, overall bowel bother, overall sexual bother, and overall quality of life.[82] However, significantly fewer men reported a clinically meaningful deterioration in weak stream (22% SBRT vs. 38% cRT; *P* =.006), emptying bladder (16% SBRT vs. 32% cRT; *P* =.04), and insomnia (12% SBRT vs. 23% cRT; *P* =.03) with cRT when compared with SBRT.[82]

Of the 14 eligible comparative studies, 4 reported on some measure of quality of life.[86,87,90,97] Overall, findings were mixed, with limited comparison with other active treatments.[86,87,90,97]

- In an analysis of the Surveillance, Epidemiology, and End Results Program (SEER)-Medicare database, men with localized prostate cancer treated with SBRT had[86]:
  - Significantly higher rates of erectile dysfunction with SBRT compared with other RT options at 1 year (16.0% SBRT vs. 11.4% brachytherapy, 7.3% IMRT, 4.7% proton beam therapy, and 9.8% combination therapy; *P* < .001) and at 2 years (23.3% SBRT vs. 18.8% brachytherapy, 12.3% IMRT, 10.8% proton beam therapy, and 17.7% combination; *P* < .001)
  - Significantly lower rates of urinary incontinence with SBRT compared with brachytherapy at 1 year (15.6% SBRT vs. 32.2% brachytherapy; *P* < .001) and at 2 years (23.9% SBRT vs. 38.6% brachytherapy; *P* < .001), but significantly higher rates than IMRT (13.1% at 1 year and 18.8% at 2 years) or proton beam therapy (6.9% at 1 year and 10.8% at 2 years; *P* < .001)

- In a study from 1 center in the US and 10 hospitals in Spain, men with localized prostate cancer were treated with SBRT in the US or with surgery (radical prostatectomy) in Spain.[87] Men receiving SBRT had significantly higher urinary-related quality of life throughout follow-up, with the largest difference at 1 month.[87] Men who underwent surgery had significantly lower sexual quality of life at all time points.[87] At 1 month, men who underwent surgery had significantly higher bowel-related quality of life than men who underwent SBRT.[87] Overall, long-term urinary and sexual quality of life declines remained clinically significantly lower for men who underwent surgery but not for those who received SBRT.[87]
- In 1 study from a single center in the US, men with low- to intermediate-risk prostate cancer treated with SBRT had similar quality of life scores (specifically, urinary and bowel) to men being actively surveilled.[90] However, significantly more men in the SBRT group received treatment for urinary symptoms (35% SBRT vs. 24% active surveillance; $P < .04$).[90] Men who received SBRT also reported a significant decline in sexual function over time when compared with active surveillance.[90]
- Men treated with SBRT for prostate cancer at a single center in the US reported quality of life over a 4-year follow-up. When compared with active surveillance, SBRT was associated with[97]:
  - Similar urinary-related quality of life; however, scores in both groups declined in the short term
  - Lower bowel-related quality of life, but at 4 years, the scores were similar between groups
  - Lower sexual-related quality of life, but at 3 and 4 years, the scores were similar between groups

Toxicity

Overall, the rates of toxicities of grade 2 or higher were relatively infrequent in SBRT, and were similar to those of other RTs.[77-80]

- In the PACE-B RCT, men in the SBRT and cRT, including moderately fractionated RT, experienced similar levels of toxicities at most time points.[77]
  - At 12 weeks, there was no difference between groups in grade 2 or higher gastrointestinal (GI) toxicities (10% SBRT vs. 12% cRT; $P = .38$) or genitourinary (GU) toxicities (23% SBRT vs. 27% cRT; $P = .16$).
  - At 24 months, there was no difference between groups in grade 2 or higher GI toxicities (2% SBRT vs. 3% cRT; $P = .32$) or GU toxicities (3% SBRT vs. 2% cRT; $P = .39$).
  - Although the cumulative rate of grade 2 or higher GI toxicities was similar between groups over the 2 years (HR, 1.02; 95% CI, 0.7 to 1.51), men in the SBRT were significantly more likely to experience a grade 2 or higher GU toxicity (18.3% SBRT vs. 10.6% cRT; HR, 1.80; 95% CI, 1.25 to 2.61).
  - There was also no difference between groups for a grade 3 or higher GI worst event (< 1% SBRT vs. 1% cRT; $P = .37$) or GU worst event (2% SBRT vs. 2% cRT; $P = .47$).
- In the ASSERT RCT[80]:
  - Men with intermediate- to high-risk localized prostate cancer treated with SBRT experienced similar levels of grade 2 or higher GI and GU toxicities to men treated with moderately fractionated RT (24% SBRT vs. 35% moderately fractionated RT; $P \geq .05$).

    - Grade 3 GI or GU or higher toxicities were much less frequent and were not significantly different between groups (2% SBRT vs. 8% moderately fractionated RT; $P \geq .05$).
    - No toxicities higher than grade 3 were observed.
- In NCT01434290, men with localized T1 to T2 stage prostate cancer experienced low rates of grade 3 toxicities in both the SBRT group and the ultrahypofractionated radiation therapy (UHRT) group.[78]
    - In the SBRT group, < 1% experienced an acute grade 3 GI toxicity, compared with 1.6% in the UHRT group (*P* value not reported).
    - In the SBRT group, < 1% experienced an acute grade 3 renal or urinary toxicity, compared with none in the UHRT group (*P* value not reported).
    - Overall, < 1% of the SBRT group and the UHRT group experienced a late grade 3 GI toxicity; similar rates (< 1%) of late grade 3 renal or urinary toxicities were also seen (*P* value not reported).
    - No acute or late grade 4 or 5 toxicities were observed in either group.
- In the HYPO-RT-PC RCT, men treated with SBRT and cRT experienced similar levels of toxicity at most time points[79]:
    - At the end of treatment, more men in the SBRT group experienced grade 2 or higher urinary toxicity than those in the cRT group (28% SBRT vs. 23% cRT); however, the results were not statistically significant (*P* = 06).
    - At 1 years, significantly more men in the SBRT group experienced grade 2 or higher urinary toxicity than those in the cRT group (6% SBRT vs. 2% cRT; *P* = 004).
    - There were no significant differences in grade 2 or higher urinary or bowel late toxicity between the 2 treatment groups at any other time point, up to 5 years after radiotherapy.

No deaths (grade 5 events) due to toxicities were observed in any of the 4 RCTs.[77-80]

Of the 14 eligible comparative studies, 5 reported on toxicities.[85,91,92,96,98] Overall, grade 3 toxicities were rare and no grade 4 or 5 events were reported.[85,91,92,96,98] However, there may be some evidence that SBRT is associated with increased urinary retention or obstruction, urinary fistula, and more GI and GU toxicity than IMRT and greater GI toxicity than brachytherapy.[85,91,92,96,98]

- SBRT was significantly associated with fewer acute GI and GU toxicities of any grade than cRT ($P \leq .002$); in the SBRT group, 3% grade 3 GU toxicity was observed compared with 3% in the CRT with no grade 3 GI toxicity in the SBRT group and 1% in the cRT group.[85]
- No acute or late GU toxicities higher than grade 3 were observed in men with localized prostate cancer treated with SBRT or IMRT, and all had subsided at the most recent follow-up.[91] No acute or late GI toxicities higher than grade 2 were observed.[91] Grade 3 erectile dysfunction persisted in 6% of patients in the SBRT group and 17% in the IMRT group.[91]
- No difference in urinary toxicity was seen between SBRT and IMRT (HR urinary, 1.08; 95% CI, 0.91 to 1.29; HR bowel, 1.11; 95% CI, 0.81 to 1.53); however, more men in the SBRT group experienced urinary obstruction or retention (HR, 1.50; 95% CI, 1.15 to 1.97) and urinary fistula (HR, 6.68; 95% CI, 1.60 to 28.0).[92]
- In a study comparing SBRT and brachytherapy, no GI toxicities higher than grade 3 were observed in either group.[96] However, SBRT was significantly associated with more GI toxicities (cumulative incidence of 4% at 3 years SBRT vs. 0 or 1% depending on the dose of brachytherapy; cumulative incidence of 5% at 5 years SBRT vs. 0 or 2% depending on the

dose of brachytherapy; $P < .05$).[96] There was no difference between groups for GU toxicities (cumulative incidence of 6% at 3 years SBRT vs. 7% or 4% depending on the dose of brachytherapy; cumulative incidence of 6% at 5 years SBRT vs. 30% or 5% depending on the dose of brachytherapy; $P = .37$).[96] The maximum prevalence of grade 3 GU toxicities was 3% In the brachytherapy group.[96]

- Using data from the Chronic Conditions Warehouse, SBRT was associated with significantly more GU toxicity than IMRT, and was also more likely to be significantly associated with claims for diagnostic procedures to investigate incontinence or obstruction and claims for urethritis, urethral strictures, and bladder outlet obstruction.[98] At 6 months, SBRT was associated with more GI toxicity than IMRT, but not at 12 or 24 months.[98] At 6 months, SBRT was associated with higher rates of any toxicities (odds ratio [OR], 1.22; 95% CI, 1.02 to 1.41).[98]

Across the 18 noncomparative studies reporting harms[99-102,104,105,108,109,111,114-118,120-123]:

- The most commonly reported toxicities related to GU and GI.
- The proportions of grade 3 toxicities ranged from none to 3%.
- No grade 4 or 5 toxicities were reported.

Full details on toxicities from each of the noncomparative studies are in Appendix C.

Lung Cancer

History

In 2013, the HTCC adopted the following coverage determination for lung cancer[7]:

- SBRT is covered for adults and children for the following conditions when the following criteria are met:
  - For inoperable NSCLC, stage 1; and
  - Evaluation includes multidisciplinary team analysis, including surgical input.

The original report included 20 noncomparative NRSs on the use of SBRT in lung cancer, other than inoperable NSCLC, stage 1 lung cancer; the populations in the studies tended to be mixed, and included both primary lung cancer and metastatic lung cancer.[125-144] The committee did not make any coverage determination for other forms of lung cancer.[7]

Study Characteristics

We identified 1 RCT, reported in 2 publications, evaluating the use of SBRT for early-stage NSCLC prior to surgery (Table 10).[145,146] We assessed the RCT as being at moderate risk-of-bias because of a lack of blinding and conflicts of interest. We also identified 1 RCT in 1 publication on the use of SBRT for advanced NSCLC.[147] We assessed the PEMBRO-RT trial as being at moderate risk-of-bias because of the lack of blinding.

We identified a further 11 comparative studies, reported in 11 publications, of SBRT for lung cancer (Table 10).[148-158] Of the 11 studies, 3 included people with operable non-small cell lung cancer (NSCLC),[153,156,157] 1 person with inoperable stage II and higher stage lung cancer,[150] 5 people with lung metastases,[148,149,151,152,155] and 2 people with large cell neuroendocrine carcinoma of the lung (LCNEC).[154,158] We assessed 4 of the studies to be at low risk-of-bias as these were complex analytic studies using data from large, national databases,[150,153,156,158] 2 at

high risk-of-bias because of the potential for confounding,[151,157] and the remaining studies at moderate risk-of-bias because although confounding had been addressed, there remained the possibility of differences between the patient populations.[148,149,152,154,155]

Table 10. Summary Study Characteristics of RCTs and Comparative Studies in Lung Cancer

Citation Setting NCT or Other Trial ID or Study Name	Duration Risk-of-bias	Patient Characteristics	Intervention	Comparator(s)
Randomized controlled trials				
Altorki et al., 2021[145,146] Single center in the US NCT02904954	Followed up to 2 years Moderate risk-of-bias	Total N = 60 people with potentially resectable early-stage NSCLC (stages IA to IIIA), comprising 30 in durvalumab plus SBRT group and 30 in durvalumab group	• SBRT plus durvalumab ○ 3 consecutive daily fractions of 8 Gy ○ 2 cycles of durvalumab 3 weeks apart at a dose of 1·12 g by IV infusion over 60 min	• Durvalumab ○ 2 cycles of durvalumab 3 weeks apart at a dose of 1·12 g by IV infusion over 60 min
Theelen et al., 2019[147] 3 centers in the Netherlands NCT02492568 PEMBRO-RT	Median follow-up of 24 months Moderate risk-of-bias	Total N = 78 people with advanced NSCLC, comprising 38 in SBRT group and 40 in control group	• SBRT plus pembrolizumab ○ 3 doses of 8 Gy delivered on alternate days to a single tumor site that did not overlap with biopsy site and was deemed most safe or convenient for patient ○ Pembrolizumab administered intravenously at 200 mg every 3 weeks	• Pembrolizumab ○ Pembrolizumab administered intravenously at 200 mg every 3 weeks
Comparative nonrandomized studies				
Filippi et al., 2016[148] Single academic center in Italy NR	Retrospective study Median follow-up of 27 months in SBRT group and 46 months in surgery group Moderate risk-of-bias	Total N = 170 people with lung oligometastases from colorectal cancer, comprising 28 in SBRT group and 124 in surgery group	• SBRT ○ 26 Gy in a single fraction (n = 31), ○ 45 Gy in 3 fractions (n = 8) ○ 55 Gy in 10 fractions (n = 2)8 ○ 60 Gy in eight fractions (n = 2)	• Surgery ○ Thoracoscopic resection (3%) ○ Wedge resection (67%) ○ Anatomical resection (26%) ○ Combined resection (3%)

Citation Setting NCT or Other Trial ID or Study Name	Duration Risk-of-bias	Patient Characteristics	Intervention	Comparator(s)
Fleming et al., 2017[149] Single center in the US NR	Retrospective study Median follow-up of 16 months Moderate risk-of-bias	Total N = 182 people with lung metastases, comprising 88 in SBRT group and 94 in cRT group	• SBRT ○ Commonly 30 Gy in 10 fractions ○ Median of 45 Gy (range, 20 to 60 Gy) in a median 5 (range, 1 to 5) fractions	• cRT ○ Maximum of 50 Gy in conventional fractionation (maximum of 40 Gy per fraction) ○ Median dose of 30 Gy (range, 20 to 50 Gy) in a median 10 (range, 5 to 25) fractions
Jacobs et al., 2020[150] National Cancer Database (2004 to 2015) NR	Retrospective database analysis Median follow-up of 19 months Low risk-of-bias	Total N = 4,401 people with inoperable stage IIB NSCLC, comprising 989 in SBRT group, 484 in HFRT group, and 2,928 in cRT	• SBRT ○ Most common dose was 50 Gy in 5 fractions	• HFRT ○ Most common dose was 60 Gy in 20 fractions • cRT ○ Most common dose was 66 Gy in 33 fractions
Kanzaki et al., 2020[151] Single academic center in Japan NR	Retrospective study Median follow-up of 28 months High risk-of-bias	Total N = 80 people with pulmonary metastasis from epithelial tumors, comprising 21 in SBRT group and 59 in PM group	• SBRT ○ Total dose of 52 Gy in 4 fractions	• PM ○ Type of resection selected according to size and location of tumor, overall general condition, and respiratory function of patient
Lee et al. 2018[152] 1 academic center in South Korea NR	Retrospective study Median follow-up of 14 months Moderate risk-of-bias	Total N = 51 people with pulmonary metastases, comprising 21 in SBRT group and 30 in surgery group	• SBRT ○ 60 Gy in 3 fractions for peripheral lesions ○ 48 Gy in 4 fractions for central lesions	• Surgery ○ Wedge resection (93%) ○ Lobectomy (4%)
Littau et al., 2022[153]	Retrospective database analysis	Total N = 25,963 people with stage I lung cancer who are otherwise healthy, comprising	• SBRT ○ Based on codes (no details reported)	• Surgery

Citation Setting NCT or Other Trial ID or Study Name	Duration Risk-of-bias	Patient Characteristics	Intervention	Comparator(s)
National Cancer Database (2004 to 2016) NR	(propensity-matched) Followed up to 5 years Low risk-of-bias	5,465 in SBRT group and 20,498 in surgery group		○ Lobar resection (wedge resection or segmentectomy) or lobectomy
Lo et al., 2020[154] National Cancer Database (2004 to 2015) NR	Retrospective (propensity-matched) database analysis Median follow-up of 39 months Moderate risk-of-bias	Total N = 3,209 people with early stage bronchopulmonary LCNEC, comprising 238 in SBRT group and 2,971 in surgery group	• SBRT ○ Dose of 48 to 60 Gy in 3 to 5 fractions	• Surgery ○ Pneumonectomy, bi/lobectomy, or sublobar resection (e.g., wedge resection or segmentectomy)
Nelson et al., 2019[155] Single academic center in the US NR	Retrospective study (propensity-matched) Median follow-up of 4.4 years Moderate risk-of-bias	Total N = 381 people with colorectal pulmonary metastases, comprising 37 in SBRT group, 327 in surgery group, and 17 patients who received both SBRT and surgery, depending on nodule	• SBRT ○ Ranged from 50 Gy to 70 Gy in 3 to 10 fractions	• Surgery ○ Wedge resection • Both surgery and SBRT
Rosen et al., 2016[156] National Cancer Database (2008 to 2012) NR	Retrospective (propensity-matched) database analysis Median follow-up of 29 months in SBRT group and 32	Total N = 15,433 people with stage I lung cancer who are otherwise healthy, comprising 1,781 in SBRT group and 13,652 in surgery group	• SBRT ○ BED of between 100 and 200 Gy in 3 to 5 treatment fractions	• Surgery ○ Lobectomy

Citation Setting NCT or Other Trial ID or Study Name	Duration Risk-of-bias	Patient Characteristics	Intervention	Comparator(s)
	months in surgery group (matched) Low risk-of-bias			
Scotti et al., 2019[157] 2 academic centers in Italy NR	Retrospective study Median follow-up of 23 months High risk-of-bias	Total N = 187 people with medically operable stage I NSCLC, comprising 93 in SBRT group and 94 in surgery group	• SBRT ○ Dose schedules were prescribed to reach a BED of at least 100 Gy (with an alpha/beta ratio of 10), and fractionation was chosen depending on lesion site and dimensions	• Surgery ○ Lobectomy
Wegner et al., 2020[158] National Cancer Database (2004 to 2015) NR	Retrospective (propensity-matched) database analysis Median follow-up of 30 months Low risk-of-bias	Total N = 754 people with early-stage LCNEC, comprising 238 in SBRT group and 516 in cRT group	• SBRT ○ Median dose 50 Gy (48 to 60 Gy) in median 4 fractions (range, 3 to 5 fractions)	• cRT ○ Median dose 65 Gy (60 to 68 Gy) in median 33 fractions (range, 27 to 35 fractions)

Abbreviations. cRT: conventional radiation therapy; BED: biologically equivalent dose; Gy: Gray; HFRT: hypofractionated radiotherapy; IV: intravenous; LCNEC: large cell neuroendocrine carcinoma of the lung; NCT: US National Clinical Trial; NR: not reported; NSCLC: non-small cell lung cancer; PM: pulmonary metastasectomy; RFA: radiofrequency ablation; SBRT: stereotactic body radiation therapy.

In addition, we identified a further 11 noncomparative studies reported in 12 publications describing the toxicities and adverse events associated with the use of SBRT for lung cancer (Table 11).[140,159-169] We assessed each of the noncomparative studies as being at high risk-of-bias because of the lack of a comparator.

Table 11. Summary Study Characteristics of Noncomparative Studies in Lung Cancer

Citation Setting NCT or Other Trial ID	Study Design and Duration Risk-of-bias	Patient Characteristics	Description of Intervention
Berkovic et al., 2020[159] Single academic center in Belgium NR	Retrospective study Median follow-up of 22 months High risk-of-bias	Total N = 104 people with oligorecurrent pulmonary metastases	• SBRT ○ Delivered 3 times a week on every other day in 3 or 5 fractions to 60 Gy
Davis et al., 2015[160] RSSearch registry, including 18 sites and academic centers in the US and Germany (2004 to 2014) NCT01885299	Retrospective registry analysis Median follow-up of 17 months High risk-of-bias	Total N = 111 people with centrally located early-stage NSCLC or lung metastases	• SBRT ○ Median 48 Gy (range, 20 to 60) in a median of 4 fractions (range, 1 to 5) for primary NSCLC ○ Median 37.5 Gy (range, 16 to 60) in a median of 3 fractions (range, 1 to 5) for metastatic disease
Duijm et al., 2018[161] 2 centers in the Netherlands (1 academic) NR	Retrospective study Median follow-up of 16 months High risk-of-bias	Total N = 231 people with central lung tumors	• SBRT ○ Tumors close to the esophagus treated with 6 to 7 fractions of 7 to 8 Gy ○ Other central tumors received 5 fractions of 9 to 12 Gy, except 2 tumors which received 3 fractions of 20 Gy
Guckenberger et al., 2009[162] Single academic center in Germany NR	Retrospective study Median follow-up of 14 months High risk-of-bias	Total N = 124 people with early-stage NSCLC and pulmonary metastases	• SBRT ○ 6 to 26 Gy in 1 to 8 fractions
Helou et al, 2017[163] Not clear NR	Prospective study Median follow-up of 22 months High risk-of-bias	Total N = 120 people with pulmonary metastases	• SBRT ○ 48 to 52 Gy in 4 fractions for peripheral pulmonary metastases; increased to 56 to 60 Gy in 4 fractions ○ 50 Gy in 5 fractions for central tumors

Citation Setting NCT or Other Trial ID	Study Design and Duration Risk-of-bias	Patient Characteristics	Description of Intervention
Lagerwaard et al., 2012[164] Single academic center in the Netherlands NR	Prospective study Median follow-up of 31 months High risk-of-bias	Total N = 177 people with potentially operable stage I NCSLC	• SBRT ○ Patients with peripheral T1 tumors without broad contact with chest wall treated with 3 fractions of 20 Gy each; ○ Patients with T1 tumors that had broad contact with chest wall and T2 tumors treated with 5 fractions of 12 Gy each. ○ Patients with centrally tumors were treated with 8 fractions of 7.5 Gy each
Lee et al., 2021[165] Single academic center in Korea NR	Retrospective study Median follow-up of 28 months High risk-of-bias	Total N = 336 people with primary, recurrent lung cancer or metastatic lung tumor	• Re-irradiation with SBRT ○ Median prescribed dose 54 Gy (range 48 to 60 Gy), and all but 1 patient had 4 fractionations • Initial SBRT ○ Median prescribed dose of 60 Gy (range 45 to 60 Gy) ○ Median fractionation number of 4 (range 4 to 8)
Osti et al., 2018[166] 1 academic center in Italy NR	Retrospective study Median follow-up of 38 months High risk-of-bias	Total N = 129 people with lung oligometastatic disease	• SBRT ○ 30 Gy in 1 dose
Sharma et al., 2018[167,169] Single center in the Netherlands NR	Retrospective study Median follow-up of 26 months High risk-of-bias	Total N = 206 people with pulmonary oligometastases	• SBRT ○ Peripheral tumors treated with 51 Gy to 6 0Gy in 3 fractions or a single fraction of 30 Gy. ○ Central tumors received 45 to 60 Gy in 5 to 8 fractions
Takeda et al., 2010[140] Single center in Japan NR	Retrospective study Median follow-up of 12 months High risk-of-bias	Total N= 128 people with lung tumors	• SBRT ○ 40 to 60 Gy in 5 to 10 fractions
Yamamoto et al. 2020[168] 68 institutions in Japan NR	Retrospective study Median follow-up of 24 months High risk-of-bias	Total N = 1,378 people with pulmonary oligometastases	• SBRT ○ Most typical dose was 48 Gy in 4-fraction

Abbreviations. Gy: Gray; NCT: US National Clinical Trial; NR: not reported; NSCLC: non-small cell lung cancer; SBRT: stereotactic body radiation therapy.

GRADE Summary of Findings

Table 12. GRADE Summary of Evidence: Effectiveness of SBRT for Lung Cancer

Number of Participants (N) Number of Studies	Findings	Certainty of Evidence	Rationale
SBRT vs. surgery or no SBRT for operable early-stage NCSLC			
Overall survival			
N = 41,583 3 comparative NRSs[153,156,157]	SBRT was associated with significantly worse outcomes than surgery for operable early-stage NCSLC; surgery was associated with around a 60 to 65% lower risk of mortality. However, 1 study did find that in patients who were medically operable, SBRT and lobectomy may be equally effective.	⨁◯◯◯ VERY LOW	Downgraded 1 level for inconsistency
Progression-free survival			
N = 187 1 comparative NRS[157]	In patients who were medically operable, SBRT and lobectomy may be equally effective (HR, 1.57; 95% CI, 0.68 to 3.64)	⨁◯◯◯ VERY LOW	Downgraded 1 level for risk-of-bias and 2 levels for imprecision (i.e., very wide CIs)[a]
Disease-control			
N = 60 1 RCT[145]	In people with potentially resectable early-stage NCSLC, SBRT in combination with durvalumab was associated with significantly higher odds of having a major pathological response (OR, 16.0; 95% CI, 3.2 to 79.6) or a partial radiographic response (46.7% SBRT with durvalumab vs. 3.3% durvalumab; *P* = .001) than durvalumab alone.	⨁⨁⨁◯ MODERATE	Downgraded 1 level for risk-of-bias
Quality of life			
Not reported			
SBRT vs. RT for inoperable stage II			
Overall survival			
N = 4,401 1 comparative NRS[150]	SBRT appears to be associated with improved survival than cRT (HR, 0.79; 95% CI, 0.71 to 0.87) or hypofractionated radiotherapy (HR, 0.57; 95% CI, 0.50 to 0.66) for inoperable stage II NSCLC.	⨁⨁◯◯ LOW	Not downgraded
Progression-free survival			
Not reported			
Disease-control			
Not reported			

Number of Participants (N) Number of Studies	Findings	Certainty of Evidence	Rationale
Quality of life			
Not reported			
SBRT vs. no SBRT for advanced NCSLC			
Overall survival			
N = 78 1 RCT[147]	People with advanced NSCLC treated with SBRT after pembrolizumab or pembrolizumab alone had a similar overall survival (median: 15.9 months SBRT vs. 7.6 months control; HR, 0.66; 95% CI, 0.37 to 1.18) However, in subgroup analyses, men (HR, 0.42; 95%CI, 0.19 to 0.96; *P* = .04) and smokers (HR, 0.48; 95% CI, 0.25 to 0.93; *P* = .03) had significantly improved survival with SBRT compared with pembrolizumab alone.	⊕⊕⊕◯ MODERATE	Downgraded 1 level for imprecision (i.e., wide CIs)[a]
Progression-free survival			
N = 78 1 RCT[147]	People with advanced NSCLC treated with SBRT after pembrolizumab or pembrolizumab alone had a similar PFS (HR, 0.71; 95% CI, 0.42 to 1.18).	⊕⊕◯◯ LOW	Downgraded 1 level each for risk-of-bias and imprecision (i.e., wide CIs)[a]
Disease-control			
Not reported			
Quality of life			
Not reported			
SBRT vs. surgery or cRT for lung metastases			
Overall survival			
N= 483 4 comparative NRSs[147-149,151,152]	In people with lung metastases, SBRT and surgery may be associated with similar overall survival (median survival at 2 years of around 68% to 77% in the SBRT group vs. 82% in the surgery group); however, SBRT may be associated with improved survival when compared with cRT (median survival of 26 months in the SBRT group vs. 9 months in the cRT group; *P* < .001).	⊕⊕◯◯ LOW	Not downgraded
Progression-free survival			
N = 301 3 comparative NRSs[148,151,152]	People with lung metastases treated with SBRT had significantly worse PFS than people treated with surgery (around 3 times more likely to have progression). However, results were mixed with 1 study showing no difference between SBRT and surgery.	⊕◯◯◯ VERY LOW	Downgraded 1 level for inconsistency

Number of Participants (N) Number of Studies	Findings	Certainty of Evidence	Rationale
Disease-control			
N = 694 4 comparative NRSs[149,151,152,155]	Results were mixed with SBRT being associated with both similar and lower levels of local control than surgery for lung metastases. SBRT, however, was significantly associated with improved local control when compared with cRT. Studies reported at different times using different statistics, precluding any summary statistics (see detailed findings below).	⊕◯◯◯ VERY LOW	Downgraded 1 level for inconsistency
Quality of life			
Not reported			
SBRT vs. surgery or cRT for LCNEC of the lung			
Overall survival			
N = 3,963 2 comparative NRSs[154,158]	In people with LCNEC of the lung, SBRT may be associated with improved survival when compared with cRT (HR, 0.83; 95% CI, 0.68 to 1.00)[b], but worse outcomes when compared with surgery (HR, 1.61; 95% CI, 1.36 to 1.92).	⊕⊕◯◯ LOW	Not downgraded
Progression-free survival			
Not reported			
Disease-control			
Not reported			
Quality of life			
Not reported			
SBRT vs. surgery and other RT for any lung cancer			
Toxicity			
N = 138 2 RCTs[145,147]	Grade 3 and higher events occurred in around 3% to 11% of SBRT group; most common were dyspnea and pneumonia, pancreatitis, and fatigue.	⊕⊕⊕◯ MODERATE	Downgraded 1 level for risk-of-bias
N = 221 2 comparative NRSs[148,152]	Grade 3 toxicities were not common with SBRT, and included lung toxicity (including radiation pneumonitis) and chest wall pain; ranging from 3% to 14% depending on the specific toxicity.	⊕⊕◯◯ LOW	Not downgraded

Notes. [a] *Inconsistency not assessable due to only 1 study;* [b] *Inverted for consistency.*
Abbreviations. CI: confidence interval; cRT: conventional radiation therapy; HR: hazard ratio; LCNEC: large-cell neuroendocrine carcinoma; NRS: nonrandomized study; NSCLC: non-small cell lung cancer; PFS: progression-free survival; RCT: randomized controlled trial; SBRT: stereotactic body radiation therapy;

Overall and Progression-free Survival

Overall and PFS were not reported for the RCT (NCT02904954); the trial of SBRT for potentially resectable early-stage NSCLC is ongoing and the authors noted data on disease-free survival were not yet mature enough for analysis.[145]

Across the 3 comparative studies in people with operable early-stage NCSLC, SBRT was associated with significantly worse outcomes than surgery. However, 1 study did find that in patients who were medically operable, SBRT and lobectomy may be equally effective.

- In an analysis from the NCDB, people with clinical stage I NSCLC who were otherwise healthy (Charlson-Deyo comorbidity index of 0 and whose treatment plan included options for either SBRT or surgery) and were treated with SBRT had significantly worse overall survival than people who underwent surgery (median survival, 57.5 months SBRT vs. 98.7 months surgery; $P < .001$; HR surgery vs. SBRT, 0.35; 95% CI, 0.33 to 0.36).[153] The survival benefit with surgery remained when analyzed by surgery type (sublobar or lobectomy).[153]
- In another analysis from the NCDB, people with clinical stage I lung cancer who had no comorbidities and were treated with SBRT had a significantly worse overall survival than people treated with lobectomy (at 5 years, 29% SBRT vs. 59% surgery; $P < .001$).[156] During the first 7.5 months after treatment, there was no difference between SBRT and lobectomy (HR, 1.14; 0.86 to 1.50); however, beyond 7.5 months, lobectomy was associated with significantly improved survival than SBRT (HR, 0.38; 0.33 to 0.43).[156]
- In a study from 2 centers in Italy, patients with medically operable stage I NSCLC treated with SBRT or lobectomy had similar overall survival (HR, 1.68; 95% CI, 0.72 to 3.90) and similar PFS (HR, 1.57; 95% CI, 0.68 to 3.64).[157]

In the 1 study in people with inoperable stage 2 NCSLC, SBRT appears to be more strongly associated with improved survival than cRT or hypofractionated radiotherapy (HFRT).

- In an analysis from the NCDB, people with inoperable stage IIB NSCLC treated with SBRT had improved overall survival when compared with people who received cRT (at 2 years, 54.2% SBRT vs. 43.3% cRT; at 5 years, 22.0% vs. 18.7%; HR, 0.79; 95% CI, 0.71 to 0.87).[150] A similar result was seen compared with people who received HFRT (at 2 years, 54.2% SBRT vs. 34.0% HFRT; at 5 years, 22.0% vs. 9.4%; HR, 0.57; 95% CI, 0.50 to 0.66).[150] For people with primary lung tumors larger than 5 cm or tumors invading the chest wall, SBRT continued to be associated with improved survival compared with HFRT, and with similar survival to cRT.[150] However, for people with multifocal tumors in the same lobe, SBRT was associated with improved survival compared with both cRT and HFRT.[150]

In the PEMBRO-RT trial, people with advanced NSCLC treated with SBRT after pembrolizumab or pembrolizumab alone had a similar overall survival (median: 15.9 months SBRT vs. 7.6 months control; HR, 0.66; 95% CI, 0.37 to 1.18).[147] However, in subgroup analyses, men (HR, 0.42; 95%CI, 0.19 to 0.96; $P = .04$) and smokers (HR, 0.48; 95% CI, 0.25 to 0.93; $P = .03$) had significantly improved survival with SBRT compared with pembrolizumab alone.[147] Between the 2 groups, PFS was similar (median, 6.6 months SBRT vs. 1.9 months control; HR, 0.71; 95% CI, 0.42 to 1.18).[147]

In total, 4 of the 5 comparative studies in people with pulmonary metastases reported on survival or PFS. In people with lung metastases, SBRT and surgery may be associated with similar

overall survival; however, PFS may be lower with SBRT than with surgery. There may be an association with SBRT and improved survival when compared with cRT.

- In a study from a single center in Italy, people with lung oligometastases treated with SBRT had similar overall survival to people treated with surgery (at 1 year, 89% SBRT vs. 96% surgery; at 2 years, 77% vs. 82%; aHR, 1.71; 95% CI, 0.82 to 3.54).[148] However, people with lung oligometastases treated with SBRT had significantly worse PFS than people treated with surgery (aHR, 2.78; 95% CI, 1.67 to 4.62).[148]
- In a study from a single center in the US, people with lung metastases treated with SBRT were significantly more likely to live longer than people treated with cRT (median, 26.2 months SBRT vs. 9.0 months cRT; $P < .001$).[149]
- In a study from a single center in Japan, people with lung metastases treated with SBRT or with surgery (pulmonary metastasectomy) had a similar overall survival at 3 years (52% SBRT vs. 77% surgery; $P = .10$).[151] However, PFS was significantly lower in the SBRT group (at 3 years, 11% SBRT vs. 42% surgery; $P = .01$).[151]
- In a study from a single center in South Korea, people with lung metastases treated with SBRT had a similar overall survival to people who underwent surgery (at 1 year, 79.5% SBRT vs. 95.0% surgery; at 2 years, 68.2% vs. 81.8%; HR univariate, 0.67; 95% CI, 0.19 to 2.35; HR multivariate, 1.58; 95% CI, 0.31 to 8.00).[152] While PFS was significantly lower in the SBRT group, this difference was not maintained in a multivariate analysis (at 1 year, 23.8% SBRT vs. 51.1% surgery; at 2 years, 11.9% vs. 46.0%; HR univariate, 0.46; 95% CI, 0.23 to 0.90; HR multivariate, 0.80; 95% CI, 0.35 to 1.80).[152] There was no significant differences between treatments in patients with or without synchronous metastases.[152]

Across the 2 comparative studies in people with LCNEC of the lung, SBRT may be associated with improved survival when compared with cRT, but worse outcomes when compared with surgery.

- In an analysis from the NCDB, people with early-stage bronchopulmonary LCNEC who received SBRT had a significantly worse overall survival than people who underwent surgery (at 5 years, 25% SBRT vs. 48% surgery; HR, 1.61; 95% CI, 1.36 to 1.92).[154] Median survival was significantly shorter in the SBRT group than in the surgery group (34.6 months SBRT vs. 57.2 months; $P < .001$).[154]
- In another analysis from the NCDB, people with early-stage LCNEC of the lung treated with SBRT had a marginally improved survival than people treated with cRT (HR, 1.21; 95% CI, 1.00 to 1.46), with a median survival of 34.7 months compared with 23.7 months for cRT ($P = .02$).[158]

Disease Control

In a RCT comparing SBRT in combination with durvalumab or with durvalumab alone in people with potentially resectable early-stage NSCLC (stages IA to IIIA), people who were treated with SBRT in combination with durvalumab were significantly more likely to have a major pathological response (53.3% SBRT with durvalumab vs. 6.7% durvalumab; OR, 16.0; 95% CI, 3.2 to 79.6).[145] People treated with SBRT in combination with durvalumab were also significantly more likely to have a partial radiographic response (46.7% SBRT with durvalumab vs. 3.3% durvalumab; $P = .001$).[145]

Four of the 5 comparative studies in people with pulmonary metastases reported some measure of disease control. Results were mixed, with SBRT being associated with both similar and lower levels of local control than surgery. However, SBRT was significantly associated with improved local control when compared with cRT.

- In a study from a single center in the US, people with lung metastases treated with SBRT were significantly less likely to experience local failure than people treated with cRT at 6 months, 5.8% SBRT vs. 31.5% cRT; at 12 months, 19.5% SBRT vs. 43.2% cRT; HR, 0.54; 95% CI, 0.32 to 0.92).[149]
- In a study from a single center in Japan, people with lung metastases treated with SBRT or with surgery (pulmonary metastasectomy) had a similar level of local control at 3 years (92% SBRT vs. 88% surgery; *P* = .48).[151]
- In a study from a single center in South Korea, people with lung metastases treated with SBRT or surgery had similar rates of local control (at 1 year 83.5% SBRT vs. 96.6% surgery; at 2 years, 75.2% vs. 91.5%; *P* = .16 for each year).[152]
- In a study from a single center in the US, people with lung metastases treated with SBRT were significantly more likely to experience local recurrence (HR, 3.28; 95% CI, 1.53 to 7.04), with a 2-year local treatment failure of 29.4% in the SBRT group and 14.1% in the surgery group, and a 5-year local treatment failure of 37.3% in the SBRT group and 18.4% in the surgery group.[155] Subgroup analysis did not identify any group in which SBRT provided a significant improvement.[155]

None of the studies in people with operable early-stage NCSLC, inoperable stage 2 NCSLC, advanced NSCLC, or LCNEC of the lung reported measures of disease control.

Quality of Life

No eligible studies reported quality of life measures.

Toxicity

In NCT02904954, there were no treatment-related deaths or deaths within 30 and 90 days of surgery for early-stage NSCLC.[145] Serious adverse events occurred in 2 (7%) patients in each group (pancreatitis and fatigue in the SBRT with durvalumab group, and pulmonary embolism and stroke in the durvalumab group).[145] In the SBRT and durvalumab group, rates of grade 3 toxicities ranged from 3% (1 case each of fatigue, adrenal insufficiency, hyperuricemia, decreased neutrophil count, and a thromboembolic event) to 10% (3 cases of hyponatremia).[145] In the durvalumab group, rates of grade 3 toxicities ranged from 3% (1 case each of fatigue, a thromboembolic event, hepatitis, and decreased platelets) to 10% (3 cases of hyperlipasemia).[145] A single grade 5 event was observed in each group; stroke (3%) in the SBRT and durvalumab group and a cardiopulmonary event in the durvalumab group.[145]

In the PEMBRO-RT trial, grade 3 and higher events occurred in around 3% to 11% of the SBRT group; the most common being dyspnea and pneumonia.[147] In the pembrolizumab group, grade 3 and higher events occurred in around 3% to 5%; the most common being dyspnea and nausea.[147]

Across the 11 comparative studies, only 2 studies reported toxicity. Grade 3 toxicities were not common with SBRT, and included lung toxicity, such as radiation pneumonitis, and chest wall pain.

- In people with pulmonary metastases, 14% of those treated with SBRT experienced grade 3 radiological lung toxicity and 4% grade 3 chest wall pain.[148] In people undergoing surgery, no major complications were observed and 1 person (< 1%) died within 30 days of surgery.[148]
- Around 3% of with pulmonary metastases who underwent surgery experienced grade 3 nausea; in the SBRT group, around 5% of people experienced grade 3 radiation pneumonitis.[152]

Across the 11 noncomparative studies reporting harms[140,159-168]:

- The most commonly reported grade 3 and higher toxicities were chest pain, cough, dyspnea, rib fractures, lung fibrosis, and hemoptysis. Specifically, radiation pneumonitis grade 3 ranged from around 1% to 5%; grade 4 was observed in around 1% of patients, and grade 5 in fewer than 1% of patients.
- The proportions of grade 3 toxicities ranged from none to 7%.
- Most studies did not observe any grade 4 or 5 toxicities; however, observed grade 4 toxicities included late radiation pneumonitis (leading to possibly treatment-related death), and grade 5 radiation pneumonitis, dyspnea, and hemoptysis.

Full details on toxicities from each of the noncomparative studies are in Appendix C.

Colorectal Cancer

History

In the 2012 report presented to the HTCC,[6] the evidence on harms was assessed as being of very low quality, based on 2 case series.[170,171].

Study Characteristics

We did not identify any eligible studies for the use of SBRT in colorectal cancer in this updated evidence review.

Uterine Cancer

History

No eligible studies on the use of SBRT in uterine cancer were included in the 2012 report.[6]

Study Characteristics

We did not identify any eligible studies for the use of SBRT in uterine cancer in this updated evidence review.

Melanoma

History

In the 2012 report presented to the HTCC,[6] the overall strength of evidence was assessed as very low for harms, based on 7 case series.[172-178] No comparative studies on the effectiveness of SBRT in this population were identified.[6]

Study Characteristics

We identified 1 RCT of SBRT in melanoma, specifically Merkel cell carcinoma (Table 13).[179] We assessed the RCT as being at moderate risk-of-bias, because of the lack of blinding.

Table 13. Summary Study Characteristics of Randomized Controlled Trials in Melanoma

Citation Setting NCT or Other Trial ID	Duration Risk-of-bias	Patient Characteristics	Description of Intervention	Description of Comparator(s)
Kim et al., 2022[179] 2 centers, 1 academic, in the US NCT03071406	Median follow-up of 15 months Moderate risk-of-bias	Total N = 50 people with advanced Merkel cell cancer, comprising 25 in SBRT group and 25 in control group	• SBRT ○ 24 Gy in 3 fractions ○ To at least 1 tumor site ○ Nivolumab and ipilimumab	○ Nivolumab and ipilimumab

Abbreviations. Gy: Gray; NCT: US National Clinical Trial; SBRT: stereotactic body radiation therapy.

GRADE Summary of Findings

Table 14. GRADE Summary of Evidence: Effectiveness of SBRT for Melanoma

Number of Participants (N) Number of Studies	Findings	Certainty of Evidence	Rationale
SBRT with nivolumab and ipilimumab vs. nivolumab and ipilimumab for Merkel cell carcinoma			
Overall survival			
N = 50 1 RCT[179]	No difference between groups by immunotherapy status: • Naïve to treatment: HR, 2.12; 95% CI, 0.13 to 34.23 • Previous treatment: HR, 2.15; 95% CI, 0.83 to 5.57	⊕⊕◯◯ LOW	Downgraded 2 levels for imprecision (i.e., very wide CIs)[a]
Progression-free survival			
N = 50 1 RCT[179]	No difference between groups by immunotherapy status: • Naïve to treatment: HR, 1.77; 95% CI, 0.11 to 28.38 • Previous treatment: HR, 1.60; 95% CI, 0.68 to 3.75	⊕⊕◯◯ LOW	Downgraded 2 levels for imprecision (i.e., very wide CIs)[a]
Disease-control			
N = 50 1 RCT[179]	Response: 50% vs. 72%; *P* = .26	⊕⊕◯◯ LOW	Downgraded 1 level each for risk-of-bias and for imprecision (i.e., not assessable)[a]
Quality of life			
Not reported			

Number of Participants (N) Number of Studies	Findings	Certainty of Evidence	Rationale
Toxicity			
N = 50 1 RCT[179]	8 (16%) discontinued the protocol treatment due to toxicity. No deaths were attributed to treatment. Grade 3 events occurred in 24% of SBRT group and 28% in control group; grade 4 events occurred in 8% and 12% by group.	⨁⨁◯◯ LOW	Downgraded 1 level each for risk-of-bias and for imprecision (i.e., not assessable)[a]

Notes. [a] *Inconsistency not assessable due to only 1 study.*
Abbreviations. CI: confidence interval; HR: hazard ratio; RCT: randomized controlled trial.

Overall and Progression-free Survival

In NCT03071406, survival outcomes were reported by immunotherapy status.[179] In people with Merkel cell carcinoma who were naïve to immunotherapy, there was no difference in overall survival between SBRT added to nivolumab and ipilimumab, or nivolumab and ipilimumab without SBRT (median, not reached in either group; HR, 2.12; 95% CI, 0.13 to 34.23).[179] In people with Merkel cell carcinoma who had prior immunotherapy, there was no difference in overall survival between SBRT added to nivolumab and ipilimumab, or nivolumab and ipilimumab without SBRT (median, not reached in either group; HR, 1.77; 95% CI, 0.11 to 28.38).[179] Similar results were seen for PFS (immunotherapy naïve: median, 9.7 months SBRT vs. 14.9 months control; HR, 2.15; 95% CI, 0.83 to 5.57; prior immunotherapy: median: 2.7 months SBRT vs. 4.2 months control; HR, 1.60; 95% CI, 0.68 to 3.75).[179]

Disease Control

In people with Merkel cell carcinoma treated with SBRT in addition to nivolumab and ipilimumab, 12 (50%) had a response to treatment compared with 18 (72%) treated with nivolumab and ipilimumab without SBRT (P = .26).[179]

Quality of Life

No eligible studies reported quality of life measures.

Toxicity

Overall, 8 (16%) discontinued the protocol treatment due to toxicity and no deaths were attributed to treatment.[179] Grade 3 toxicities occurred in 4% to 8% of patients in the SBRT added to nivolumab and ipilimumab group and 4% to 12% of patients in the nivolumab and ipilimumab without SBRT group.[179] The most common grade 3 toxicities were colitis and elevated pancreatic enzymes in the SBRT group and arthralgia and elevated transaminases in the control group.[179] Overall, 5 (10%) grade 4 events occurred; 2 in the SBRT group and 3 in the control group. Grade 4 events included elevated pancreatic enzymes in both groups, and hyponatremia and acute kidney injury in the control group.[179]

Renal Cancer

History

In the 2012 report presented to the HTCC,[6] no primary studies reported on the effectiveness of SBRT for renal cancer alone.

Study Characteristics

We identified 1 eligible comparative study and 1 noncomparative study reporting on the use SBRT in renal cell carcinoma (Table 15 and Table 16). We assessed the comparative study to be at low risk-of-bias as it was a complex analytic study using data from large, national databases. We assessed the noncomparative study as being at high risk-of-bias because of the lack of a comparator of interest.

Table 15. Summary Study Characteristics of Comparative Studies in Renal Cancer

Citation Setting NCT or Other Trial ID	Duration Risk-of-bias	Patient Characteristics	Description of Intervention	Description of Comparator(s)
Uhlig et al., 2020[180] National Cancer Database (2004 to 2015) NR	Retrospective database analysis (propensity-matched) Median follow-up of 58 months Low risk-of-bias	Total N = 91,965 people with stage I RCC, comprising 174 in SBRT group, 3,432 in RFA group, 5,446 in CA group, and 82,913 in PN group	• SBRT ○ Median dose of 40 Gy (IQR, 32 to 48) in median of 3 fractions (IQR, 2 to 4)	• RFA • CA • PN

Abbreviations. CA: cryoablation; Gy: Gray; PN: partial nephrectomy; RCC: renal cell carcinoma; RFA: radiofrequency ablation; SBRT: stereotactic body radiation therapy.

Table 16. Summary Study Characteristics of Noncomparative Studies in Renal Cancer

Citation Setting NCT or Other Trial ID	Study Design and Duration Risk-of-bias	Patient Characteristics	Description of Intervention
Siva et al., 2022[181] 12 sites in 5 countries NR	Retrospective and prospective data analysis Minimum of 2 years follow-up High risk-of-bias	Total N = 190 people with primary renal cell carcinoma	• SBRT ○ Single or multiple fractions of greater than 5 Gy

Abbreviations. Gy: Gray; NR: not reported; SBRT: stereotactic body radiation therapy

GRADE Summary of Findings

Table 17. GRADE Summary of Evidence: Effectiveness of SBRT for Renal Cancer

Number of Participants (N) Number of Studies	Findings	Certainty of Evidence	Rationale
SBRT vs. cRT in stage I RCC			
Overall survival			
N = 91,965 1 comparative NRS[180]	In people with stage I RCC, SBRT was associated with a significantly worse overall survival than people treated with ablation or surgery[180]: • Partial nephrectomy vs. SBRT: HR, 0.29 (95% CI, 0.19 to 0.46) • Cryoablation vs. SBRT: HR, 0.40 (95% CI, 0.26 to 0.60) • Radiofrequency ablation or microwave ablation vs. SBRT: HR, 0.46 (95% CI, 0.31 to 0.67)	⨁⨁◯◯ LOW	Not downgraded[a]
Progression-free survival			
Not reported			
Disease-control			
Not reported			
Quality of life			
Not reported			
Toxicity			
Not reported			

Notes. [a] *Inconsistency not assessable due to only 1 study*
Abbreviations. CI: confidence interval; HR: hazard ratio; NRS: nonrandomized study; RCC: renal cell carcinoma; SBRT: stereotactic body radiation therapy.

Overall and Progression-free Survival

In people with stage I RCC, SBRT was associated with a significantly worse overall survival than people treated with ablation or surgery[180]:

- Partial nephrectomy vs. SBRT: HR, 0.29 (95% CI, 0.19 to 0.46)
- Cryoablation vs. SBRT: HR, 0.40 (95% CI, 0.26 to 0.60)
- Radiofrequency ablation or microwave ablation vs. SBRT: HR, 0.46 (95% CI, 0.31 to 0.67)

Disease Control

No eligible studies reported measures of disease control.

Quality of Life

No eligible studies reported quality of life measures.

Toxicity

In the noncomparative study, none of the 190 people treated with SBRT for primary renal cell carcinoma experienced grade 3 toxic effects or treatment-related deaths.[181] Only 1 patient

developed a treatment-related acute grade 4 duodenal ulcer and late grade 4 gastritis after SBRT.[181]

Pancreatic Cancer

History

In the 2012 report presented to the HTCC,[6] the overall strength of evidence for pancreatic cancer was assessed as very low for effectiveness and harms, based on 1 systematic review and 4 case series.[182-186] The 2012 report[6] also concluded that the overall strength of evidence on cost-effectiveness for pancreatic cancer was very low, based on 1 economic modeling study.[187]

Study Characteristics

We identified 3 eligible comparative studies of SBRT in pancreatic cancer (Table 18). We assessed each of the studies to be at low risk-of-bias as these were complex analytic studies using data from large, national databases.[188-190]

Table 18. Summary Study Characteristics of Comparative Studies in Pancreatic Cancer

Citation Setting NCT or Other Trial ID	Duration Risk-of-bias	Patient Characteristics	Description of Intervention	Description of Comparator(s)
de Geus et al., 2017[188] National Cancer Database (2004 to 2012) NR	Retrospective database analysis (propensity matched) Followed up to 20 months Low risk-of-bias	Total N = 14,331 people with unresected pancreatic cancer, comprising 322 in SBRT group, 5,464 in CT group, 6,418 in cRT group, and 2,127 in IMRT group	• SBRT ○ Median dose of 30.0 Gy (IQR, 24.0 to 35.0) ○ Median of 3 fractions (IQR, 3 to 5)	• CT • cRT ○ Median dose of 45.0 Gy (IQR, 45.0 to 50.4) ○ Median of 28 fractions (IQR, 25 to 29) • IMRT ○ Median dose of 50.4 Gy (IQR, 45.0 to 50.4) ○ Median of 28 fractions (IQR, 25 to 30)
Moningi et al., 2022[189] Surveillance, Epidemiology, and End Results (SEER) and Texas Cancer Registry, linked with Medicare; MarketScan Commercial Claims and Encounter database NR	Retrospective database analysis Follow-up of at least 9 months Low risk-of-bias	Total N = 5,624 people with non-metastatic, unresectable pancreatic cancer comprising 2,552 older patients (105 SBRT, 1,187 CT, 1,230 cRT) and 3,102 younger patients (101 SBRT, 1,519 CT, 1,482 cRT)	• SBRT	• CT • cRT

Citation Setting NCT or Other Trial ID	Duration Risk-of-bias	Patient Characteristics	Description of Intervention	Description of Comparator(s)
Zhong et al., 2017[190] National Cancer Database (2004 to 20123 NR	Retrospective database analysis (propensity matched) Median follow-up of 26 months Low risk-of-bias	Total N = 8,450 people with locally advanced pancreatic cancer, comprising 631 in SBRT group and 7,819 in cRT group	• SBRT ○ Median of 8.0 Gy ([1]0th percentile of 5.0 and [9]0th percentile of 20.0) in median 5 fractions ([1]0th percentile of 2 and [9]0th percentile of 5)	• cRT ○ Median of 1.8 Gy ([1]0th percentile of 1.8 and [9]0th percentile of 1.9) in median 28 fractions ([1]0th percentile of 21 and [9]0th percentile of 31)

Abbreviations. cRT: conventional RT; CT: chemotherapy; Gy: Gray; IMRT: intensity-modulated radiotherapy; IQR: interquartile range; NCT: US National Clinical Trial; NR: not reported; SBRT: stereotactic body radiation therapy.

GRADE Summary of Findings

Table 19. GRADE Summary of Evidence: Effectiveness of SBRT for Pancreatic Cancer

Number of Participants (N) Number of Studies	Findings	Certainty of Evidence	Rationale
SBRT vs. CT or IMRT for unresected pancreatic cancer			
Overall survival			
N = 14,331 1 comparative NRS[188]	In people with unresected pancreatic cancer treated with SBRT had significantly better overall survival than people treated with CT (13.9 months SBRT vs. 10.2 months CT; *P* < .001) or IMRT (13.9 months SBRT vs. 12.2 months IMRT; *P* = .049). However, there was no difference in overall survival between SBRT with multi-agent CT and multi-agent CT alone (14.8 months SBRT with multi-agent CT vs. 12.9 months multi-agent CT alone; *P* = .09).	⨁⨁◯◯ LOW	Not downgraded[a]
Progression-free survival			
Not reported			
Disease-control			
Not reported			
Quality of life			
Not reported			

Number of Participants (N) Number of Studies	Findings	Certainty of Evidence	Rationale
SBRT vs. cRT for locally advanced pancreatic cancer			
Overall survival			
N = 8,450 1 comparative NRS[190]	People with locally advanced pancreatic cancer treated with SBRT had significantly better overall survival than people treated with cRT at 2 years (HR, 0.84; 95% CI, 0.75 to 0.93), with a significantly longer median survival.	⨁⨁◯◯ LOW	Not downgraded[a]
Progression-free survival			
Not reported			
Disease-control			
Not reported			
Quality of life			
Not reported			
SBRT vs. CT or cRT for pancreatic cancer			
Toxicity			
N = 5,624 1 comparative NRS[189]	In people with nonmetastatic, unresectable pancreatic cancer, SBRT was associated with significantly more GI bleeds than CT alone (HR, 4.13; 95% CI, 2.58 to 6.61) and GI strictures (HR, 1.58; 95% CI, 1.18 to 2.21). However, risk varied by age, with SBRT being associated with similar rates of GI complications to cRT in younger people.	⨁⨁◯◯ LOW	Not downgraded

Notes. [a] *Inconsistency not assessable due to only 1 study*
Abbreviations. CI: confidence interval; cRT: conventional radiation therapy; CT: chemotherapy; GI: gastrointestinal; HR: hazard ratio; IMRT: intensity-modulated radiation therapy; NRS: nonrandomized study; SBRT: stereotactic body radiation therapy.

Overall and Progression-free Survival

In an analysis from the National Cancer Database, people with unresected pancreatic cancer treated with SBRT had significantly better overall survival than people treated with chemotherapy (CT; 13.9 months SBRT vs. 10.2 months CT; $P < .001$), cRT (13.9 months SBRT vs. 11.6 months cRT; $P = .02$), or intensity-modulated radiation therapy (IMRT; 13.9 months SBRT vs. 12.2 months IMRT; $P = .049$).[188] However, there was no difference in overall survival between SBRT with multi-agent CT and multi-agent CT alone (14.8 months SBRT with multi-agent CT vs. 12.9 months multi-agent CT alone; $P = .09$).[188]

In another analysis from the National Cancer Database, people with locally advanced pancreatic cancer treated with SBRT had significantly better overall survival than people treated with cRT at 2 years (20.3% SBRT vs. 16.3% cRT; HR, 0.84; 95% CI, 0.75 to 0.93), with a significantly longer median survival (13.9 months SBRT vs. 11.6 months cRT; $P < .001$).[190] In a subgroup analysis, there was a significant survival benefit with SBRT for people aged 69 and younger, tumor stages

T3 or T4, nodal stage N1, tumor size of 3 cm or less, people with no comorbidities, people who had not undergone surgery and CT use.[190]

Disease Control

No eligible studies reported measures of disease control.

Quality of Life

No eligible studies reported quality of life.

Toxicity

Only 1 of the eligible studies included safety outcomes.[189] In an analysis of SEER and Texas Cancer Registry (linked with Medicare) and the MarketScan Commercial Claims and Encounter database, toxicities were compared by age (patients aged older than 65 and patients aged 18 to 64 years).[189] Overall, SBRT was associated with significantly more GI bleeds than CT alone (HR, 4.13; 95% CI, 2.58 to 6.61) and GI strictures (HR, 1.58; 95% CI, 1.18 to 2.21).[189] When compared with cRT, SBRT was associated with higher rates of biliary stricture (42.9% SBRT vs. 31.8% cRT; *P* = .02) in older people.[189] In younger people, SBRT was associated with similar rates of GI complications to cRT.[189]

Head and Neck Cancer

History

In the 2012 report presented to the HTCC,[6] the overall strength of evidence was assessed as very low for harms for head and neck cancers (specifically, ocular and glomus jugulare), based on 1 systematic review and 7 case series.[172-178,191] No comparative effectiveness or economic studies were identified.[6]

Study Characteristics

We identified 5 eligible comparative studies (1 RCT and 4 NRSs, in 6 publications) of SBRT in head and neck cancer (Table 20).[192-197] We assessed the RCT as being at moderate risk-of-bias because of a lack of reporting around randomization and allocation concealment. We assessed 1 study to be at high risk-of-bias because of the potential for confounding,[195] and the remaining studies were at moderate risk-of-bias because although confounding had been addressed, there remained the possibility of differences between the patient populations.[192,196,197]

Table 20. Summary Study Characteristics of Randomized Controlled Trials and Comparative Studies in Head and Neck Cancer

Citation Setting NCT or Other Trial ID	Duration Risk-of-bias	Patient Characteristics	Description of Intervention	Description of Comparator(s)
Randomized controlled trials				
McBride et al., 2021[194] Single center in the US	RCT Median follow-up of 20 months	Total N = 62 people with metastatic or recurrent head and neck squamous cell carcinoma, comprising	• SBRT in combination with nivolumab ○ 9 Gy in 3 fractions	• Nivolumab

Citation Setting NCT or Other Trial ID	Duration Risk-of-bias	Patient Characteristics	Description of Intervention	Description of Comparator(s)
NCT02684253	Moderate risk-of-bias	32 in SBRT group and 30 in control group	delivered every other day	
Comparative nonrandomized studies				
Al-Mamgani et al., 2013[195] Single center in the Netherlands NR	Retrospective study Median follow-up of 56 month in the SBRT group and 57 months in the BT group High risk-of-bias	Total N = 250 people with for early-stage oropharyngeal cancer, comprising 102 in SBRT group and 148 in BT group	• SBRT boost after RT ○ 3 fractions, 5.5 Gy per fraction within 1 week to primary tumor	• BT boost after RT
Ozyigit et al., 2011[197] Single academic center in Turkey NR	Retrospective study Median follow-up of 24 months Moderate risk-of-bias	Total N = 51 people with locally recurrent nasopharyngeal carcinoma, comprising 24 in SBRT group and 27 in conformal RT group	• SBRT ○ 30 Gy delivered over 5 consecutive days	• Conformal RT
Vargo et al., 2018[196] 8 academic centers in the US NR	Retrospective study Median follow-up of 24 months in the SBRT group and 28 months in the IMRT group Moderate risk-of-bias	Total N = 414 people with unresectable recurrent or second primary head and neck cancer, comprising 197 in SBRT group and 217 in IMRT group	• SBRT ○ Median 40 Gy (range, 16 to 50) in median of 5 fractions (range, 1 to 8)	• IMRT ○ Median 60 Gy (range, 40 to 72) in median of 33 fractions (range, 12 to 60)
Yamazaki et al., 2017[192,193] 3 centers, including an academic center, in Japan NR	Retrospective study Median follow-up of 8 months Moderate risk-of-bias	Total N = 176 people with recurrent head and neck cancers, comprising 117 in SBRT group, 33 in IMRT group and 26 in charged particle RT group	• SBRT ○ Median 32 Gy (range, 25 to 39) in median of 5 fractions (range, 3 to 8)	• IMRT ○ Median 60 Gy (range, 30 to 69) in median of 20 fractions (range, 5 to 30) • Charged particle RT ○ Median 57.6 Gy (range, 43.2 to 70.2) in median of 16 fractions

Citation Setting NCT or Other Trial ID	Duration Risk-of-bias	Patient Characteristics	Description of Intervention	Description of Comparator(s)
				(range, 12 to 30)

Abbreviations. BT: brachytherapy; Gy: Gray; IMRT: intensity-modulated radiation therapy; NCT: US National Clinical Trial; RCT: randomized controlled trial; RT: radiation therapy; SBRT: stereotactic body radiation therapy

GRADE Summary of Findings

Table 21. GRADE Summary of Evidence: Effectiveness of SBRT for Head and Neck Cancer

Number of Participants (N) Number of Studies	Findings	Certainty of Evidence	Rationale
SBRT vs. brachytherapy in early-stage oropharyngeal cancer			
Overall survival			
N = 250 1 comparative NRS[195]	SBRT boost or brachytherapy boost after cRT were associated with a similar overall survival at 3 years (81% SBRT vs. 83% BT; *P* = .83).	⊕⊕◯◯ LOW	Not downgraded[a]
Progression-free survival			
N = 250 1 comparative NRS[195]	SBRT boost or brachytherapy boost after cRT were associated with a similar disease-free survival at 3 years (92% SBRT vs. 86% BT; *P* = .15).	⊕⊕◯◯ LOW	Not downgraded[a]
Disease-control			
N = 250 1 comparative NRS[195]	SBRT boost or brachytherapy boost after cRT were associated with a similar local control rate at 3 years (97% SBRT vs. 94% BT; *P* = .33).	⊕⊕◯◯ LOW	Not downgraded[a]
Quality of life			
N = 250 1 comparative NRS[195]	No significant difference in quality of life in patients with early-stage oropharyngeal cancer boosted with SBRT or brachytherapy after cRT.	⊕⊕◯◯ LOW	Downgraded 1 level for imprecision (i.e., not assessable)
SBRT vs. other treatment options for recurrent or metastatic head and neck cancer			
Overall survival			
N = 62 1 RCT[194]	No difference between nivolumab in combination with SBRT or nivolumab alone (at 12 months, 54.4% SBRT vs. 50.2% control; *P* = .75)	⊕⊕⊕◯ MODERATE	Downgraded 1 level for imprecision (i.e., not assessable)[a]
N = 641 3 comparative NRSs[192,196,197]	SBRT appears to be associated with a significantly worse overall survival than charged particle RT, (HR, 0.35; 95% CI, 0.13 to 0.94), but a similar cancer-	⊕⊕◯◯ LOW	Not downgraded

Number of Participants (N) Number of Studies	Findings	Certainty of Evidence	Rationale
	specific survival to IMRT (HR, 0.88; 95% CI, 0.70 to 1.10) and conformal RT (at 2 years, 64% SBRT vs. 47% conformal RT; *P* = .40).		
Progression-free survival			
N = 62 1 RCT[194]	No difference between nivolumab in combination with SBRT or nivolumab alone (at 12 months, 16.8% SBRT vs. 32.2% control; *P* = .79)	⨁⨁⨁◯ MODERATE	Downgraded 1 level for imprecision (i.e., not assessable)[a]
Disease-control			
N = 62 1 RCT[194]	No difference between nivolumab in combination with SBRT or nivolumab alone (at 12 months, OR, 0.80; 95% CI, 0.24 to 2.61)	⨁⨁◯◯ LOW	Downgraded 2 levels for imprecision (i.e., very wide CIs)[a]
N = 641 3 comparative NRSs[192,196,197]	SBRT appears to be associated with similar levels of disease control to IMRT (HR, 1.15; 95% CI, 0.89 to 1.50), conformal RT (at 2 years, 82% SBRT; 80% conformal RT; *P* = .57), and charged particle RT (at 1 year, 67% SBRT vs. 67% charged particle RT; *P* value not reported)	⨁⨁◯◯ LOW	Not downgraded
Quality of life			
Not reported			
SBRT vs. other options for early and recurrent head and neck cancers			
Toxicity			
N = 62 1 RCT[194]	No difference between nivolumab in combination with SBRT or nivolumab alone (grade 3, and higher 9.7% SBRT vs. 13.3% control; *P* = .70)	⨁⨁⨁◯ MODERATE	Downgraded 1 level for imprecision (i.e., not assessable)[a]
N = 891 4 comparative NRSs[192,195-197]	SBRT had a favorable toxicity profile, with similar or fewer toxicities than other treatment options (brachytherapy, conformal RT, IMRT, charged particle RT); however, grade 5 events were relatively high, with 1 study reporting 12.5% grade 5 events in the SBRT group	⨁⨁◯◯ LOW	Not downgraded

Notes. [a] *Inconsistency not assessable due to only 1 study*
Abbreviations. CI: confidence interval; cRT: conventional radiation therapy; IMRT: intensity-modulated radiation therapy; NRS: nonrandomized study; OR: odds ratio; RCT: randomized controlled trial; RT: radiation therapy; SBRT: stereotactic body radiation therapy.

Overall and Progression-free Survival

In a single center study from the Netherlands, patients with early-stage oropharyngeal cancer boosted with SBRT or brachytherapy after cRT had similar overall survival at 3 years (81% SBRT vs. 83% BT; *P* = .83) and disease-free survival at 3 years (92% SBRT vs. 86% BT; *P* = .15).[195]

In the RCT, people with metastatic or recurrent head and neck squamous cell carcinoma treated nivolumab in combination with SBRT or nivolumab alone had a similar overall survival (at 12 months, 54.4% SBRT vs. 50.2% control; median survival, 13.9 months SBRT vs. 14.2 months control; *P* = .75).[194]Incidence of PFS was also similar between groups (at 12 months, 16.8% SBRT vs. 32.2% control; median survival, 2.6 months SBRT vs. 1.9 months control; *P* = .79).[194]

Across the 3 comparative studies, SBRT appears to be associated with a significantly worse overall survival than charged particle RT, but a similar cancer-specific survival to IMRT and conformal RT.

- In a single center study from Turkey, patients with locally recurrent nasopharyngeal carcinoma reirradiated with SBRT or conformal RT (with or without brachytherapy) had a similar cancer-specific survival at 2 years (64% SBRT vs. 47% conformal RT; *P* = .40).[197]
- In a multicenter study from the US, people with unresectable recurrent or second primary head and neck cancer had a significantly worse overall survival when treated with SBRT compared with those treated with IMRT (at 2 years: 16.3% SBRT vs. 35.4% IMRT; *P* < .001), with a median survival of 7.8 months compared with 13.3 months.[196] However, this difference did not remain significant on multivariate analysis (HR, 0.88; 95% CI, 0.70 to 1.10).[196] In patients with unresectable tumors with an intertreatment interval greater than 2 years or those with 2 years or less and without feeding tube or tracheostomy dependence had significantly improved survival with IMRT when compared with SBRT (18.6% SBRT; 39.1% IMRT; *P* < .001).[196]
- In a multicenter study from Japan, people with recurrent head and neck cancers reirradiated with photon RT (majority treated with SBRT) had similar overall survival to people treated with charged particle RT (at 1 year, 54% SBRT vs. 68% charged particle RT; HR, .49; 95% CI, 0.86 to 2.57).[192] However, in a matched analysis, charged particle RT was associated with significantly improved survival when compared with photon RT (HR, 0.35; 95% CI, 0.13 to 0.94).[192]

Disease Control

In a single center study from the Netherlands, patients with early-stage oropharyngeal cancer boosted with SBRT or brachytherapy after cRT had similar local control at 3 years (97% SBRT vs. 94% BT; *P* = .33), regardless of tumor T stage.[195]

In the RCT, people with metastatic or recurrent head and neck squamous cell carcinoma treated nivolumab in combination with SBRT or nivolumab alone had similar objective response rates (at 12 months, 29.0% SBRT vs. 34.5% control; OR, 0.80; 95% CI, 0.24 to 2.61).[194]

Across the 3 comparative studies, SBRT appears to be associated with similar levels of disease control to IMRT, conformal RT, and charged particle RT.

- In a single center study from Turkey, patients with locally recurrent nasopharyngeal carcinoma reirradiated with SBRT or conformal RT (with or without brachytherapy) had a similar rate of local control at 2 years (82% SBRT; 80% conformal RT; *P* = .57).[197]
- In a multicenter study from the US, people with unresectable recurrent or second primary head and neck cancer had a significantly higher locoregional failure when treated with SBRT compared with those treated with IMRT (cumulative incidence: 57.0% SBRT vs. 45.4% IMRT; *P* = .01); this difference did not remain significant on multivariate analysis (HR, 1.15; 95% CI, 0.89 to 1.50).[196] Patients with unresectable tumors with an intertreatment interval greater than 2 years or those with 2 years or less and without feeding tube or tracheostomy dependence had significantly lower locoregional failure with IMRT when compared with SBRT (*P* = .006).[196]
- In a multicenter study from Japan, people with recurrent head and neck cancers reirradiated with photon RT (majority treated with SBRT) had similar rates of local control at 1 year to people treated with charged particle RT (at 1 year, 67% SBRT vs. 67% charged particle RT; *P* value not reported; CIs overlap).[192]

Quality of Life

There was no significant difference in quality of life in patients with early-stage oropharyngeal cancer boosted with SBRT or brachytherapy after cRT at any measured time point.[195]

Toxicity

In the RCT, people with metastatic or recurrent head and neck squamous cell carcinoma treated nivolumab in combination with SBRT or nivolumab alone experienced similar levels of toxicity (grade 3, and higher 9.7% SBRT vs. 13.3% control; *P* = .70).[194]

Across the 4 comparative studies, SBRT had a favorable toxicity profile, with similar or fewer toxicities than other treatment options (brachytherapy, conformal RT, IMRT, charged particle RT); however, grade 5 events were relatively high, with 1 study reporting 12.5% grade 5 events in the SBRT group.

- Acute and late grade 3 toxicities were similar in the SBRT- and brachytherapy-boosted groups.[195] No grade 4 or higher toxicities were observed.[195]
- SBRT was associated with fewer late grade 3 or higher toxicities than conformal RT (21% SBRT vs. 48% conformal RT; *P* = .04), and these included cranial neuropathy, carotid blow-out syndrome, and brain necrosis in the SBRT group; brain necrosis, trismus, cranial neuropathy, and carotid blow-out syndrome in the conformal RT group.[197] Overall, fatal complications were similar between groups (12.5% SBRT vs. 14.8% conformal RT; *P* = .80).[197]
- Acute grade 3 or higher toxicities were similar for SBRT and IMRT (11.7% SBRT vs. 16.6% IMRT; *P* = 15) but grade 4 and higher toxicities were significantly higher in the IMRT group (0.5% SBRT vs. 5.1% IMRT; *P* < .01).[196] Grade 4 toxicities included fistula development, intensive care unit admission, or life-threatening bleeding.[196] Acute grade 5 deaths (specifically bleeding) were similar between groups (0.5% SBRT vs. 1.8% IMRT; *P* = .42), as were late grade 3 or higher toxicities (11.6% SBRT vs. 12.4% IMRT: *P* = .69).[196]
- Charged particle RT was associated with higher rates of grade 3 or higher toxicities (21% SBRT vs. 23% IMRT vs. 46% charged particle RT; *P* = .04; HR univariate, 2.71; 95% CI, 1.15

to 6.39); however, this difference did not remain on multivariate analysis (HR, 1.2; 95% CI, 0.42 to 3.41).[192] Overall, there were 13 (9%: 10 bleeding, 1 ulceration, 1 mucositis, 1 trismus and abscess) grade 5 toxicities in the photon RT group, whereas 4 (15%: 2 bleeding, 1 skin/bone necrosis and infection, 1 soft tissue necrosis and infection) in the charged particle RT group

Ovarian Cancer

History

No eligible studies on the use of SBRT in ovarian cancer were included in the 2012 report.[6]

Study Characteristics

We did not identify any eligible studies for the use of SBRT in breast cancer in this updated evidence review.

Liver Cancer

History

In the 2012 report presented to the HTCC,[6] the evidence for effectiveness and harms of SBRT for hepatocellular carcinoma was assessed as being of very low certainty, with any conclusions about benefit and harms being uncertain. The report included 2 poor-methodological-quality systematic reviews of case series[185,198] and 7 case series for hepatocellular carcinoma.[199-205]

Study Characteristics

We did not identify any RCTs evaluating the use of SBRT for liver cancer. We identified 20 comparative studies, reported in 21 publications, on the use of SBRT for liver cancer (Table 22).[206-226] The populations varied across studies, with 8 evaluating the use of SBRT in unresectable hepatocellular carcinoma (HCC),[209,211,213,215-217,222,224] 4 in early-stage HCC,[207,218,219,223] 4 in small HCCs,[208,210,212,214] 2 as bridge therapy to liver transplantation for HCC,[220,225] 1 in advanced HCC,[206] and 1 in unresectable intrahepatic cholangiocarcinoma.[221] We assessed 4 of the studies to be at low risk-of-bias as these were complex analytic studies using data from large, national databases,[217-219,221] 5 at high risk-of-bias because of the potential for confounding,[208,209,211,220,225] and the remaining studies were at moderate risk-of-bias because although confounding had been addressed, there remained the possibility of differences between the patient populations.[206,207,210,212-216,222-224]

Table 22. Summary Study Characteristics of Comparative Studies in Liver Cancer

Citation Setting NCT or Other Trial ID	Duration Risk-of-bias	Patient Characteristics	Description of Intervention	Description of Comparator(s)
Comparative nonrandomized studies				
Bettinger et al., 2019[206] 15 centers, including academic centers across Germany, the UK, Italy, Switzerland, Japan and South Korea NR	Retrospective analysis (propensity-matched) Median follow-up NR Moderate risk-of-bias	Total N = 1,023 participants with advanced HCC, comprising 122 in SBRT group and 901 in sorafenib group	• SBRT ○ Median total dose of 44 Gy (range, 21 to 66) in 3 to 12 fractions	• Sorafenib ○ 800 mg per day
Hara et al., 2019[207] Two centers (1 academic) in Japan NR	Retrospective study (propensity-matched) Median follow-up of 30 months in the SBRT group and 34 months in the RFA group Moderate risk-of-bias	Total N = 374 participants with early-stage HCC, with 143 in SBRT group and 231 in RFA group	• SBRT ○ Total dose of 40 GY and 35 Gy in 5 fractions ○ Also a minority treated with 36 to 45 Gy in 12 to 15 fractions	• RFA ○ Performed percutaneously under ultrasound guidance ○ 1 to 3 insertions performed to achieve complete ablation, requiring a 5 mm ablative safety margin for each tumor
Honda et al., 2013[208] Single academic center in Japan NR	Retrospective study Median follow-up of 12 months for SBRT and 30 months for TACE High risk-of-bias	Total N = 68 participants with small (3 cm or smaller), solitary, and hypervascular HCC, comprising 30 in TACE-SBRT group and 38 in TACE group	• TACE-SBRT ○ Total dose of 48 or 60 Gy delivered in 4 or 8 fractions in 4 to 10 days	• TACE ○ All treatment naïve
Jacob et al., 2015[209] Single academic center in the US NR	Retrospective study Median follow-up not reported High risk-of-bias	Total N = 161 participants with nonresectable HCC tumors of 3 cm or greater, comprising 37 in TACE-SBRT group and 124 in TACE group	• TACE-SBRT ○ 36 to 60 Gy in 3 fractions	• TACE

Citation Setting NCT or Other Trial ID	Duration Risk-of-bias	Patient Characteristics	Description of Intervention	Description of Comparator(s)
Jeong et al., 2021[210,226] Single center in South Korea NR	Retrospective study (also retrospective noncomparative cohort from the same institution reporting on harms) Median follow-up of 50 months Moderate risk-of-bias	Total N = 266 participants with small (3 cm or smaller) HCC, comprising 87 in SBRT group and 179 in RFA group	• SBRT ○ Median total dose was 45 Gy (range 30 to 60) ○ Median dose of 15 Gy (range, 10 to 15) per fraction given over 3 to 4 consecutive days	• RFA ○ Performed percutaneously under ultrasonographic guidance ○ Radiofrequency current was emitted for 10 to 15 min using a 200W generator set
Ji et al., 2022[211] Single academic center in Hong Kong NR	Retrospective study Median follow-up of 26 months High risk-of-bias	Total N = 60 participants with unresectable HCC, comprising 22 in SBRT group and 38 in RFA group	• SBRT ○ 5.5 to 10 Gy per day for 5 doses in 1 week, to a total of 27.5 to 50 Gy	• RFA ○ RFA through percutaneous approach under ultrasound or CT guidance ○ Each cycle lasted for 8 to 12 minutes
Jun et al, 2018[212] 4 centers in South Korea, including 3 academic centers NR	Retrospective study Median follow-up NR Moderate risk-of-bias	Total N = 199 participants with HCC smaller than 5 cm, comprising 85 in SBRT-TACE group and 114 in TACE group	• SBRT ○ Total dose of 40 to 60 Gy (median, 55 Gy) administered in 3 to 5 fractions over consecutive days or twice a week ○ In combination with TACE	• TACE alone
Kim et al., 2020[213] 7 centers in Korea, Taiwan, China, and Hong Kong NR	Retrospective (propensity-matched) study Median follow-up of 28 months	Total N = 2,064 participants with unresectable HCC, comprising 496 in SBRT group and 1,568 in RFA group	• SBRT ○ Median dose of 72.0 Gy (IQR 65.6 to 88.0) in 2.0 Gy fractions	• RFA ○ Performed percutaneously under ultrasound guidance ○ Complete ablation with a 0.5 to 1.0 cm margin

Citation Setting NCT or Other Trial ID	Duration Risk-of-bias	Patient Characteristics	Description of Intervention	Description of Comparator(s)
	Moderate risk-of-bias			
Kimura et al., 2018[214] 2 centers in Japan (1 academic center) NR	Retrospective study Median follow-up of 16 month in the SBRT group and 29 months in the combination group Moderate risk-of-bias	Total N = 150 participants with small (up to 5 cm) HCC who were ineligible for resection or ablation therapies, comprising 28 in SBRT group and 122 in combination group	• SBRT ○ 48 Gy in 4 fractions at the isocenter and 40 Gy in 4 or 5 fractions at the dose covering 95% of the planning target volume	• SBRT in combination with TACE
Nabavizadeh et al., 2021[215] Single academic center in the US NR	Retrospective, propensity-matched analysis Median follow-up of 48 months Moderate risk-of-bias	Total N = 190 participants with a single inoperable HCC, comprising 90 in TACE-SBRT group and 100 in TACA-TA group	• TACE-SBRT ○ 5 fractions	• TACE-TA ○ Performed using CT and ultrasound guidance
Nieuwenhuizen et al., 2021[216] AmCORE (2007 to 2020) NR	Prospective registry analysis Median follow-up of 29 months Moderate risk-of-bias	Total N = 199 participants with unresectable liver metastases, comprising 55 in SBRT group and 144 in TA group	• SBRT ○ 60 Gy in 3, 5, 8 or 12 fractions	• TA ○ RFA or microwave ablation
Oladeru et al., 2016[217] Surveillance, Epidemiology, and End Results Program (SEER)-Medicare (2004 to 2011) NR	Retrospective database analysis Median follow-up NR Low risk-of-bias	Total N = 189 participants with unresectable HCC, comprising 112 in SBRT group and 77 in SIRT group	• SBRT ○ No details	• SIRT

Citation Setting NCT or Other Trial ID	Duration Risk-of-bias	Patient Characteristics	Description of Intervention	Description of Comparator(s)
Parikh et al., 2018[218] Surveillance, Epidemiology, and End Results Program (SEER)-Medicare (2004 to 2011) NR	Retrospective database analysis (propensity-matched) Median follow-up of 16 months in the SBRT group and 25 months in the RFA group Low risk-of-bias	Total N = 440 participants with early-stage HCC, comprising 32 in SBRT group and 408 in RFA group	• SBRT ○ No details	• RFA
Rajyaguru et al., 2018[219] National Cancer Database (2004 to 2013) NR	Retrospective database analysis Median follow-up of 25 months Low risk-of-bias	Total N = 3,980 participants with nonsurgically managed stage I or II HCC, comprising 296 in SBRT group and 3,684 in RFA group	• SBRT ○ Dose range from < 30 Gy in 1 to 2 fractions to 50 or more Gy (no. of fractions NR)	• RFA
Sapisochin et al., 2017[220] Single center in Canada NR	Retrospective (assumed) study Median follow-up of 47 months High risk-of-bias	Total N = 594 participants with HCC treated as a bridge to transplant, comprising 36 in SBRT group, 99 in TACE group, and 244 in RFA group	• SBRT ○ Median prescribed dose was 36 Gy in 6 fractions (IQR, 30 to 40 in 6 fractions)	• TACE • RFA
Sebastian et al., 2019[221] National Cancer Database (2004 to 2014) NR	Retrospective database analysis Median follow-up of 17 months Low risk-of-bias	Total N = 141 participants with unresectable intrahepatic cholangiocarcinoma, comprising 27 in SBRT group, 60 in TARE group and 54 in cRT group	• SBRT ○ 30 Gy or higher delivered in 5 or fewer fractions ○ Median dose and number of fractions was 45 Gy (IQR, 40 to 50 Gy) and 5 fractions (IQR, 3 to 5)	• TARE • cRT ○ Median dose and number of fractions was 50.4 Gy (IQR, 45 to 54 Gy) and 28 fractions (IQR 25 to 30)

Citation Setting NCT or Other Trial ID	Duration Risk-of-bias	Patient Characteristics	Description of Intervention	Description of Comparator(s)
Wahl et al., 2016[222] Single academic center in the US NR	Retrospective study Median follow-up of 13 months for SBRT and 20 months for RFA Moderate risk-of-bias	Total N = 224 participants with inoperable, nonmetastatic HCC, comprising 63 in SBRT group and 161 in RFA group	• SBRT ○ 3 or 5 fractions delivered 2 to 3 times per week with median doses of 30 or 50 Gy, with a range of 27 to 60 Gy	• RFA ○ Majority percutaneous (97%)
Wang et al., 2021[223] Single academic center in Japan NR	Retrospective study (propensity-matched) Median follow-up of 36 months Moderate risk-of-bias	Total N = 98 participants with Barcelona Clinical Liver Cancer stages 0 to B1, comprising 26 in SBRT group and 72 in RFA group	• SBRT ○ Total dose of 35 Gy delivered in 5 fractions over 5 to 7 days	• RFA
Wong et al., 2019[224] 2 centers (1 academic) in Hong Kong NR	Retrospective study (propensity-matched) Median follow-up of 13 months Moderate risk-of-bias	Total N = 251 participants with nonresectable HCC, comprising 49 in TACE + SBRT and 202 in TACE group	• SBRT ○ Total dose ranged from 5 to 8.5 Gy for 6 fractions to 4 Gy for 6 to 10 fractions	• TACE
Wong et al., 2021[225] Single academic center in Hong Kong NCT03950102	Prospective study using retrospective comparison groups Minimum follow-up of 12 months High risk-of-bias	Total N = 150 participants who received bridge treatment to liver transplantation for HCC, comprising 40 in SBRT group, 59 in TACE group, and 51 in HIFU group	• SBRT ○ Median dose of 50 Gy in 5 fractions	• TACE ○ Median number per patient was 3 (range, 1 to 9) • RFA

Abbreviations. Gy: Gray; HCC: hepatocellular carcinoma; HIFU; high-intensity focused ultrasound; NCT: US National Clinical Trial; NR: not reported; RFA: radiofrequency ablation; SBRT: stereotactic body radiation therapy; TACE: transarterial chemoembolization.

In addition, we identified a further 11 noncomparative studies, reported in 13 publications, describing the toxicities and adverse events associated with the use of SBRT for liver cancer (Table 23).[227-239] We assessed each of the noncomparative studies at being at high risk-of-bias because of the lack of a comparator.

Table 23. Summary Study Characteristics of Noncomparative Studies in Liver Cancer

Citation Setting NCT or Other Trial ID	Study Design and Duration Risk-of-bias	Patient Characteristics	Description of Intervention
Andratschke et al., 2018[236] 17 centers in Germany and Switzerland NR	Retrospective study Median follow-up of 15 months High risk-of-bias	Total N = 474 people with liver oligometastases	• SBRT ○ Median 18.5 Gy (range, 3 to 37.5 Gy) in median 1 fraction (range, 1 to 13)
Berber et al., 2013[237] 4 academic centers in the US NR	Retrospective (assumed) study Median follow-up of 25 months High risk-of-bias	Total N = 153 people with metastatic liver lesions	• SBRT ○ 27 to 46.5 Gy in around 3 to 10 fractions
Bujold et al., 2013[230,231,239] Single academic center in Canada NCT00914355 and NCT00152906	Prospective study Median follow-up of 31 months High risk-of-bias	Total N = 102 people with locally advanced HCC	• SBRT ○ Median dose of 36 Gy in 6 fractions
Kibe et al., 2022[227] Single center in Japan NR	Retrospective study Median follow-up of 39 months High risk-of-bias	Total N = 180 people with locally untreated HCC tumors	• SBRT ○ 35 Gy in 5 fractions or 40 Gy in 5 fractions
Lock et al., 2022[234] Single academic center in Canada NR	Prospective study Followed up to 2 years High risk-of-bias	Total N = 397 people with liver tumors	• SBRT ○ Median dose of 42 Gy
Loi et al., 2021[228] Single center in Italy NR	Retrospective study Median follow-up of 19 months High risk-of-bias	Total N = 128 people with HCC	• SBRT ○ 3 to 30 fractions
Mahadevan et al., 2018[233] RSSearch registry, including 25 sites and	Retrospective registry analysis	Total N = 427 people with liver metastases	• SBRT ○ Median dose of 45 Gy (range, 12 to 60) in a

Citation Setting NCT or Other Trial ID	Study Design and Duration Risk-of-bias	Patient Characteristics	Description of Intervention
academic centers in the US, Germany, and Australia (2005 to 2017) NCT01885299	Median follow-up of 14 months High risk-of-bias		median of 3 fractions (range, 1 to 5)
Méndez Romero et al., 2021[238] 13 centers, including academic centers, in the Netherlands and Belgium NR	Mixed (some data entered retrospectively) study Median follow-up of 2.3 years High risk-of-bias	Total N = 515 people with liver metastases	• SBRT ○ 18 to 20 Gy in 3 fractions ○ 11 to 12 Gy in 5 fractions ○ 7.5 Gy in 8 fractions ○ 5 Gy in 12 fractions
Munoz-Schuffenegger et al., 2021[235] Single center in Canada NR	Retrospective study Median follow-up of 11 months High risk-of-bias	Total N = 128 people with HCC with macrovascular invasion	• SBRT ○ Median dose of 33 Gy (range, 27 to 54) in a median of 5 fractions (range, 5 to 6)
Stintzing et al., 2019[232] Single center in Germany NR	Prospective study Median follow-up of 30 months High risk-of-bias	Total N = 126 people with oligo-metastatic disease limited to liver	• SBRT ○ 20 to 45 Gy in 1 to 3 fractions
Voglhuber et al., 2021[229] Single academic center in Germany NR	Retrospective study Median follow-up of 11 months High risk-of-bias	Total N = 115 people with liver metastases	• SBRT ○ Median cumulative dose of 35 Gy (range, 12 to 60 Gy) with a median single dose of 7 Gy (range, 2.5 to 20 Gy) in 5 (range, 2 to 16)

Abbreviations. Gy: Gray; HCC: hepatocellular carcinoma; NCT: US National Clinical Trial; NR: not reported; SBRT: stereotactic body radiation therapy.

GRADE Summary of Findings

Table 24. GRADE Summary of Evidence: Effectiveness of SBRT for Liver Cancer

Number of Participants (N) Number of Studies	Findings	Certainty of Evidence	Rationale
SBRT vs. RFA for early-stage HCC			
Overall survival			
N = 4,892 4 comparative NRSs[207,218,219,223]	In people with early-stage HCC, results were mixed.	⨁◯◯◯ VERY LOW	Downgraded 1 level for inconsistency

Number of Participants (N) Number of Studies	Findings	Certainty of Evidence	Rationale
	SBRT may be associated with similar overall survival to RFA (at 5 years, 78.4% vs. 46.3%; *P* = .09 over the 5 years); however, 1 study showed that SBRT may be associated with worse survival than RFA at 5 years (HR, 0.67; 95% CI, 0.55 to 0.81).		(i.e., mixed results)
Progression-free survival			
N = 98 1 comparative NRS[223]	In people with early-stage HCC, SBRT after RFA may be associated with similar PFS to repeated RFA (at 2 years, 31.4% vs. 28.6%; *P* = .31).	⨁◯◯◯ VERY LOW	Downgraded 1 level for imprecision (i.e., not assessable)[a]
Disease-control			
N = 472 2 comparative NRSs[207,223]	In people with early-stage HCC, SBRT may be associated with similar rates of intrahepatic recurrence (at 3 years, 59.3% RT vs. 57.6% RFA; *P* = .64) and local recurrence (0 SBRT vs. 25.7% RFA; *P* = .06).	⨁⨁◯◯ LOW	Not downgraded
Quality of life			
Not reported			
SBRT vs. TACE and RFA in small HCCs			
Overall survival			
N = 683 4 comparative NRSs[208,210,212,214]	In people with small HCCs, SBRT, alone or in combination with TACE is associated with a similar overall survival to TACE alone, TACE in combination with TACE, or to RFA. Studies reported at different times using different statistics, precluding any summary statistics (see detailed findings below).	⨁◯◯◯ VERY LOW	Downgraded 1 level for imprecision (i.e., wide CIs)
Progression-free survival			
N = 615 3 comparative NRSs[210,212,214]	In people with small HCCs, SBRT is associated with a similar PFS to RFA. SBRT in combination with TACE is associated with similar or improved PFS to TACE alone or SBRT alone. Studies reported at different times using different statistics, precluding any summary statistics (see detailed findings below).	⨁⨁◯◯ LOW	Not downgraded
Disease-control			
N = 683 4 comparative NRSs[208,210,212,214]	In people with small HCC, SBRT added to TACE appears to be associated with improved local control, but results are mixed. Studies reported at different times using different statistics, precluding any	⨁◯◯◯ VERY LOW	Downgraded 1 level for inconsistency (i.e., mixed results)

Number of Participants (N) Number of Studies	Findings	Certainty of Evidence	Rationale
	summary statistics (see detailed findings below).		
Quality of life			
Not reported			
SBRT vs. other treatments for unresectable HCC			
Overall survival			
N = 3,338 8 comparative NRSs[209,211,213,215-217,222,224]	In people with unresectable HCC, SBRT, alone or in combination with TACE, appears to be associated with similar or improved survival compared with TACE alone, RFA, or SIRT. When compared with TA, SBRT appears to be associated with a lower survival rate. Studies reported at different times using different statistics, precluding any summary statistics (see detailed findings below).	⊕⊕◯◯ LOW	Not downgraded
Progression-free survival			
N = 889 5 comparative NRSs[211,215-217,224]	In people with unresectable HCC, SBRT, alone or in combination with TACE, appears to be associated with similar or improved PFS compared with TACE alone, RFA, or SIRT. When compared with TA, SBRT appears to be associated with a lower PFS. Studies reported at different times using different statistics, precluding any summary statistics (see detailed findings below).	⊕⊕◯◯ LOW	Not downgraded
Disease-control			
N = 3,149 8 comparative NRSs[209,211,213,215,216,222,224]	In people with unresectable HCC, SBRT, alone or in combination with TACE, may have similar or improved rates of disease control and recurrence when compared with RFA or TACE alone. When compared with TA, results are mixed, with 1 study showing no difference and 1 showing a significant decrease in local control with SBRT. Studies reported at different times using different statistics, precluding any summary statistics (see detailed findings below).	⊕⊕◯◯ LOW	Not downgraded
Quality of life			
Not reported			

Number of Participants (N) Number of Studies	Findings	Certainty of Evidence	Rationale
SBRT vs. sorafenib for advanced HCC			
Overall survival			
N = 1,023 1 comparative NRS[206]	In people with advanced HCC, SBRT was associated with improved survival when compared with sorafenib (HR, 0.53; 95% CI, 0.36 to 0.77)	⨁⨁◯◯ LOW	Not downgraded[a]
Progression-free survival			
N = 1,023 1 comparative NRS[206]	In people with advanced HCC, SBRT was associated with improved PFS when compared with sorafenib (HR, 0.59; 95% CI, 0.42 to 0.86)	⨁◯◯◯ VERY LOW	Downgraded 1 level imprecision (i.e., wide CIs)[a]
Disease-control			
Not reported			
Quality of life			
Not reported			
SBRT vs. other treatment as bridging therapy for people on waiting list for liver transplantation due to HCC			
Overall survival			
N = 744 2 comparative NRSs[220,225]	SBRT, as bridge therapy, appears to be associated with a similar overall survival to other options for bridge therapy (TACE, RFA, or HIFU; at around 61% to 73% at 3 years).	⨁⨁◯◯ LOW	Not downgraded
Progression-free survival			
N = 150 1 comparative NRS[225]	SBRT, as bridge therapy, appears to be associated with improved PFS when compared with TACE or HIFU (progression at 3 years, 18.5% SBRT vs. 54.9% TACE vs. 62.8% HIFU; *P* < .001).	⨁◯◯◯ VERY LOW	Downgraded 1 level for imprecision (i.e., not assessable)[a]
Disease-control			
N = 744 2 comparative NRSs[220,225]	SBRT, as bridge therapy, appears to be associated with a better disease control than other options for bridge therapy (TACE or HIFU) but may be associated with worse disease control than RFA. Studies reported at different times using different statistics, precluding any summary statistics (see detailed findings below).	⨁◯◯◯ VERY LOW	Downgraded 1 level for imprecision (i.e., not assessable)[a]
Quality of life			
Not reported			

Number of Participants (N) Number of Studies	Findings	Certainty of Evidence	Rationale
SBRT vs. TARE or cRT for unresectable intrahepatic cholangiocarcinoma			
Overall survival			
N = 141 1 comparative NRS[221]	SBRT was associated with improved survival compared with TARE (HR, 0.40; 95% CI, 0.22 to 0.74) or cRT (HR, 0.37; 95% CI, 0.20 to 0.68)	⨁⨁◯◯ LOW	Not downgraded[a]
Progression-free survival			
Not reported			
Disease-control			
Not reported			
Quality of life			
Not reported			
SBRT vs. other treatments for HCC			
Toxicity			
N = 6,071 16 comparative NRSs[206-216,220,222-225]	Rates of toxicities of grade 3 or higher were relatively infrequent in SBRT, and were similar to those of other RTs or treatment options. SBRT may be associated with some increased toxicities, but it is also associated with some decreased toxicities when compared with other options. Rates of toxicities varied by type of toxicity and time frame.	⨁⨁◯◯ LOW	Not downgraded

Notes. [a] *Inconsistency not assessable due to only 1 study*
Abbreviations. CI: confidence interval; cRT: conventional radiation therapy; HCC: hepatocellular carcinoma; HIFU: high-intensity focused ultrasound; HR: hazard ratio; NRS: nonrandomized study; PFS: progression-free survival; RFA: radiofrequency ablation; SBRT: stereotactic body radiation therapy; TA: thermal ablation; TACE: transarterial chemoembolization.

Overall and Progression-free Survival

Overall, across the 4 comparative studies in people with early-stage HCC, results were mixed. SBRT may be associated with similar overall survival and PFS to RFA; however, some studies showed that SBRT may be associated with worse survival than RFA.

- In a study from 2 centers in Japan, people with early-stage HCC treated with RT (the majority received SBRT) or with radiofrequency ablation (RFA) had similar survival (overall survival, cancer-specific survival, liver-failure survival, and nonspecific survival) at 3 years (overall survival, 70.4% RT vs. 69.1% RFA; $P = .86$).[207]
- Outcomes for patients with early-stage HCC treated with SBRT or RFA were compared using the SEER-Medicare database.[218] Patients treated with SBRT had a similar overall survival to patients treated with RFA (at 1 year, 78.1% SBRT vs. 79.4% RFA; $P \geq .05$); however, over the 3 years, patients in the RFA had significantly better survival (HR, 1.80; 95% CI, 1.15 to

2.82).[218] This difference disappeared in the matched cohort (HR, 1.28; 95% CI, 0.60 to 2.72).[218]

- In an analysis of the NCDB, patients with stage I or II HCC without surgery treated with SBRT had a significantly lower overall survival than patients treated with RFA (at 5 years, 19.3% SBRT vs. 29.8% RFA; HR, 0.67; 95% CI, 0.55 to 0.81).[219] The benefit of RFA was consistent across all subgroups examined and was robust to the effects of severe fibrosis or cirrhosis.[219]
- In a study from a single center in Japan, people with Barcelona Clinical Liver Cancer stage 0 to B1 HCC treated with SBRT after RFA had similar survival to people treated with repeated RFA (at 1 year, 95.2% SBRT vs. 90.5% RFA; at 2 years, 87.3% vs. 73.5%; at 5 years, 74.8% vs. 46.3%; *P* = .09).[223] PFS was also similar (at 1 year, 66.7% SBRT vs. 52.4% RFA; at 2 years, 31.4% vs. 28.6%; *P* = .31), with a median time to progression of 13.9 months in the SBRT group and 8.3 months in the RFA group (*P* = .11).[223]

Across the 4 comparative studies in people with small HCC, overall survival and PFS appeared to be similar for people treated with SBRT when compared with other therapies (transarterial chemoembolization [TACE] and RFA). There also may be some subgroups who would benefit from SBRT in combination with TACE.

- In a study from a single center in Japan, people with small (3 cm and smaller), solitary, and hypervascular HCC were treated with SBRT in combination with TACE or with TACE alone.[208] People treated with SBRT in combination with TACE had improved survival over the 3-year study period; however, the results were not statistically significant (at 1 year, 100% SBRT with TACE vs. 88.9% TACE alone, at 2 years, 100% vs. 73.6%; at 3 years, 100% vs. 66.1%; *P* = .47).[208] The median overall survival was not reached for SBRT in combination with TACE, compared with 40.9 months in the TACE alone group.[208] In people naïve to treatment, SBRT in combination with TACE was associated with a significantly better disease-free survival (at 1 year, 71.4% SBRT with TACE vs. 24.8% TACE alone, at 2 years, 42.0% vs. 14.2%; at 3 years, 0 vs. 7.0%; *P* = .03).[208] The median disease-free survival was 15.2 months in the SBRT in combination with TACE group compared with 4.2 months in the TACE group.[208]
- In a study from a single center in South Korea, people with small HCC (3 cm or smaller) were treated with SBRT or RFA.[210] At 4 years, people treated with SBRT had significantly lower overall survival (64.1% SBRT vs. 78.1% RFA; *P* = .01).[210] However, treatment did not remain a significant prognostic factor in a multivariate analysis (HR, 1.46; 95% CI, 0.85 to 2.52).[210] PFS was also similar between the 2 treatment groups (HR, 0.46; 95% CI, 0.15 to 1.45).[210]
- People with small (5 cm or smaller) HCC were treated with SBRT in combination with TACE or TACE alone across 4 centers in South Korea.[212] The overall survival was similar in both groups over a 5-year period (HR, 0.72; 95% CI, 0.38 to 1.38).[212] However, patients in the SBRT in combination with TACE group had significantly improved PFS compared with TACE alone (at 1 year, 56.5% SBRT with TACE vs. 42.2% TACE; at 3 years, 32.3% vs. 21.6%; HR, 0.67; 95% CI, 0.48 to 0.99).[212] The difference was marginally significant in a multivariate analysis (HR, 0.69; 95% CI, 0.48 to 1.00).[212] In patients with 2 or fewer HCCs, SBRT in combination with TACE was associated with significantly better PFS compared with TACE alone (HR, 0.59; 95% CI, 0.39 to 0.89).[212]

- In a study from 2 centers in Japan, people with small HCC who were ineligible for resection or ablation therapies treated with SBRT in combination with TACE or SBRT alone had similar overall survival (at 1 year, 94.8% SBRT with TACE vs. 100% SBRT; at 2 years, 80.3% vs. 78.6%; *P* = .66).[214] PFS and local PFS was also similar between groups (PFS at 1 year, 61.3% SBRT with TACE vs. 74.4% SBRT; at 2 years, 42.9% vs. 49.0%; *P* = .19).[214]

Across the 8 comparative studies in people with unresectable HCC, SBRT, alone or in combination with TACE, appears to be associated with similar or improved survival compared with TACE alone, RFA, or selective internal radiotherapy (SIRT). When compared with TA, SBRT appears to be associated with a lower survival rate; however, there may be subgroups of people who would have similar outcomes if treated by SBRT or TA for unresectable HCC.

- People with nonresectable HCC tumors of 3 cm or larger were treated with SBRT in combination with TACE or with TACE alone at a single academic center in the US.[209] There was no 30-day mortality in either group, and at 90 days, the mortality was similar between the groups (0 SBRT with TACE vs. 65 TACE; *P* = .35).[209] However, after censoring for liver transplantation, people in the SBRT in combination with TACE group lived significantly longer, with a median survival of 33 months compared with 20 months in the TACE group (*P* = .02).[209]
- In a study from a single center in Hong Kong, patients with unresectable HCC treated with SBRT or RFA had a similar overall survival rate (at 1 year, 88.2% SBRT vs. 100% RFA; at 2 years, 85.7% vs. 75.0%; *P* = .58).[211] PFS was also similar between groups (at 1 year, 50.0% SBRT vs. 44.7% RFA; at 2 years, 13.6% vs. 7.9%; *P* = .81).[211]
- Across 7 centers in Korea, Taiwan, China, and Hong Kong, patients with unresectable HCC were treated with SBRT or RFA.[213] In the unmatched cohort, patients in the SBRT group had significantly better 2-year overall survival than those in the RFA group (25.7% SBRT vs. 18.9% RFA; HR, 1.57; 95% CI, 1.36 to 1.81).[213] However, after matching, there was no significant difference between groups (22.4% SBRT vs. 28.9% RFA; HR, 0.86; 95% CI, 0.70 to 1.06).[213]
- In a single academic center in the US, people with a single inoperable HCC were treated with SBRT in combination with TACE or thermoablation (TA) in combination with TACE.[215] At 2 years, patients in the SBRT in combination with TACE group had significantly worse survival than patients in the TA in combination with TACE group (at 1 year, 74% SBRT with TACE vs. 89% TA with TACE; at 2 years, 49% vs. 77%; subdistribution HR, 2.55; 95% CI, 1.80 to 3.61).[215] PFS was also significantly worse in the SBRT in combination with TACE group compared with the TA in combination with TACE group (at 1 year, 65% SBRT with TACE vs. 85% TA with TACE; at 2 years, 5049% vs. 76%; subdistribution HR, 1.85; 95% CI, 1.25 to 2.76).[215] In the subgroup of patients with Barcelona Clinic Liver Cancer (BLCL) stage A HCC and Child-Pugh score A cirrhosis, there was no difference in overall survival or PFS between groups.[215]
- In an analysis of the AmCORE database, the Amsterdam colorectal liver metastases registry, patients with colorectal liver metastases were treated with SBRT or TA.[216] Over 5 years, patients treated with SBRT had a significantly lower survival rate (at 1 year, 84% SBRT vs. 94% TA; at 2 years, 61% vs. 80%; at 3 years, 37% vs. 65%; at 5 years, 19% vs. 41%; HR, 1.29; 95% CI, 1.12 to 1.49).[216] Similarly, PFS was significantly lower in the SBRT group compared

with TA (HR, 1.58; 95% CI, 1.31 to 1.90).[216] Limiting the analysis to treatment-naïve patients or patients with small tumors did not change the results for overall survival or PFS.[216]
- In an analysis of the SEER-Medicare database, outcomes for people with unresectable HCC were compared by treatment received, SBRT or SIRT.[217] Patients in the SBRT and SIRT groups had similar overall survival (median survival, 14 months SBRT vs. 12 months SIRT; HR, 0.72; 95% CI, 0.49 to 1.07) and PFS (median PFS, 14 months SBRT vs. 14 months SIRT; HR, 0.70; 95% CI, 0.46 to 1.05).[217]
- In a study from a single center in the US, patients with inoperable, nonmetastatic HCC treated with SBRT or RFA had similar overall survival (at 1 year, 74.1% SBRT vs. 69.6% RFA; at 2 years, 43.6% vs. 52.9%; P≥ .05).[222]
- In a study from 2 centers in Hong Kong, patients with unresectable HCC were treated with SBRT in combination with TACE or TACE alone.[224] Patients treated with SBRT after TACE had a significantly better overall survival than patients treated with TACE alone (at 1 year, 67.2% SBRT with TACE vs. 43.9% TACE; at 2 years, 47.1% vs. 24.2%; at 3 years, 47.1% vs, 13.3%; HR, 0.55; 95% CI, 0.37 to 0.82).[224] Median survival was 23.9 months in the SBRT in combination with TACE group and 10.4 months in the TACE group.[224] PFS was also significantly better in the SBRT in combination with TACE group (at 1 year, 32.5% SBRT with TACE vs. 21.4% TACE; at 2 years, 20.1% vs. 12.1%; at 3 years, 15.1% vs. 5.1%; HR, 0.62; 95% CI, 0.42 to 0.90).[224] Median PFS was 7.6 months in the SBRT in combination with TACE group and 5.7 months in the TACE group.[224]

In 1 comparative study in people with advanced HCC, SBRT was associated with improved survival and PFS when compared with sorafenib.[206]
- In a multicenter, international study, people with advanced HCC treated with SBRT (after TACE failure, as an alternative to sorafenib, or after progression under sorafenib) lived significantly longer than people treated with sorafenib (16.0 months SBRT vs. 9.6 months sorafenib; HR, 0.53; 95% CI, 0.36 to 0.77).[206] Survival remained significantly improved with SBRT in people with extrahepatic metastases but not in people with portal vein thrombosis.[206]
- People with advanced HCC treated with SBRT also had significantly longer PFS than those treated with sorafenib (9.0 months SBRT vs. 6.0 months sorafenib; HR, 0.59; 95% CI, 0.42 to 0.86).[206]

Of the 20 comparative studies, 2 reported on the use of SBRT as bridging therapy for people on the waiting list for liver transplantation due to HCC. As a bridge therapy, SBRT appears to be associated with a similar overall survival to other options (TACE, RFA, or high-intensity focused ultrasound [HIFU]) and may be associated with improved PFS.
- In a study from a single center in Canada, patients treated with SBRT as a bridge therapy while waiting for a liver transplant for HCC had a similar overall survival to patients who received TACE or RFA bridge therapy (at 1 year, 83% SBRT vs. 86% TACE vs. 86% RFA; at 3 years, 61% vs. 61% vs. 72%; at 5 years, 61% vs. 56% vs. 61%; *P* = .40).[220] Mortality post-transplant was also similar between groups (*P* = .70).[220]
- In a study from a single center in Hong Kong, patients treated with SBRT as a bridge therapy while waiting for a liver transplant for HCC had a similar overall survival to patients who received TACE or HIFU bridge therapy (at 1 year, 84.9% SBRT vs. 88.1% TACE vs. 80.4% HIFU; at 2 years, 76.4% vs. 72.7% vs. 60.8%; at 3 years, 73.0% vs. 65.6% vs. 54.9%;

P = .29).[225] However, SBRT was associated with significantly better PFS than TACE or HIFU (progression at 1 year, 10.8% SBRT vs. 45.0% TACE vs. 47.6% HIFU; at 2 years, 18.5% vs. 50.6% vs. 62.8%; at 3 years, 18.5% vs. 54.9% vs. 62.8%; *P* < .001).[225] After transplantation, patients in all groups had similar rates of overall survival (*P* = .91) and recurrence-free survival (*P* = .85).[225]

In 1 comparative study in people with unresectable intrahepatic cholangiocarcinoma, SBRT was associated with improved survival compared with transarterial radioembolization (TARE) or cRT.

- In an analysis of the NCDB, the median overall survival for patients with unresectable intrahepatic cholangiocarcinoma was 48 months for people treated with SBRT, 20 months for people treated with TARE, and 14 months for people treated with cRT.[221] Overall, SBRT was associated with significantly better overall survival than TARE (HR, 0.40; 95% CI, 0.22 to 0.74) and cRT (HR, 0.37; 95% CI, 0.20 to 0.68).[221] Similar results were seen in a multivariate analysis and after adjusting for propensity weighting.[221]

Disease Control

Across the 4 comparative studies in people with early-stage HCC, 2 reported some measure of disease control. Overall, SBRT may be associated with similar rates of intrahepatic and local recurrence as RFA.

- In a study from 2 centers in Japan, people with early-stage HCC treated with RT (the majority received SBRT) had significantly lower local recurrence than people treated with RFA at 3 years (5.3% RF vs. 12.9% RFA; *P* < .001).[207] Local recurrence remained significantly lower for HCC attached to vessels and those adjacent to vessels.[207] However, there was no difference between groups for intrahepatic recurrence at 3 years (59.3% RT vs. 57.6% RFA; *P* = .64).[207]
- In a study from a single center in Japan, people with Barcelona Clinical Liver Cancer stage 0 to B1 HCC treated with SBRT after RFA had similar rates of intrahepatic recurrence to repeated RFA (at 1 year, 33.3% SBRT vs. 29.5% RFA; *P* = .97) and although local recurrence was lower in the SBRT group, the difference was not statistically significant (0 SBRT vs. 25.7% RFA; *P* = .06).[223]

Overall, across the 4 comparative studies in people with small HCC, SBRT added to TACE appears to be associated with improved local control, but results are mixed.

- In a study from a single center in Japan, people with small (3 cm and smaller), solitary, and hypervascular HCC were treated with SBRT in combination with TACE or with TACE alone.[208] People treated with SBRT in combination with TACE had significantly better local control (complete response, 96.3% SBRT with TACE vs. 3.3% TACE; *P* < .001).[208]
- In a study from a single center in South Korea, people with small HCC (3 cm or smaller) treated with SBRT or RFA had similar rates of intrahepatic recurrence (27.6% SBRT vs. 36.7% RFA; HR, 0.82; 95% CI, 0.56 to 1.18).[210] Perivascular location was a significant negative prognostic factor for recurrence in people treated with RFA but not in those treated with SBRT.[210]
- People with small (5 cm or smaller) HCC were treated with SBRT in combination with TACE had significantly improved local control when compared with people in the TACE alone group (at 1 year, 91.1% SBRT with TACE vs. 69.9% TACE; at 3 years 89.9% vs. 48.8%; at 5 years, 89.9% vs. 48.8%; *P* < .001).[212]

- In a study from 2 centers in Japan, people with small HCC who were ineligible for resection or ablation therapies treated with SBRT in combination with TACE or SBRT alone had similar rates of local control (at 1 year, 99.2% SBRT with TACE vs. 100% SBRT; at 2 years, 98.5% vs. 95.4%; *P* = .42).[214]

Across the 8 comparative studies in people with unresectable HCC, 7 reported on some measure of disease control. Overall, SBRT, alone or in combination with TACE, may have similar or improved rates of disease control and recurrence when compared with RFA or TACE alone. When compared with TA, the results are mixed, with 1 study showing no difference and 1 showing a significant decrease in local control with SBRT.

- People with nonresectable hepatocellular carcinoma tumors of 3 cm or larger were treated with SBRT in combination with TACE or with TACE alone at a single academic center in the US.[209] People in the SBRT in combination with TACE group had significantly lower rates of local recurrence (10.8% SBRT with TACE vs. 25.8% TACE; *P* = .04).[209]
- In a study from a single center in Hong Kong, patients with unresectable HCC treated with SBRT or RFA had similar rates of complete response (82% SBRT vs. 89% RFA; *P* = .04).[211] At 26 months, there was no significant difference between groups for the local tumor control rate, intrahepatic recurrence, or the median time to recurrence (median time, 16 months SBRT vs. 14 months RFA; *P* = .93).[211] However, people treated with SBRT were significantly more likely to have extrahepatic occurrence (27% SBRT vs. 0 RFA; *P* < .001).[211]
- Across 7 centers in Korea, Taiwan, China, and Hong Kong, patients with unresectable HCC treated with SBRT had significantly lower rates of local recurrence compared with those treated with RFA (19.4% SBRT vs. 23.7% RFA; HR, 0.45; 95% CI, 0.35 to 0.58).[213] Similar results were seen after matching.[213] In subgroup analysis, SBRT was significantly associated with superior local control in small tumors (3 cm or smaller) irrespective of location, large tumors located in the subphrenic region, and tumors that progressed after TACE.[213]
- In a single academic center in the US, people with a single inoperable HCC treated with SBRT in combination with TACE or TA in combination with TACE had similar levels of local control (at 1 year, 99% SBRT with TACE vs. 90% TA with TACE; at 2 years, 94% vs. 87%; *P* = .28).[215]
- In an analysis of the AmCORE database, the Amsterdam colorectal liver metastases registry, patients with colorectal liver metastases were treated with SBRT had significantly worse local control than people treated with TA (HR, 1.60, 95% CI 1.23 to 2.08).[216]
- In a study from a single center in the US, patients with inoperable, nonmetastatic HCC treated with RFA were significantly more likely to have local progression than people treated with SBRT (HR, 2.63; 95% CI, 1.20 to 5.75).[222] When analyzed by tumor size, there was no difference between groups for tumors smaller than 2 cm, but SBRT was significantly better than RFA for larger tumors.[222]
- In a study from 2 centers in Hong Kong, patients with unresectable HCC were treated with SBRT in combination with TACE or TACE alone.[224] Overall, 98% of patients treated with SBRT after TACE achieved radiological control compared with 57% of patients treated with TACE alone (no *P* value reported).[224]

Of the 20 comparative studies, 2 reported on the use of SBRT as a bridging therapy for people on the waiting list for liver transplantation due to HCC. SBRT, as a bridge therapy, appears to be

associated with a better disease control than other options for bridge therapy (TACE or HIFU) but may be associated with worse disease control than RFA).

- In a study from a single center in Canada, patients treated with SBRT as a bridge therapy while waiting for a liver transplant for HCC had a significantly lower recurrence rate than patients who received TACE but a higher rate than patients who received RFA bridge therapy (at 1 year, 7% SBRT vs. 18% TACE vs. 8% RFA; at 3 years, 26% vs. 28% vs. 13%; 26% vs. 35% vs. 14%; $P = .03$).[220]
- In a study from a single center in Hong Kong, patients treated with SBRT as a bridge therapy while waiting for a liver transplant for HCC had significantly improved local control than patients who received TACE or HIFU bridge therapy (at 1 year, 92.3% SBRT vs. 43.5% TACE vs. 33.3% HIFU; $P = .02$).[225] Patients treated with SBRT also had significantly better local control (at 1 year, 53.8% SBRT vs. 17.4% TACE vs. 13.3% HIFU; $P \leq .05$) and objective response (at 1 year, 76.9% SBRT vs. 39.1% TACE vs. 26.7% HIFU; $P = .02$).[225] In the SBRT group, 4 patients were 'delisted' because the HCC was assessed as having been treated.[225]

No eligible studies reported on disease control with SBRT for advanced cancer or unresectable intrahepatic cholangiocarcinoma.

Quality of Life

No eligible studies reported quality of life measures.

Toxicity

Across the 20 comparative studies, the rates of toxicities of grade 3 or higher were relatively infrequent in SBRT, and were similar to those of other RTs or treatment options. While SBRT may be associated with some increased toxicities, it is also associated with some decreased toxicities when compared with other options.

- In a multicenter, international study, people with advanced HCC treated with SBRT or sorafenib experienced low rates of grade 3 toxicities (11% SBRT vs. 30% sorafenib; no formal statistical analysis conducted); the most common being an increase in bilirubin in the SBRT group (6%) and diarrhea in the sorafenib group (11%).[206] Overall, 24 grade 4 toxicities were observed; 2 in the SBRT group (1 liver abscess and 1 hepatic decompensation, leading to radiation-induced liver disease) and 22 in the sorafenib group (2 hand-foot skin reactions, 10 of diarrhea, 5 of fatigue, and 5 of weight loss).[206] Sorafenib was stopped in 175 (19.4%) of patients because of adverse events.[206] In the SBRT group, 1 patient developed a cholangitis probably deemed to be treatment-related. No grade 5 events were reported.[206]
- In a study from 2 centers in Japan, people with early-stage HCC treated with RT (the majority received SBRT) and RFA had the same rate of liver toxicity (8.2% RT vs. 8.2% RFA; $P = .23$).[207] However, when liver-failure death was included, people in the RT group experienced significantly worse outcomes, with 4 deaths within 12 months in the RT group and 1 in the RFA group ($P < .001$).[207]
- In a study from a single center in Japan, around 10% of people with small, solitary, and hypervascular HCC treated with SBRT in combination with TACE experienced a grade 3 toxicity (7% leukocytopenia, 3% thrombocytopenia). In the TACE group, around 13% of people experienced grade 3 toxicities (8% thrombocytopenia. 5% hyperbilirubinemia).[208] No grade 4 toxicities were observed and no patients treated with SBRT developed radiation-induced liver disease.[208]

- In patients with nonresectable hepatocellular carcinoma tumors of 3 cm or larger treated with SBRT in combination with TACE, 1 patient (3%) experienced grade 3 GI toxicity.[209] No other grade 3 or higher toxicities were reported.[209] However, 1 patient died of pulmonary sepsis within 4 weeks of SBRT.[209] Toxicities after TACE were not reported.[209]
- In a study from a single center in South Korea, 1 grade 3 biliary stricture in the SBRT group and 1 grade 4 abdominal hemorrhage in the RFA group were observed (< 1% SBRT vs. 1.1% RFA).[210] Overall, 1 patient died due to hepatic failure of unknown cause at 4 months after SBRT.[210]
- In a study from a single center in Hong Kong, patients with unresectable HCC treated with SBRT or RFA experienced some complications in the first week after treatment (23% SBRT vs. 21%; *P* = .88); and no grade 3 toxicities were observed.[211] During follow-up, patients in both the SBRT and RFA groups died of liver failure and in the RFA group, of hepatorenal syndrome and gastrointestinal bleeding.[211] No further details were reported.[211]
- People with small (5 cm or smaller) HCC treated with SBRT in combination with TACE and TACE alone had similar levels of liver toxicity (Child-Pugh deterioration of 2 or more, 9.4% SBRT with TACE vs. 5.5% TACE; *P* = .12; elevated liver transaminases, 9.4% vs. 4.8%; *P* = .24).[212]
- In patients with unresectable HCC treated with SBRT or RFA, acute grade 3 or higher toxicities occurred in 1.6% of the SBRT group and 2.6% of the RFA group (*P* = .27).[213] However, SBRT was significantly associated with greater liver toxicity (change in Child-Pugh score of more than 2, 11.2% SBRT vs. 4.7% RFA; *P* < .001).[213]
- The rate of grade 3 or higher toxicities in people with small HCC who were ineligible for resection or ablation therapies treated with SBRT in combination with TACE or SBRT alone was similar (18.9.% SBRT with TACE vs. 17.9% SBRT; *P* = .90).[214] After SBRT in combination with TACE, patients experienced grade 3 elevated bilirubin (5%; 2 cases after SBRT and 4 cases after TACE), grade 3 elevated aspartate transaminase and alanine transaminase levels (10%; 1 case after SBRT and 11 cases after TACE), grade 3 decreased platelets (27%; 16 cases after SBRT and 17 after TACE), grade 4 decreased platelets (2%; 2 cases after SBRT), grade 3 decreased albumin (2%; 2 cases after SBRT), grade 3 ascites (2%; 3 after SBRT), grade 3 portal vein thrombosis (1%; 1 after SBRT), and grade 3 other toxicities (2%; 2 after SBRT and 1 after TACE).[214] After SBRT alone, patients experienced grade 3 decreased platelets (11%), grade 4 decreased platelets (4%), grade 3 portal vein thrombosis (4%), and grade 3 other toxicities (4%).[214] No radiation pneumonitis was observed.[214]
- People with a single inoperable HCC treated with SBRT in combination with TACE had significantly greater liver toxicity than people treated with TA in combination with TACE (27% SBRT with TACE vs. 9% TA with TACE; *P* = .01).[215]
- Patients with colorectal liver metastases treated with SBRT had lower rates of grade 3 toxicity than patients treated with TA (0 SBRT vs. 66.3% TA; *P* = .06); however, the results were not statistically significant.[216] In both groups, the 90-day mortality was 0.[216]
- Patients awaiting liver transplantation for HCC who received SBRT bridge therapy had significantly more liver impairment than those who received TACE or RFA bridge therapy (38.9% SBRT vs. 19.5% TACE vs. 13.0% RFA; *P* = .001).[220] Fewer patients in the SBRT group experienced fatigue and nausea compared with TACE but not RFA (fatigue, 5.6% SBRT vs. 23.7% TACE vs. 2.1% RFA; *P* < .001; nausea, 8.3% SBRT vs. 10.8% TACE vs. 1.7% RFA; *P* = .001).[220] Patients who received SBRT bridge therapy had significantly less pain than those

who received TACE or RFA bridge therapy (2.8% SBRT vs. 53.8% TACE vs. 21.5% RFA; $P < .001$).[220] However, there was no differences between groups for other toxicities, and no patient was "delisted" due to treatment toxicity.[220]

- In people with inoperable, nonmetastatic HCC, grade 3 and higher toxicities were similar for SBRT and RFA (5% SBRT vs. 11% RFA; $P = .31$.[222] In the SBRT group, grade 3 and higher toxicities were radiation-induced liver disease (n = 1), GI bleeding (n = 1), and worsening ascites (n = 1); no deaths were observed related to SBRT treatment.[222] In the RFA group, grade 3 and higher toxicities were pneumothorax (n = 1), sepsis (n = 2), duodenal and colonic perforation (n = 2), and bleeding (n = 3) and resulted in 2 deaths within 1 month of treatment.[222] No late grade 5 toxicities were observed in either group.[222] Liver toxicity was similar between the SBRT and RFA groups; however, at 12 months, Child-Pugh scores worsened significantly in the SBRT group compared with RFA (deterioration, 1.2 SBRT vs. 0.3; $P = .005$).[222] In a multivariate model, SBRT was not significantly associated with worsening (OR, 1.02; $P = .97$); nor was SBRT dose associated with worsening Child-Pugh scores.[222]
- Patients with Barcelona Clinical Liver Cancer stage 0 to B1 HCC treated with either SBRT or RFA had similar levels of liver toxicity (Child-Pugh deterioration of 2 or more, 23.8% SBRT vs. 33.3% RFA; $P > .05$).[223] No grade 3 or higher events were observed in either group.[223]
- In people with unresectable HCC, SBRT with TACE and TACE alone had similar levels of liver toxicity (Child-Pugh A, 93.9% SBRT with TACE vs. 86.7% TACE; $P = .17$).[224] No patients developed classic radiation-induced liver disease.[224] Patients treated with SBRT in combination with TACE were more likely to experienced fatigue and hematological abnormality in hemoglobin, platelet, and white cell count; patients treated with TACE were more likely to experience renal and liver impairment and fever.[224] Grade 3 or higher events ranged from 1% (INR in the TACE group, decreased white cell count in the TACE group) to 33% (elevated aspartate aminotransferase in the TACE group); however, grade 3 or higher toxicities were generally low or not observed.[224]
- In people receiving bridge therapy while waiting for a liver transplant for HCC, there was no 30-day mortality in any of the treatment groups (SBRT, TACE, and HIFU) and no difference between groups for readmission with 30 days of treatment (5% SBRT vs. 8% TACE vs. 9% HIFU; $P = .70$).[225] SBRT was associated with more grade 3 decreases in platelets (57% SBRT vs. 41% TACE vs. 27% HIFU; $P < .001$) and more grade 3 decreases in white blood cell count (17% SBRT vs. 4% TACE vs. 5% HIFU; $P = .003$).[225] SBRT was also associated with fewer grade 3 increased in bilirubin (3% SBRT vs. 18% TACE vs. 3% HIFU; $P = .03$).[225]

Across the 11 noncomparative studies reporting harms[227-229,231-238]:

- The most commonly reported toxicities related to liver toxicities, including elevated liver enzymes.
- The proportions of grade 3 toxicities ranged from none to 27%.
- Classic and nonclassic radiation-induced liver disease was rare.
- Most studies did not observe any grade 4 or 5 toxicities; however, 1 study reported that 3% of participants experienced a grade 4 adverse event and 7% a grade 5 adverse event.

Full details on toxicities from each of the noncomparative studies are in Appendix C.

Cervical Cancer

History

No eligible studies on the use of SBRT in cervical cancer were included in the 2012 report.[6]

Study Characteristics

We did not identify any eligible studies for the use of SBRT in cervical cancer in this updated evidence review.

Esophageal Cancer

History

No eligible studies on the use of SBRT in esophageal cancer were included in the 2012 report.[6]

Study Characteristics

We did not identify any eligible studies for the use of SBRT in esophageal cancer in this updated evidence review.

Oligometastatic Cancer

History

The original report included 2 noncomparative studies on the use of SBRT for oligometastatic disease[240,241]; no specific coverage determinations were made for the use of SBRT in people with oligometastatic disease.[7]

Study Characteristics

We identified 3 RCTs, reported in 9 publications, evaluating the use of SBRT for oligometastatic cancers (Table 25). Of the 3 RCTs, 2 included men with oligometastatic prostate cancer (STOMP and ORIOLE)[242,243] and 1 included people with a controlled primary tumor and 1 to 5 oligometastatic lesions (SABR-COMET).[244] We assessed the 3 RCTs as being at moderate risk-of-bias because of a lack of blinding.[242-244]

We also identified a further 3 comparative studies, reported in 3 publications, on the use of SBRT for oligometastatic prostate cancer (Table 25). We assessed 1 study to be at high risk-of-bias because of the potential for confounding,[245] and the remaining 2 studies were at moderate risk-of-bias because although confounding had been addressed, there remained the possibility of differences between the patient populations.[246,247]

Table 25. Summary Study Characteristics of Randomized Controlled Trials and Comparative Studies in Oligometastatic Cancer

Citation Setting NCT or Other Trial ID or Study Name	Duration Risk-of-bias	Patient Characteristics	Intervention	Comparator(s)
Randomized controlled trials				
Ost et al., 2017[242,248] 6 centers, including academic centers, in Belgium NCT01558427 STOMP	Median follow-up of 3 years Moderate risk-of-bias	Total N = 62 men with recurrent oligometastatic prostate cancer, comprising 31 in treatment arm (majority received SBRT; remainder underwent surgery) and 31 in active surveillance arm	• SBRT ○ Total dose of 30 Gy (80%of maximal dose) delivered in 3 fractions ○ 25 (81%) • Metastectomy ○ 6 (19%)	• Surveillance
Palma et al., 2019[244,249-252] 10 hospitals in Canada, the Netherlands, Scotland, and Australia NCT01446744 SABR-COMET	Followed up to 10 years Moderate risk-of-bias	Total N = 99 people with a controlled primary tumor and 1 to 5 oligometastatic lesions, comprising 66 in SBRT group and 33 in control group Primary sites were mostly adrenal, bone, liver, and lung	• SBRT ○ Doses ranged from 30 to 60 Gy in 3 to 8 fractions, depending on target size and location ○ Single fractions of 16 to 24 Gy permitted for targets in brain and vertebrae ○ Concurrent chemotherapy or targeted therapy was not permitted within 4 weeks before SBRT • Standard of care, tailored to individual clinical circumstance	• Standard of care, tailored to individual clinical circumstance • Radiotherapy delivered according to standard principles of palliative radiation, with goal of alleviating symptoms or preventing anticipated complications of progression
Phillips et al., 2020[243,248,253] 3 academic centers in the US NCT02680587 ORIOLE	Followed up to 24 months Moderate risk-of-bias	Total N = 54 men with oligometastatic prostate cancer, comprising 36 in group and 18 in observation group	• SBRT ○ Dose and fractionation based on size and location of each lesion, with prescription doses ranging from 19.5 to 48.0 Gy in 3 to 5 fractions ○ Salvage RT was allowed ○ Patients were allowed to have received ADT or other systemic	• Observation ○ Salvage RT was allowed ○ Patients were allowed to have received ADT or other systemic therapy during initial management or salvage treatment but

Citation Setting NCT or Other Trial ID or Study Name	Duration Risk-of-bias	Patient Characteristics	Intervention	Comparator(s)
			therapy during initial management or salvage treatment but not within 6 months of enrollment	not within 6 months of enrollment
Comparative nonrandomized studies				
Bouman-Wammes et al., 2017[245] Single center in the Netherlands NR	Retrospective study Median follow-up of 2.6 years High risk-of-bias	Total N = 63 men with metachronous oligometastases of hormone-sensitive prostate cancer, comprising 43 in SBRT group and 20 in control group (no SBRT)	• SBRT ○ 3 Gy in 10 fractions (67%) ○ 3 Gy in 15 fractions (9%) ○ 5 Gy in 7 fractions (23%)	• No SBRT
De Bleser et al., 2019[246] 15 centers, including academic centers, across Europe NR	Retrospective study Median follow-up of 36 months Moderate risk-of-bias	Total N = 506 men with nodal oligorecurrent prostate cancer, comprising 309 in SBRT group and 197 in ENRT group	• SBRT ○ High dose of RT (minimum 5Gy per fraction) directed to suspicious node(s) in maximum 10 fractions	• ENRT ○ RT to suspicious and elective nodes with a minimum dose of 45 Gy in 25 fractions
Hurmuz et al., 2020[247] Multiple centers in Turkey TROD-09-002	Retrospective study Median follow-up of 23 months Moderate risk-of-bias	Total N = 176 men with oligometastatic or oligorecurrent prostate cancer, comprising 129 in SBRT group and 47 in cRT group	• SBRT ○ Median total dose of 27 Gy (range, 15 to 40) in median of 3 (range, 1 to 5) fractions	• cRT

Abbreviations. ADT: androgen deprivation therapy; cRT: conventional radiation therapy; ENRT: elective nodal radiation therapy; Gy: Gray; NCT: US National Clinical Trial; NR: not reported; RT: radiation therapy; SBRT: stereotactic body radiation therapy.

In addition, we identified a further 12 noncomparative studies, reported in 13 publications, describing the toxicities and adverse events associated with the use of SBRT for oligometastatic cancer (Table 26).[240,254-265] We assessed each of the noncomparative studies at being at high risk-of-bias because of the lack of a comparator.

Table 26. Summary Study Characteristics of Noncomparative Studies in Oligometastatic Cancer

Citation Setting NCT or Other Trial ID	Study Design and Duration Risk-of-bias	Patient Characteristics	Description of Intervention
Bowden et al., 2020[254] Single center in Australia ACTRN12618000566235 TRANSFORM	Prospective study Median follow-up of 35 months High risk-of-bias	Total N = 199 men with up to 5 prostate cancer oligometastases	• SBRT ○ 50 Gy in 10 daily fractions
Chalkidou et al., 2021[255] 17 centers in England NR	Prospective study Median follow-up of 13 months High risk-of-bias	Total N = 1,422 people with solid cancer and extracranial oligometastases Primary sites were mostly prostate, colorectal, renal, breast, lung, and melanoma	• SBRT ○ Median BED 105 Gy (IQR, 72 to 130) in 3 to 8 fractions
Franzese et al., 2021[256] Multiple centers in Italy NR	Retrospective study Median follow-up of 19 months High risk-of-bias	Total N = 207 people with metastatic kidney cancer (oligorecurrent and oligoprogressive)	• SBRT ○ Median dose of 36 Gy (range, 10 to 75) in median of 5 fractions (range, 1 to 10)
Macchia et al., 2020[257] Multiple centers, including academic centers, in Italy MITO RT1	Retrospective study Median follow-up of 22 months High risk-of-bias	Total N =261 women with oligometastatic ovarian cancer	• SBRT ○ Median total dose 25 Gy (range, 5 to 75) in median of 4 fractions (range, 1 to 13)
Milano et al., 2008[240,265] Single academic center in the US NR	Prospective study Followed-up for up to 10 years High risk-of-bias	Total N = 121 people with 5 or fewer oligometastatic lesions Primary sites were mostly breast, colorectal, head or neck, lung, and esophageal	• SBRT ○ Median of 38 Gy (range, 0.3 to 422) ○ Most treated with 10 fractions of 5 Gy
Nicosia et al., 2020[258] Multiple centers, including academic	Retrospective study Median follow-up of 16 months High risk-of-bias	Total N = 109 men with a maximum of 5 lymph node metastases from prostate cancer	• SBRT ○ Median does of 36 Gy (range, 25 to 48) in median of 7 fractions (range, 5 to 12)

Citation Setting NCT or Other Trial ID	Study Design and Duration Risk-of-bias	Patient Characteristics	Description of Intervention
centers, in Italy and Germany NR			
Olsen et al., 2022[259] 6 centers in Canada NCT02933242 SABR-5	Retrospective (assumed) study Median follow-up of 25 months High risk-of-bias	Total N = 381 people with oligometastatic or oligoprogressive disease (up to 5 lesions) Primary sites were mostly prostate, colorectal, breast, lung, and kidney	• SBRT ○ 48 or 54 Gy in 4 or 3 fractions daily or every other day, peripheral lung ○ 60 Gy in 8 fractions daily, lung ○ 35 or 24 Gy in 5 or 2 fractions daily or every other day, bone ○ 54 Gy in 3 fractions every other day, liver ○ 40 or 60 Gy in 5 or 8 fractions daily, adrenal ○ 40 Gy in 5 fractions daily, lymph node or soft tissue ○ SRS protocol, brain
Ost et al., 2016[260] Multicenter study (sites not clear) NR	Retrospective study Median follow-up of 36 months High risk-of-bias	Total N = 119 men with oligometastatic prostate cancer treatment-naïve recurrence	• SBRT ○ At least 5 Gy per fraction to a BED of at least 80 Gy using an alpha:beta ratio of 3
Poon et al., 2020[261] 6 high-volume academic centers in the US, Canada, Australia, and Italy NR	Retrospective study Median follow-up of 24 months High risk-of-bias	Total N = 1,033 people with 5 or fewer extracranial oligometastases whose primary tumor was treated curatively Primary sites were mostly breast, colorectal, kidney, lung, prostate, melanoma, sarcoma, head and neck, thyroid, pancreas, hepatic or biliary, and gynecological	• SBRT ○ Varied over time and by institution
Sogono et al., 2021[262] Single center in Australia NR	Retrospective study Median follow-up of 3.1 years High risk-of-bias	Total N = 371 people with to 5 sites of oligometastatic disease Primary sites were mostly bone or soft tissue, breast,	• SBRT ○ Median dose of 20 Gy (range, 16 to 28) in a single fraction

Citation Setting NCT or Other Trial ID	Study Design and Duration Risk-of-bias	Patient Characteristics	Description of Intervention
		gastrointestinal, genitourinary (not prostate), prostate, lung, and skin	
Sutera et al., 2019[263] Single academic center in the US NCT01345552	Prospective study Median follow-up of 41.3 months High risk-of-bias	Total N = 147 people with oligometastatic disease (1 to 5 metastases) Primary sites were mostly lung, colorectal, head and neck, breast, prostate, kidney, esophagus, uterus, ovaries, and bladder	• SBRT ○ Median dose of 48 Gy (IQR, 41 to 54) in median of 4 fractions (IQR, 3 to 5)
Triggiani et al., 2017[264] 9 centers, including academic centers, in Italy NR	Retrospective study Median follow-up of 20 months High risk-of-bias	Total N = 100 men with oligometastatic prostate cancer	• SBRT ○ Median of 116 Gy (range, 80 to 217); fractions NR

Abbreviations. BED: biologically equivalent dose; Gy: Gray; IQR: interquartile range; NCT: US National Clinical Trial; NR: not reported; SBRT: stereotactic body radiation therapy; SRS: stereotactic radiosurgery.

GRADE Summary of Findings

Table 27. GRADE Summary of Evidence: Effectiveness of SBRT for Oligometastatic Cancer

Number of Participants (N) Number of Studies	Findings	Certainty of Evidence	Rationale
SBRT vs. standard of care for oligometastatic cancer (primaries mostly adrenal, bone, liver, and lung)			
Overall survival			
N = 99 1 RCT[244]	At 5 years, no difference between groups (HR, 0.57; 95% CI, 0.30 to 1.10) At 6 years, improved survival with SBRT (HR, 0.47; 95% CI, 0.27 to 0.81)	⊕⊕⊕◯ MODERATE	Downgraded 1 level for imprecision (i.e., wide CIs)[a]
Progression-free survival			
N = 99 1 RCT[244]	At 5 years, improved PFS with SBRT (HR, 0.47; 95% CI, 0.30 to 0.76) At 6 years, improved PFS with SBRT (HR, 0.48; 95% CI, 0.31 to 0.76)	⊕⊕⊕◯ MODERATE	Downgraded 1 level for risk-of-bias
Disease-control			
N = 99	SBRT is associated with improved disease control (absence of progression, 75% SBRT vs. 49%	⊕⊕◯◯ LOW	Downgraded 1 level each for risk-of-bias

Number of Participants (N) Number of Studies	Findings	Certainty of Evidence	Rationale
1 RCT[244]	standard of care; *P* = .001; lesional control by location).		and imprecision (i.e., not assessable)[a]
Quality of life			
N = 99 1 RCT[244]	People with a controlled primary tumor and 1 to 5 oligometastatic lesions treated with SBRT or standard of care had a similar quality of life at each subsequent follow-up.	⨁⨁◯◯ LOW	Downgraded 1 level each for risk-of-bias and imprecision (i.e., not assessable)[a]
SBRT vs. observation for oligometastatic prostate cancer			
Overall survival			
N = 116 2 RCTs[242,243]	In a pooled analysis of 2 RCTs, the median for overall survival was not reached in either group, with similar overall survival between groups (HR, 0.53; 95% CI, 0.13 to 2.11).	⨁⨁◯◯ LOW	Downgraded 2 levels for imprecision (i.e., very wide CIs)[a]
Progression-free survival			
N = 116 2 RCTs[242,243]	SBRT may be associated with similar or improved PFS (11.9 months MDT vs. 5.9 months surveillance; HR, 0.44; 95% CI, 0.29 to 0.66), and other measures of disease-related survival (ADT-free and castration-resistant prostate cancer-free survival).	⨁⨁◯◯ LOW	Downgraded 1 level each for risk-of-bias and imprecision (i.e., wide CIs)
Disease-control			
N = 54 1 RCT[243]	Men treated with SBRT had higher complete response (28% SBRT vs. 8% observation) and partial response rates (43% vs. 39% observation) at 6 months; however, no formal statistical testing was reported.	⨁⨁◯◯ LOW	Downgraded 1 level each for risk-of-bias and imprecision (i.e., not assessable)[a]
Quality of life			
N = 116 2 RCTs[242,243]	No difference between groups.	⨁⨁◯◯ LOW	Downgraded 1 level each for risk-of-bias and imprecision (i.e., not assessable)
SBRT vs. RT or no SBRT for oligometastatic prostate cancer			
Overall survival			
N = 506 1 comparative NRS[247]	Men with oligometastatic or oligorecurrent prostate cancer treated with SBRT or cRT had a similar overall survival at 2 years (87.7% SBRT vs. 87.3% cRT; *P* = .91)	⨁⨁◯◯ LOW	Not downgraded[a]
Progression-free survival			
N = 682 2 comparative NRSs[246,247]	SBRT appears to be associated with a worse metastasis-free survival when compared with elective nodal RT but similar or improved PFS when compared with cRT.	⨁◯◯◯ VERY LOW	Downgraded 1 level for imprecision (i.e., not assessable)

Number of Participants (N) Number of Studies	Findings	Certainty of Evidence	Rationale
Disease-control			
N = 239 2 comparative NRSs[245,246]	SBRT appears to be associated with worse outcomes (local and lymph node progression, relapse) when compared with elective nodal RT (68% SBRT vs. 77% with elective nodal RT; *P* = .01) but similar or improved outcomes (time to ADT or castration-resistance) when compared with no SBRT.	⨁◯◯◯ VERY LOW	Downgraded 1 level for imprecision (i.e., not assessable)
Quality of life			
Not reported			
SBRT vs. other treatment for oligometastatic cancer (primary sites included prostate, breast, lung, and other sites)			
Toxicity			
N = 215 3 RCTs[242-244]	No grade 3 and higher toxicities were seen in 2 of the 3 trials, , but some SBRT-related deaths were observed.	⨁⨁◯◯ LOW	Downgraded 1 level each for risk-of-bias and imprecision (i.e., not assessable)
N = 745 3 comparative NRSs[245-247]	No grade 3 and higher toxicities were reported, lower than those experienced with elective nodal RT (up to 2%).	⨁◯◯◯ VERY LOW	Downgraded 1 level for imprecision (i.e., not assessable)

Notes. [a] *Inconsistency not assessable due to 1 pooled analysis or 1 study*
Abbreviations. ADT: androgen deprivation therapy; CI: confidence interval; HR: hazard ratio; NRS: nonrandomized study; RCT: randomized controlled trial; RT: radiation therapy; SBRT: stereotactic body radiation therapy.

Overall and Progression-free Survival

In the SABR-COMET trial, people with a controlled primary tumor and 1 to 5 oligometastatic lesions had[244,249-252]:

- Similar overall survival at 5 years to people who received standard of care (including palliative RT)
  - Median overall survival; 41 months SBRT vs. 28 months standard of care; HR, 0.57; 95% CI, 0.30 to 1.10
- Significantly improved survival at 6 years compared with people who received standard of care (including palliative RT)
  - Median overall survival; 50 months SBRT vs. 28 months standard of care; HR, 0.47; 95% CI, 0.27 to 0.81
- Significantly improved PFS compared with people who received standard of care (including palliative RT) at both the 5- and 6-year time point
  - Median PFS; 12 months SBRT vs. 6 months standard of care; over 5 years, HR, 0.47; 95% CI, 0.30 to 0.76

- Median PFS; 12 months SBRT vs. 5 months standard of care; over 6 years, HR, 0.48; 95% CI, 0.31 to 0.76

In men with oligometastatic prostate cancer, SBRT may be associated with improved PFS; however, overall survival was similar between the SBRT and observation groups.

- Overall survival was not reported in the STOMP trial.[242] Men treated with metastatic-directed therapy (MDT; the majority of whom received SBRT) had a similar ADT-free survival to men undergoing surveillance (21 months MDT vs. 13 months surveillance; HR, 0.60; 95% CI, 0.31 to 1.11).[242] However, MDT was associated with significantly improved biochemical recurrence-free survival (HR, 0.53; 95% CI, 0.30 to 0.94).[242]
- Overall survival was not reported in the ORIOLE trial.[242] Men treated with SBRT for oligometastatic prostate cancer had a significantly lower rate of progression to those undergoing observation (progression at 6 months, 19% SBRT vs. 61% observation; median time to progression, not reached SBRT vs. 5.8 months observation; HR, 0.30; 95% CI, 0.11 to 0.81).[243]
- In a pooled analysis of ORIOLE and STOMP, at a median follow-up of 53 months[248]:
  - Median for overall survival was not reached in either group (HR, 0.53; 95% CI, 0.13 to 2.11).
  - MDT was associated with improved PFS when compared with observation (11.9 months MDT vs. 5.9 months surveillance; HR, 0.44; 95% CI, 0.29 to 0.66).
  - There was no difference between groups for castration-resistant prostate cancer-free survival (median not reached, MDT vs .63 months surveillance; HR, 0.67; 95% CI, 0.34 to 1.31) or for radiographic PFS (18 months MDT vs. 17 months surveillance; HR, 0.81; 95% CI, 0.50 to 1.29).

From the 2 comparative studies in oligometastatic prostate cancer, SBRT appears to be associated with a worse outcome when compared with elective nodal RT, but with similar or improved outcomes to cRT.

- In a multicenter study from Europe, men with nodal oligorecurrent prostate cancer treated with SBRT had significantly worse metastasis-free survival than men treated with elective nodal RT (68% SBRT vs. 77% with elective nodal RT; $P = .01$).[246] When analyzed by the number of nodes affected at recurrence, the survival benefit was seen only in men with 1 lymph node at recurrence.[246]
- In a multicenter study from Turkey, men with oligometastatic or oligorecurrent prostate cancer treated with SBRT or cRT had a similar overall survival at 2 years (87.7% SBRT vs. 87.3% cRT; $P = .91$).[247] However, PFS at 2 years was significantly higher in the SBRT group (86.2% SBRT vs. 54.9%; $P < .001$).[247]

Disease Control

In the SABR-COMET trial, people with a controlled primary tumor and 1 to 5 oligometastatic lesions were[244]:

- Significantly more likely to have improved disease control
  - Absence of progression in lesions present at randomization (75% SBRT vs. 49% standard of care; $P = .001$)
  - Longer-term absence of progression in lesions present at randomization (63% SBRT vs. 46% standard of care; $P = .04$)

- Significantly higher lesional control by lesion location (adrenal, 100%; bone, 72%; lung, 51%; liver, 50%; *P* = .04)

In the ORIOLE trial, men treated with SBRT had higher complete response (28% SBRT vs. 8% observation) and partial response rates (43% vs. 39% observation) at 6 months; however, no formal statistical testing was reported.[243]

From the 2 comparative studies reporting on disease control, SBRT appears to be associated with worse outcomes when compared with elective nodal RT but improved outcomes when compared with no SBRT.

- In a study from a single center in the Netherlands, men with metachronous oligometastases of hormone-sensitive prostate cancer treated with SBRT had a significantly longer time to ADT (17.3 months SBRT vs. 4.2 months no SBRT; *P* < .001) but a similar time to castration resistance once ADT was started (31.5 months SBRT vs. 26.9 months no SBRT; *P* = .54).[245]
- In a multicenter study from Europe, men with nodal oligorecurrent prostate cancer treated with SBRT were significantly more likely to experience local progression (16% SBRT vs. 5% elective nodal RT; *P* < .001) and lymph node progression (details not reported; *P* < .001).[246] Men with nodal oligorecurrent prostate cancer treated with SBRT were also significantly more likely to experience relapse compared with those treated with elective nodal RT (57% SBRT vs. 38% elective nodal RT; *P* < .001).[246]

Quality of Life

In the SABR-COMET trial, people with a controlled primary tumor and 1 to 5 oligometastatic lesions treated with SBRT or standard of care had a similar quality of life at each subsequent follow-up.[244]

In STOMP, men in the MDT and surveillance groups had a similar quality of life at baseline that remained comparable at 3-month and 1-year follow-up.[242] In ORIOLE, no differences in quality of life were observed between the SBRT and observation arms or within either arm over time.[243]

Toxicity

In the eligible RCTs, toxicities were rare, but some SBRT-related deaths were observed.

- More people treated with SBRT experienced a grade 2 or higher toxicity (29% SBRT vs. 9% standard of care; *P* = .03).[244] In the SBRT group, 3 people died of SBRT-related toxicity (1 each of radiation pneumonitis, pulmonary abscess, subdural hemorrhage after surgery to repair a SBRT-related perforated gastric ulcer).[244]
- No grade 2 to 5 toxicity was observed in the STOMP trial.[242]
- In the ORIOLE trial, no grade 3 or higher events were observed.[243]

In the eligible comparative studies, toxicities were rare, and may be lower than those experienced with elective nodal RT.

- No men with metachronous oligometastases of hormone-sensitive prostate cancer treated with SBRT experienced a grade 3 toxicity.[245]
- Elective nodal RT was associated with significantly higher acute (*P* = .002) and late toxicities (*P* < .001).[246] In the elective nodal RT group, men experienced around 1% to 2% grade 3 events compared with none in the SBRT group.[246]

- No men with men with oligometastatic or oligorecurrent prostate cancer treated with SBRT or cRT experienced a grade 3 toxicity.[247]

Across the 12 noncomparative studies reporting harms[240,254-264]:
- The most commonly reported toxicities related to fatigue and radiation pneumonitis.
- Many studies reported no grade 3 or higher toxicities; where grade 3 toxicity was observed, it was in around 1% to 2% of people.
- Very few grade 4 or 5 toxicities were observed; however, there were 2 deaths related to SBRT, including 1 patient who died of bile duct stenosis.

Full details on toxicities from each of the noncomparative studies are in Appendix C.

Adrenal Cancer

History

In the 2012 report presented to the HTCC,[6] the overall strength of evidence was assessed as very low for effectiveness and harms for adrenal metastases, based on 2 case series.[266,267] No economic studies were identified.[6]

Study Characteristics

We only identified 1 noncomparative study on the use of SBRT for adrenal metastases (Table 28).[268] We assessed the study at being at high risk-of-bias because of the lack of a comparator.

Table 28. Summary Study Characteristics of Noncomparative Studies in Adrenal Cancer

Citation Setting NCT or Other Trial ID	Duration Risk-of-bias	Patient Characteristics	Description of Intervention
Franzese et al., 2021[268] 3 centers, including academic centers, in Italy NR	Retrospective study Median follow-up of 14 months High risk-of-bias	Total N = 142 people with adrenal metastases	• SBRT ○ Median dose of 40 Gy (range, 10 to 60) in median 4 fractions (1 to 10)

Abbreviations. Gy: Gray; NR: not reported; SBRT: stereotactic body radiation therapy.

GRADE Summary of Findings

Table 29. GRADE Summary of Evidence: Effectiveness of SBRT for Adrenal Cancer

Number of Participants (N) Number of Studies	Findings	Certainty of Evidence	Rationale
SBRT vs. other treatment options for adrenal cancer			
Overall survival			
No eligible comparative studies were identified.			

Number of Participants (N) Number of Studies	Findings	Certainty of Evidence	Rationale
Progression-free survival			
No eligible comparative studies were identified.			
Disease-control			
No eligible comparative studies were identified.			
Quality of life			
No eligible comparative studies were identified.			
Toxicity			
No eligible comparative studies were identified.			

Overall and Progression-free Survival

No eligible RCTs or comparative studies were identified.

Disease Control

No eligible RCTs or comparative studies were identified.

Quality of Life

No eligible RCTs or comparative studies were identified.

Toxicity

In the study from 3 centers in Italy, no grade 3 or higher toxicities were observed in people treated with SBRT for adrenal metastases, with 1 (0.7%) patient having a lesional hemorrhage after SBRT.[268]

Large Tumors

History

The original report did not include any studies specifically in people with large tumors.[6]

Study Characteristics

We only identified 1 noncomparative study on the use of SBRT for large tumors (Table 30).[269] We assessed the study at being at high risk-of-bias because of the lack of a comparator.

Table 30. Summary Study Characteristics of Noncomparative Studies in Large Tumors

Citation Setting NCT or Other Trial ID	Duration Risk-of-bias	Patient Characteristics	Description of Intervention
Grozman et al., 2021[269] Single academic center in Sweden	Retrospective study Median follow-up of 17 months High risk-of-bias	Total N = 164 people with large tumors (gross tumor volume of at least 70 cc)	• SBRT ○ 40 Gy in 5 fractions ○ 40 Gy in 4 fractions

Citation Setting NCT or Other Trial ID	Duration Risk-of-bias	Patient Characteristics	Description of Intervention
NR			

Abbreviations. Gy: Gray; NR: not reported; SBRT: stereotactic body radiation therapy.

GRADE Summary of Findings

Table 31. GRADE Summary of Evidence: Effectiveness of SBRT for Large Tumors

Number of Participants (N) Number of Studies	Findings	Certainty of Evidence	Rationale
SBRT vs. other treatment options for large tumors			
Overall survival			
No eligible comparative studies were identified.			
Progression-free survival			
No eligible comparative studies were identified.			
Disease-control			
No eligible comparative studies were identified.			
Quality of life			
No eligible comparative studies were identified.			
Toxicity			
No eligible comparative studies were identified.			

Abbreviation. SBRT; stereotactic body radiation therapy.

Overall and Progression-free Survival

No eligible RCTs or comparative studies were identified.

Disease Control

No eligible RCTs or comparative studies were identified.

Quality of Life

No eligible RCTs or comparative studies were identified.

Toxicity

In a study from a single center in Sweden, around 15% of people with large tumors experienced a grade 3 or higher toxicity, 2% grade 4, and 6% grade 5 toxicities.[269] The grade 4 and higher toxicities included radiation pneumonitis or pneumonia, esophago-tracheal fistula, gastric perforation, hemoptysis, gastrointestinal bleeding, and duodenal perforation.[269]

Mixed Cancers

History

In the 2012 report presented to the HTCC,[6] no comparative studies were identified on mixed or multiple cancer sites. The report included 5 case series of SBRT for multiple tumor sites.[240,241,270-272] The report concluded that the overall strength of evidence was very low for effectiveness and harms.[6]

Study Characteristics

We identified 2 noncomparative studies in mixed cancer (primary or metastatic tumors in the lung or liver, and primary and metastatic tumors in the abdomen and pelvis; Table 32).[271,273] We assessed each of the studies at being at high risk-of-bias because of the lack of a comparator.

Table 32. Summary Study Characteristics of Noncomparative Studies in Mixed Cancers

Citation Setting NCT or Other Trial ID	Duration Risk-of-bias	Patient Characteristics	Description of Intervention
McCammon et al., 2009[271] Single academic center in the US NR	Retrospective study Median follow-up of 8 months High risk-of-bias	Total N = 141 people with primary or metastatic tumors in lung or liver	• SBRT ○ Most common dose of 60 Gy in 3 fractions (range, < 30 to 60)
Yoon et al., 2021[273] Single academic center in the US NR	Retrospective study Median follow-up of 20 months High risk-of-bias	Total N = 106 people with primary and metastatic tumors in abdomen and pelvis	• SBRT ○ Median total dose of 40 Gy (range, 24 to 60) in median 5 fractions (range, 3 to 5)

Abbreviations. Gy: Gray; NCT: US National Clinical Trial; NR: not reported; SBRT: stereotactic body radiation therapy.

GRADE Summary of Findings

Table 33. GRADE Summary of Evidence: Effectiveness of SBRT for Mixed Cancers

Number of Participants (N) Number of Studies	Findings	Certainty of Evidence	Rationale
SBRT vs. other treatment options for mixed cancers			
Overall survival			
No eligible comparative studies were identified.			
Progression-free survival			
No eligible comparative studies were identified.			
Disease-control			
No eligible comparative studies were identified.			

Number of Participants (N) Number of Studies	Findings	Certainty of Evidence	Rationale
Quality of life			
No eligible comparative studies were identified.			
Toxicity			
No eligible comparative studies were identified.			

Overall and Progression-free Survival

No eligible RCTs or comparative studies were identified.

Disease Control

No eligible RCTs or comparative studies were identified.

Quality of Life

No eligible RCTs or comparative studies were identified.

Toxicity

In the 2 noncomparative studies, acute and late grade 3 toxicities ranged from 1% to 5%, including grade 3 pneumonitis, dermatitis, and higher soft-tissue or muscle inflammation or fibrosis.[271,273] Grade 4 events were rare, around 1% to 2%, including 2 cases of sepsis.[271,273] In 1 study, 2 patients developed vertebral fractures within the radiation field most likely attributable to treatment.[271] There did not appear to be any association between acute or late toxicities by grade and dose.[273]

Bone Cancer

History

In the 2012 report presented to the HTCC,[6] no primary studies reported on the effectiveness of SBRT for bone metastases.

Study Characteristics

We identified 1 RCT evaluating the use of SRBT in mostly nonspine bone metastases (Table 34).[274] We assessed the RCT as being at moderate risk of bias, because of the lack of blinding.

Table 34. Summary Study Characteristics of Randomized Controlled Trials in Bone Cancers

Citation Setting NCT or Other Trial ID	Duration Risk of Bias	Patient Characteristics	Description of Intervention	Description of Comparator(s)
Nguyen et al., 2019[274] Single academic center in the US	Followed up to 24 months	Total N = 160 people with radiologically confirmed painful bone metastases, comprising 81 in the	• SBRT ○ Single-fraction 12 Gy for lesions >4 cm or 16 Gy for lesions ≤4 cm	• Standard MFRT ○ 30 Gy delivered in 10 3-Gy fractions ○ Standard concurrent chemotherapy,

Citation Setting NCT or Other Trial ID	Duration Risk of Bias	Patient Characteristics	Description of Intervention	Description of Comparator(s)
NCT02163226	Moderate risk of bias	SBRT group and in the 79 control group	○ Standard concurrent chemotherapy, immunotherapy, or targeted therapy was allowed	immunotherapy, or targeted therapy was allowed

Abbreviations. Gy: Gray; MFRT: mutitfraction radiation therapy; NCT: US National Clinical Trial; SBRT: stereotactic body radiation therapy.

GRADE Summary of Findings

Table 35. GRADE Summary of Evidence: Effectiveness of SBRT for Bone Cancer

Number of Participants (N) Number of Studies	Findings	Certainty of Evidence	Rationale
SBRT vs. cRT for bone metastases			
Overall survival			
N = 160 1 RCT[274]	People with radiologically confirmed painful bone metastases (mostly nonspine) treated with SBRT or MFRT had a similar overall survival (median, 6.7 months in both groups).	⊕⊕⊕◯ MODERATE	Downgraded 1 level imprecision (i.e., not assessable)[a]
Progression-free survival			
Not reported			
Disease-control			
N = 160 1 RCT[274]	When compared with MFRT, SBRT was found to be noninferior for both local failure (HR, 0.18; 95% CI, 0.02 to 1.47).	⊕◯◯◯ VERY LOW	Downgraded 1 level for risk of bias and 2 levels for imprecision (i.e., very wide CIs)[a]
Quality of life			
N = 160 1 RCT[274]	No significant difference in quality of life for patients treated with SBRT or with MFRT.	⊕⊕◯◯ LOW	Downgraded 1 level each for risk of bias and imprecision (i.e., not assessable)
Toxicity			
N = 160 1 RCT[274]	No significant difference in toxicities for patients treated with SBRT or with MFRT. SBRT was associated with around 1% grade 3 or higher toxicities, and up to 10% for fatigue grade 3 and higher.	⊕⊕◯◯ LOW	Downgraded 1 level each for risk of bias and imprecision (i.e., not assessable)

Notes. [a] *Inconsistency not assessable as only 1 study*
Abbreviations. CI: confidence interval; MFRT: multifraction radiation therapy; SBRT: stereotactic body radiation therapy.

Overall and Progression-free Survival

People with radiologically confirmed painful bone metastases (mostly nonspine) treated with SBRT or multifraction RT had a similar overall survival (median, 6.7 months in both groups); however, quality-life adjusted survival analysis found overall survival was significantly higher in the SBRT group when compared to the MFRT group (*P* value not reported).[274]

Disease Control

People with radiologically confirmed painful bone metastases (mostly nonspine) treated with SBRT were significantly less likely to experience local failure (0 SBRT vs. 4.2% multifraction RT at 6 months; 0 vs. 4.9% at 12 months; 0 vs. 9.7% at 24 months; *P* = .02).[274] When compared with multifraction RT, SBRT was found to be noninferior for both local failure (HR, 0.18; 95% CI, 0.02 to 1.47).[274]

Quality of Life

There was no significant difference in quality of life for patients treated with SBRT or with multifraction RT.[274]

Toxicity

Patients in both the SBRT and multifraction RT group experienced similar levels of toxicity, with no grade 4 or higher toxicities being reported.[274] SBRT was associated with around 1% grade 3 or higher toxicities, and up to 10% for fatigue grade 3 and higher.

FDA Reported Harms for Stereotactic Body Radiation Therapy

We also searched the U.S. FDA MAUDE database from the past 5 years and the Medical Device Recall reports (Appendix F). We found 618 entries in the MAUDE database, including voluntary, user facility, distributor, and manufacturer reports of adverse events relating to SBRT use in the past 5 years. We were not able to analyze the reports by cancer type, but the types of adverse events appeared similar to those reported in our eligible studies as well, as device failures and process errors.

Key Question 3

Please see the findings for Key Questions 1 and 2 by cancer site for evidence on SBRT and differential efficacy or harms in subpopulations.

Key Question 4

We identified 9 eligible studies reporting economic outcomes (health care resource use or costs) or the results of an economic model (Table 36).[92,189,218,275-279].

- 2 on the use of SBRT for prostate cancer
  - Pan and colleagues[92] compared the toxicities and cost of proton radiation and SBRT with IMRT for prostate cancer among men younger than 65 years of age with private insurance.
  - Parikh and colleagues[280] compared the cost-effectiveness of treating patients with oligorecurrent hormone-sensitive prostate cancer with upfront MDT before standard-of-care systemic therapy.
  - We assessed the cost comparison study by Pan and colleagues[92] as being at low risk-of-bias; however, no formal economic modeling was conducted. The modeling study by Parikh and colleagues was assessed as being at low risk-of-bias.
- 1 on the use of SBRT for oligometastatic NSCLC
  - Kim and colleagues[276] aimed to evaluate the cost-effectiveness of the routine addition of SBRT to upfront therapy in stage IV NSCLC by mutational subgroup.
  - We assessed this study as being at low risk-of-bias.
- 1 on the use of SBRT for pancreatic cancer
  - Moningi and colleagues[189] compared health care payments for RT and chemotherapy for unresectable pancreatic cancer.
  - We assessed this study as being at low risk-of-bias; however, no formal economic modeling was conducted.
- 1 on the use of SBRT for head and neck cancer
  - Kim and colleagues[275] evaluated the cost-effectiveness of salvage therapies for patients with recurrent head and neck cancer.
  - We assessed this study as being at low risk-of-bias.
- 1 on the use of SBRT in liver cancer
  - Parikh and colleagues[218] compared costs for SBRT and RFA in early-stage HCC.
  - We assessed this study as being at low risk-of-bias.
- 2 on the use of SBRT in oligometastatic cancer
  - Kumar and colleagues[277] evaluate the cost-effectiveness of the addition of SBRT compared with standard therapy alone among cancer patients with oligometastatic disease.

- Mehrens and colleagues[278] examined the cost-effectiveness of SBRT for oligometastatic disease, based on the SABR-COMET RCT.[244]
- We assessed the studies as being at low risk-of-bias.

- 1 on the use of SBRT for bone metastases[279]
  - Santos and colleagues[279] assessed US national radiation therapy trends, including SBRT, for bone metastases and the associated expenditures.
  - We assessed the study as being at low risk of bias.

Table 36. Summary Study Characteristics of Economic Studies of SBRT

Study ID Study Risk-of-bias	Population	Intervention	Comparators	Economic Analytic Method
Prostate cancer				
Pan et al., 2018[92] Low risk-of-bias	Men with localized prostate cancer	• SBRT	• IMRT	Cost comparison
Parikh et al., 2020[280] Low risk of bias	Men with oligorecurrent hormone-sensitive prostate cancer	• SBRT	• Abiraterone acetate plus prednisone and ADT • Docetaxel and ADT	Cost-effectiveness analysis (Markov state transition model)
Lung cancer				
Kim et al., 2019[276] Low risk-of-bias	People with oligometastatic stage IV NSCLC, grouped by mutation status	• SBRT plus maintenance therapy	• Maintenance therapy alone	Cost-effectiveness analysis (Markov state transition model)
Pancreatic cancer				
Moningi et al., 2022[189] Low risk-of-bias	People with non-metastatic, unresectable pancreatic cancer	• SBRT	• cRT • Chemotherapy	Cost comparison
Head and neck cancer				
Kim et al., 2018[275] Low risk-of-bias	People with unresectable locally recurrent previously irradiated head and neck cancers	• SBRT • SBRT plus cetuximab	• Platinum-based chemotherapy alone • Chemotherapy plus cetuximab • IMRT plus chemotherapy	Cost-effectiveness analysis (Markov state transition model)
Liver cancer				
Parikh et al., 2018[218]	People with early-stage liver cancer	• SBRT	• RFA	Cost-effectiveness analysis

Study ID Study Risk-of-bias	Population	Intervention	Comparators	Economic Analytic Method
Low risk-of-bias				
Oligometastatic cancer				
Kumar et al., 2021[277] Low risk-of-bias	People with oligometastatic disease	• SBRT	• Standard care	Cost-effectiveness analysis (Markov model)
Mehrens et al., 2021[278] Low risk-of-bias	People with oligometastatic disease	• SBRT	• Standard care	Cost-effectiveness analysis (partitioned survival model)
Bone cancer				
Santos et al., 2021[279] Low risk of bias	People with bone metastases	• SBRT	• EBRT • IMRT	Cost comparison

Abbreviations. ADT: androgen deprivation therapy; cRT: conventional radiation therapy; EBRT: external beam radiation therapy; IMRT: intensity-modulated radiation therapy; RFA: radiofrequency ablation; SBRT: stereotactic body radiation therapy.

GRADE Summary of Findings

Table 37. GRADE Summary of Evidence: Economic Outcomes of SBRT by Cancer Site

Number of Participants (N) Number of Studies	Findings	Certainty of Evidence	Rationale
SBRT vs. IMRT for prostate cancer			
Outcome: cost-effectiveness			
N = 3 hypothetical cohorts 1 economic modelling study[280]	Upfront SBRT may be a cost-effective option for people who wish to avoid systemic therapy; however, it was the cost-effective strategy in only 53.6% of microsimulations at a WTP of $100,000 per QALY	⨁⨁◯◯ LOW	Downgraded 1 level for indirectness[a] (i.e., oligometastatic hormone-resistant prostate cancer) and for imprecision (i.e., wide CIs)
Outcome: costs			
N = 12,128 1 comparative NRS[92]	SBRT had lower costs for both the payer ($49,504 for SBRT and $57,244 for IMRT; P < .001) and patient than	⨁◯◯◯ VERY LOW	Downgraded 1 level for indirectness[a] (i.e., localized prostate cancer in

Number of Participants (N) Number of Studies	Findings	Certainty of Evidence	Rationale
	IMRT ($1,015 for SBRT and $1,560 for IMRT; *P* < .001) No difference between treatments in complication costs or overall health care costs at 2 years		younger men with private insurance)
SBRT plus maintenance therapy vs maintenance therapy for lung cancer			
Outcome: cost-effectiveness			
N = 3 hypothetical cohorts 1 economic modelling study[276]	SBRT was assessed as not being cost-effective at a WTP threshold of $100,000 when added to maintenance therapy for people with oligometastatic NSCLC.	⊕⊕⊕◯ MODERATE	Downgraded 1 level for indirectness[a] (i.e., oligometastatic NSCLC only, by mutation status)
SBRT vs. cRT or chemotherapy for pancreatic cancer			
Outcome: cost-effectiveness			
Not reported			
Outcome: costs			
N = 5,624 1 comparative NRS[189]	Healthcare payments were greatest for SBRT when compared with cRT or chemotherapy under US Medicare (*P* < .001) and employer-based insurance (*P* < .001).	⊕◯◯◯ VERY LOW	Downgraded 1 level for indirectness[a] (i.e., nonmetastatic, unresectable pancreatic cancer)
SBRT plus maintenance therapy vs salvage therapies for head and neck cancer			
Outcome: cost-effectiveness			
N = 1 hypothetical cohort 1 economic modelling study[275]	None of treatment strategies were cost-effective. However, SBRT-based reirradiation has potential to be cost-effective, as model was sensitive to median survival.	⊕⊕⊕◯ MODERATE	Downgraded 1 level for indirectness[a] (i.e., locoregional previously irradiated head and neck cancer)
SBRT vs. RFA for liver cancer			
Outcome: cost-effectiveness			
N = 440 1 comparative NRS[218]	SBRT was not cost-effective compared with RFA in overall population of people with early-stage HCC; however, 85.5% of bootstrap ICER estimates were lower than WTP threshold of $100,000.	⊕⊕⊕◯ MODERATE	Downgraded 1 level for indirectness (i.e., early-stage HCC only)[a]
SBRT vs. standard care for oligometastatic cancer			
Outcome: cost-effectiveness			
N = 2 hypothetical cohorts based on SABR-COMET data	Addition of SBRT increased costs and improved quality adjusted survival, overall leading to a cost-effective	⊕⊕⊕◯ MODERATE	Downgraded 1 level for indirectness (i.e., based on

Number of Participants (N) Number of Studies	Findings	Certainty of Evidence	Rationale
2 economic modelling studies[277,278]	treatment strategy for patients with oligometastatic cancer.		a single trial for patient outcomes)
SBRT vs. other forms of RT for bone cancer			
Outcome: cost-effectiveness			
Not reported			
Outcome: costs			
N = 40,993 cases 1 comparative NRS	For people with bone metastases, the cost of SBRT was significantly higher for both professional and technical fees ($679 lower provider costs and $6,422 lower technical costs for external beam RT; $36 lower provider costs and $2,534 lower technical costs for IMRT; *P* < .001).	⨁◯◯◯ VERY LOW	Downgraded 1 level for indirectness (i.e., no indication how many were nonspine metastases)

Notes. [a] *Inconsistency not assessable due to only 1 study*
Abbreviations. cRT: conventional radiation therapy; HCC: hepatocellular carcinoma; ICER: incremental cost-effectiveness ratio; IMRT: intensity-modulated radiation therapy; NCSLC: non-small cell lung cancer; NRS: nonrandomized study; RFA: radiofrequency ablation; RT: radiation therapy; SBRT: stereotactic body radiation therapy WTP: willingness-to-pay.

Prostate Cancer

We identified 1 formal economic model assessing the comparative cost-effectiveness of SBRT for prostate cancer[280] and 1 study that reported the costs of treatment to the payer and to the patient.[92]

The economic model compared 3 treatment strategies[280]:

- Upfront metastasis-directed therapy, followed by salvage abiraterone acetate plus prednisone (AAP) with ADT followed by salvage docetaxel with ADT (strategy 1)
- Upfront AAP with ADT, followed by salvage docetaxel with ADT (strategy 2)
- Upfront docetaxel with ADT, followed by salvage AAP with ADT (strategy 3)

The base care model was that of the perspective of a US payer, with cost estimates taken directly from Medicare sources.[280] All cost estimates were converted into 2020 US dollars by using a Consumer Price Index inflation calculator from the US Bureau of Labor Statistics.[280] Costs and effectiveness were discounted using appropriate discount rates, but no further details were reported.[280] The time horizon was 10 years, and cost-effectiveness was evaluated using net monetary benefit, and a willingness-to-pay (WTP) threshold of $100,000 per QALY.[280]

At 10 years, the total cost was $141,148 for upfront SBRT, $166,807 for upfront AAP and ADT, and $136,154 for upfront docetaxel and ADT, with total QALYs of 4.63, 4.89, and 4.00, respectively.[280] These resulted in net monetary benefit values of $322,240 for upfront SBRT,

$322,018 for upfront AAP and ADT, and $263,407 for upfront docetaxel and ADT.[280] In a one-way sensitivity analysis, the model was sensitive to the cost of AAP, with modest variations in cost resulting in greater net monetary benefit with the upfront AAP and ADT when compared with upfront SBRT.[280] In probabilistic sensitivity analysis, the mean net monetary benefit values were $351,476 (95% CI, $239,652 to $531,551) for upfront SBRT, $326,983 (95% CI, $234,344 to $417,815) for upfront AAP and ADT, and $272,437 (95% CI, $174,239 to $381,610) for upfront docetaxel and ADT.[280] Upfront MDT was the cost-effective strategy in 53.6% of microsimulations at a WPT of $100,000 per QALY.[280]

In the study by Pan and colleagues,[92] using the MarketScan Commercial Claims and Encounters database, they found:

- The mean radiation cost to the payer was $49,504 for SBRT and $57,244 for IMRT ($P < .001$).
- The mean radiation cost to the patient was $1,015 for SBRT and $1,560 for IMRT ($P < .001$).
- The mean complication costs were similar at 2 years for SBRT and IMRT ($3,084 SBRT vs. $2,079; $P = .25$) as were mean total health care costs ($80,786 SBRT vs. $77,539 IMRT; $P = .36$).

However, this analysis was limited to younger patients with localized prostate cancer (aged 65 years and younger) and to patients with private insurance, thus limiting the generalizability of the findings beyond this population.[92]

Lung Cancer

We identified 1 eligible formal cost-effectiveness model comparing SBRT plus maintenance therapy with maintenance therapy alone for oligometastatic NSCLC.[276] The model analyzed 3 hypothetical cohorts:

- Epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) mutation-positive group
- Programmed death ligand (PDL-1) expressing group
- EGFR and ALK mutation-negative and PDL-1 negative (mutation-negative) group

The base case model was developed from a payer's perspective for health care services (considering only direct medical costs), using unadjusted national 2018 Medicare reimbursement rates.[276] Both costs and utilities were discounted at an annual rate of 3%.[276] With a lifetime time horizon, the model cycled until the entire cohort had died.[276] Treatment strategies were compared using the incremental cost-effectiveness ratio (ICER), the ratio of cost difference to quality-adjusted life-years (QALYs) difference between strategies.[276] The analysis used a WTP threshold of $100,000 per QALY gained, and a dominant strategy was defined as one that was more effective and less costly than the alternative strategy.[276]

In base case analysis[276]:

- In the EGFR or ALK-positive cohort, SBRT plus maintenance therapy cost $64,511 more than maintenance therapy alone while gaining 0.11 QALYs, resulting in an ICER of $564,186 per QALY gained.
- For the PDL-1-positive cohort, the cost difference was $56,066 with 0.17 QALYs gained, resulting in an ICER of $299,248 per QALY gained with SBRT plus maintenance therapy.

- In the mutation-negative cohort, SBRT plus maintenance therapy cost $30,075 more than maintenance therapy alone while gaining 0.23 QALYs, resulting in an ICER of $128,424 per QALY gained.

In one-way sensitivity analyses of the mutation-positive cohorts, results were most sensitive to the costs of maintenance therapy, as well as the utility of hospice or terminal care, median survival, and median PFS.[276] However, none of the parameters, when varied, caused SBRT plus maintenance therapy to be a cost-effective option. In probabilistic sensitivity analysis, SBRT plus maintenance therapy was favored in 31% of model iterations and maintenance therapy alone favored in 69% at a WTP threshold of $100,000 per QALY gained for both the EGFR/ALK mutation-positive and PDL-1-positive cohorts.[276]

In the mutation-negative cohort, the results were found to be most sensitive to cost of maintenance therapy, PFS, and medial survival.[276] If the cost of maintenance therapy was reduced by 25% or more, the ICER would be below $50,000 per QALY gained, and if the median survival when treated with SBRT was more than 1.5 times that of maintenance therapy alone, the ICER would be below $100,000 per QALY gained.[276] Probabilistic sensitivity analysis demonstrated SBRT plus maintenance was favored in 45% of model iterations and maintenance therapy alone favored in 55% at a WTP threshold of $100,000 per QALY gained.[276]

SBRT therefore was assessed as not being cost-effective at a WTP threshold of $100,000 when added to maintenance therapy for people with oligometastatic NSCLC.[276]

Pancreatic Cancer

We did not identify any formal economic model assessing the comparative cost-effectiveness of SBRT for pancreatic cancer. We did identify 1 eligible study that reported the comparative costs of treatment for unresectable pancreatic cancer.[189] In an analysis of the SEER and Texas Cancer Registry (linked with Medicare) and the MarketScan Commercial Claims and Encounter database, health care costs per patient were higher with treatment using SBRT or CFRT compared with chemotherapy alone[189]:

- Median 12-month total payments per patient (fee-for-service Medicare insurance coverage) were $57,502 for chemotherapy alone (IQR, $34,179 to $84,888), $66,366 for cRT (IQR, $60,645 to $118,298), and $80,282 for SBRT (IQR, $45,244 to $93,684; $P < .001$).
- Median payments per patient (under employer-based insurance coverage) were $127,438 for chemotherapy alone (IQR, $76,001 to $194,98), $172,547 for cRT (IQR, $117,987t o $248,735) and $212,579 for SBRT (IQR, $144,177 to $303,268; $P < .001$).

Age-adjusted models did not significantly affect mean cost differences by treatment.[189]

Head and Neck Cancer

We identified 1 eligible formal cost-effectiveness model comparing 5 salvage treatment strategies for locoregional previously irradiated head and neck cancer[275]:

- Platinum-based chemotherapy alone
- Chemotherapy plus cetuximab
- SBRT alone
- SBRT plus cetuximab
- IMRT plus chemotherapy

Cohorts were followed for 3 years and the Markov cycle length was 1 month.[275] Cost estimates for each treatment strategy were based on Medicare reimbursement unadjusted national rates, derived from current procedural terminology codes, in 2016.[275] Medicare reimbursement data accounted for technical (hospital) and professional (physician) fees for each treatment strategy.[275] Total costs were estimated from the Center for Medicare & Medicaid Services and the Agency for Healthcare Research and Quality, and Healthcare Cost and Utilization Project data.[275] Both costs and utilities were discounted at an annual rate of 3%.[275] The analysis was based on a payer's perspective for the health care services (direct medical costs), with WTP threshold of $100 000 per QALY gained.[275]

The common baseline therapy was chemotherapy alone (the least costly and the least effective).[275] No treatment strategy was cost-effective at the WTP threshold of $100 000 per QALY gained.[275]

- SBRT alone had an ICER of $150,866 per QALY gained.
- SBRT plus cetuximab had an ICER of $219,509 per QALY gained.
- IMRT plus chemotherapy was absolutely dominated (i.e., less effective and more costly than SBRT alone and SBRT plus cetuximab).
- Chemotherapy plus cetuximab (current standard of care) was the least cost-effective therapy among all other therapies.

In one-way sensitivity analyses, results were most sensitive to median survival and utility of tumor progression.[275] If median survival was 11 months or longer, the SBRT alone strategy was lower than $100,000 per QALY gained.[275] If median survival was 13 months or longer, SBRT plus cetuximab was lower than $100,000 per QALY gained.[275] No variation in the tumor progression utility values caused a strategy to meet the WTP threshold.[275] Probabilistic sensitivity analysis demonstrated chemotherapy alone was favored in 65% of model iterations, in 16% for SBRT alone, 15% for IMRT plus chemotherapy, 6% for SBRT plus cetuximab, and in 0.5% of model iterations for chemotherapy plus cetuximab at the $100,000 WTP threshold.[275]

Liver Cancer

We identified 1 study comparing costs and resource use for patients with early-stage HCC treated with SBRT or RFA using the SEER Program-Medicare database.[218] Rates of 90-day hospitalization were higher in the RFA group, but the results were not statistically significant (27.2% in the RFA group; $P = .06$).[218] When costs were compared:

- Total costs were significantly lower in the SBRT group ($51,746 SBRT vs. $85,016 RFA; $P = .02$)
- Inpatient costs were significantly lower in the SBRT group ($23,360 SBRT vs. $54,053 RFA; $P = .02$)
- 90-day outpatient costs were significantly higher in the SBRT group ($15,478 SBRT vs. $5,760 RFA; $P < .001$)
- There was no difference between SBRT and RFA for outpatient costs, Part D medication costs, 90-day overall costs, 90-day inpatient costs, or in the median cost per median life-year gained ($38,810 SBRT vs. $40,777; *P* value not reported).[218]

The full sample bootstrap median ICER was $61,164 (95% CI, $420,299 to 367,960), meaning that SBRT was not cost-effective compared with RFA in the overall population; however, 85.5% of the bootstrap ICER estimates were lower than the WTP threshold of $100,000.[218]

Oligometastatic Cancer

The economic analysis aimed to assess whether adding SBRT to standard therapy represents a cost-effective strategy among cancer patients with oligometastatic disease.[277] The Markov cost-effectiveness model used a monthly cycle length and extended the model over a lifetime horizon.[277] Patient outcomes were based on findings from the SABR-COMET trial.[244] The costs of SBRT were estimated from current Medicare reimbursement rates, which included the cost of a radiation oncology consultation, simulation, radiation planning, and a 5-day course of treatment.[277] Costs were converted to 2019 dollars using the Consumer Price Index to account for inflation.[277] The analysis used a 3% annual discount rate for all costs and QALYs, and reported cost-effectiveness from the health care sector and societal perspectives, with a WTP threshold of $100,000.[277]

From the health care sector perspective, the base case analysis found SBRT increased the overall cost of treatment by $54,260, from $405,901 with standard therapy to $460,161 with SBRT.[277] From the societal perspective, SBRT increased the overall cost of treatment by $72,799, from $472,544 with standard therapy to $545,343 with SBRT[277]. Effectiveness was increased with SBRT by 1.88 QALYs, from 2.96 QALY on standard therapy to 4.84 QALY with SBRT. The ICER for SBRT compared with standard therapy was $28,906 per QALY (health care sector perspective) and $38,783 per QALY (societal perspective); both were considered cost-effective at a WTP threshold of $100,000 per QALY.[277] The model was modestly sensitive to assumptions about tumor progression, although the model was not sensitive to assumptions about survival or cost of treatment.[277] Probabilistic sensitivity analyses demonstrated SBRT was the cost-effective treatment option 99.8% (health care sector perspective) or 98.7% (societal perspective) of the time.[277]

In another analysis based on the SABR-COMET trial,[244] the model was designed to assess the cost-effectiveness of SBRT compared with standard care over the trial duration of 6 years, using a cycle length of 1 month.[278] The analysis was performed in a US setting from a health care perspective, and adopted a WTP of $100,000.[278] In the base case analysis of the total study population over the trial duration of 6 years, SBRT led to an increased effectiveness of 0.78 QALY at increased costs of $1,133, with an ICER of $1,446 per QALY.[278] When additional long-term SEER data were applied, SBRT led to an increased effectiveness of 1.34 QALY at additional costs of $52,180.[278] Results were sensitive to systemic therapy costs, with higher costs of oligometastatic disease and lower costs of polymetastatic disease leading to unfavorable ICER values, lower costs for therapy of oligometastatic state, and higher costs of polymetastatic state leading to favorable ICERs.[278] It remained cost-effective even when the costs for SBRT and salvage SBRT were increased up to around 8 times for the study duration and for long-term survival.[278] Overall, SBRT was cost-effective in 100% of Monte Carlo simulation runs.[278]

Bone Cancer

Using a claims-based Medicare data set for the years 2015 to 2017, the costs of SBRT were estimated to be $11,868 ($1,774 in provider fees and $10,094 in technical fees).[279] For people

with bone metastases, the cost of SBRT was significantly higher for both professional and technical fees ($679 lower provider costs and $6,422 lower technical costs for external beam RT; $36 lower provider costs and $2,534 lower technical costs for IMRT; $P < .001$).[279]

Summary

Based on the studies included in this review, we conclude that SBRT:

- May be similarly or more effective than other options for men with localized prostate cancer (very low to moderate certainty of evidence [CoE], based on 3 RCTs and 7 comparative NRSs)
- May be similarly or more effective than radiation therapy for inoperable stage II NSCLC (low CoE, based on 1 comparative NRS) or in combination with pembrolizumab than pembrolizumab alone for advanced NSCLC (low to moderate CoE, based on 1 RCT). SBRT also appears to be similarly or more effective than cRT for people with lung metastases (very low to low CoE, based on 4 comparative NRSs) or LCNEC of the lung (low CoE, based on 2 comparative NRSs). In general, surgery appears to be more effective than SBRT for resectable lung cancer (very low to low CoE, based on 10 comparative NRSs)
- In combination with nivolumab and ipilimumab, may be as effective as nivolumab and ipilimumab for Merkel cell carcinoma (low CoE, based on 1 RCT)
- May be less effective than ablation (RFA, microwave, or cryoablation) or surgery for stage 1 renal cell carcinoma (low CoE, based on 1 comparative NRS)
- May be more effective than chemotherapy or intensity-modulated radiation therapy for unresected pancreatic cancer (low CoE, based on 1 comparative NRS);
- May be more effective than conventional RT for pancreatic cancer (low CoE, based on 1 comparative NRS);
- May be similarly effective to brachytherapy, when used as a boost treatment after cRT for early-stage oropharyngeal cancer (low CoE, based on 1 comparative NRS)
- May be less effective than charged particle RT for recurrent or metastatic head and neck cancer, but similar in effectiveness to IMRT and conformal RT (low to moderate CoE, based on 1 RCT and 3 comparative NRSs)
- May be as effective as RFA for early-stage liver cancer; however, results were mixed (very low to low CoE, based on 4 comparative NRSs)
- Alone, or in combination with TACE, may be as effective as RFA or TACE alone for small liver cancers (very low to low CoE, based on 4 comparative NRSs) and for unresectable liver cancer (low CoE, based on 8 comparative NRSs)
- May be more effective than sorafenib for advanced liver cancer (very low to low CoE, based on 1 comparative NRS)
- May be similarly or more effective than other options (RFA, TACE, HIFU) when used as a bridging therapy for people on the waiting list for liver transplantation due to liver cancer (very low to low CoE, based on 2 comparative NRSs)
- May be more effective than sorafenib for advanced liver cancer (very low to low CoE, based on 1 comparative NRS)
- May be more effective than TARE for unresectable intrahepatic cholangiocarcinoma (low CoE, based on 1 comparative NRS)
- Appears to be more effective than standard of care or observation for oligometastatic cancer (low to moderate CoE, based on 3 RCTs); however, for oligometastatic prostate cancer,

elective nodal radiation therapy may be more effective than SBRT (very low to low CoE, based on 2 comparative NRSs)
- May be as effective as multifraction RT for painful bone metastases (moderate CoE, based on 1 RCT)

No comparative studies were identified on the use of SBRT for adrenal cancer or large tumors. Few studies reported on clinical subgroups of interest, but there was some indication that specific populations (by cancer site) may be more likely to benefit from SBRT compared with other populations. However, subgroups varied by cancer type and treatment site, and were often only reported in single studies.

Overall, SBRT was not associated with significantly higher rates of toxicity than other treatment options. The types of toxicity varied by treatment site, and rates of grade 4 and 5 toxicities were rare.

While the economic literature was sparse, SBRT appears to be:
- Possibly cost-effective for oligometastatic hormone-resistant prostate cancer (low CoE, based on 1 economic modeling study)
- Lower in costs than IMRT for prostate cancer (very low CoE, based on 1 comparative NRS)
- Cost-ineffective when compared with maintenance therapy for oligometastatic lung cancer (moderate CoE, based on 1 economic modeling study)
- Higher in costs than cRT or chemotherapy for pancreatic cancer (very low CoE, based on 1 comparative NRS)
- Cost-ineffective as reirradiation when compared with other salvage therapies, including IMRT with chemotherapy, for head and neck cancer (moderate CoE, based on 1 economic modeling study)
- Cost-ineffective when compared with RFA for liver cancer (low CoE, based on 1 economic modeling study)
- Cost-effective when compared with standard of care for oligometastatic cancer (moderate CoE, based on 2 economic modeling studies)
- More expensive than EBRT and IMRT for bone cancer

FDA Reported Harms

Very few reports in the FDA's Medical Device Recall database were classified as Class 1 (defined as a situation where there is a reasonable chance that a product will cause serious health problems or death), and these were related to software and placement issues. Similar safety issues were reported to the FDA's MAUDE database (Appendix F).

Clinical Practice Guidelines

A total of 25 eligible guidelines made recommendations on the use of SBRT (also referred to as ultrahypofractionated radiotherapy). By cancer type and by order of disease prevalence in Washington state, these include:
- 3 on prostate cancer, in 5 publications[29,281-284]
  - We rated 2 of the guidelines as being of good methodological quality[29,281-283] and 1 as poor methodological quality because detailed methods and processes were not described.[284]

- 4 on lung cancer, in 5 publications[285-289]
  - We assessed 2 of the guidelines as being of good methodological quality[285,288] and 2 as being of moderate methodological quality because of limited reporting around methods and processes.[287,289]
- 3 on colorectal cancer[290-292]
  - We assessed 2 of the guidelines as being of good methodological quality[290,292] and 1 as being of moderate methodological quality because of limited reporting around methods and processes.[291]
- 2 on gynecological cancer[293,294]
  - We assessed both of the guidelines to be of good methodological quality.[293,294]
- 1 on melanoma[295]
  - We assessed this guideline as being of being of moderate methodological quality because of limited reporting around methods and processes.[295]
- 4 on renal cancer[296-300]
  - We assessed 2 of the guidelines as being of good methodological quality[296,297,299] and 2 as being of moderate methodological quality because of limited reporting around methods and processes.[298,300]
- 1 on pancreatic cancer[301]
  - We assessed this guideline as being of being of good methodological quality.[301]
- 4 on liver & biliary tract cancer[302-305]
  - We assessed 2 of the guidelines as being of good methodological quality[302,303] and 2 as being of moderate methodological quality because of limited reporting around methods and processes.[304,305]
- 2 on nonspine bone cancer[306,307]
  - We assessed 1 guideline as being of moderate methodological quality because of limited reporting around methods and processes[306] and 1 as being of poor methodological quality, with no information on methods or processes.[307]
- 1 on testicular cancer[308]
  - We assessed the guideline as being of moderate methodological quality because of because of limited reporting around methods and processes.[308]

Prostate Cancer

The eligible guidelines made primarily conditional recommendations on the use of SBRT as an option for treating prostate cancer (Table 38).

- The recommendations in the 2022 joint American Society for Radiation Oncology and American Urological Association (ASTRO/AUA) guidelines are described as strong recommendations on the use of SBRT for low- or intermediate-risk localized prostate cancer; however, the wording suggests a more conditional approach with SBRT being offered as an option.[29,281,282]
- The European Association of Urology (EAU) joint guidelines recommend SBRT solely as a subject for future investigation.[283]
- The guidelines from the Australian and New Zealand Faculty of Radiation Oncology Genito-Urinary Group (FROGG) recommend SBRT an option for metastatic disease or as salvage therapy with inconsistent, low-quality evidence.[284] The guideline also highlights the need for more clinical trials.[284]

Table 38. Excerpted Clinical Practice Recommendations on Stereotactic Body Radiation Therapy for Prostate Cancer

Organization and Year Title Methodological Quality	Recommendations	
American Society for Radiation Oncology and American Urological Association (ASTRO/AUA), 2022 Clinically localized prostate cancer: AUA/ASTRO guideline, part I[281]; part II[282]; and part III[29] Good methodological quality	Clinicians may offer ultrahypofractionated EBRT for patients with low- or intermediate-risk prostate cancer who elect EBRT.	Strong recommendation; evidence level: grade A
	In patients with low- or favorable intermediate-risk prostate cancer electing radiation therapy, clinicians should offer dose-escalated hypofractionated EBRT (moderate or ultra), permanent low-dose rate (LDR) seed implant, or temporary high-dose rate (HDR) prostate implant as equivalent forms of treatment.	Strong recommendation; evidence level: grade B
Prostate Cancer Guidelines Panel, 2022 EAU - EANM - ESTRO - ESUR - ISUP - SIOG guidelines on prostate cancer[283] Good methodological quality	SBRT was discussed in literature review but panel concluded there was not enough evidence to make recommendations on its use.	Available evidence is of low quality; strong recommendations cannot be made.
Australian and New Zealand Faculty of Radiation Oncology Genito-Urinary Group (FROGG), 2018 Radiotherapy for recurrent prostate cancer: 2018 Recommendations of the Australian and New Zealand Radiation Oncology Genito-Urinary group[284] Poor methodological quality	3.4. Recurrence limited to pelvic lymph nodes after curative local treatment: SBRT alone to involved node(s) may be considered in selected patients, but these patients should be informed that they are at high risk of relapse which may be harder to treat with curative intent	5, D • Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles" • Level 5 evidence or troublingly inconsistent or inconclusive studies of any level
	Radiotherapy management of oligometastases: 4.3. Patients should be encouraged to enter clinical trials where available to ascertain potential benefit of SBRT in addition to standard of care systemic therapy	4, D • Case-series (and poor-quality cohort and case-control studies • Level 5 evidence or troublingly inconsistent or inconclusive studies of any level
	5.4. If considering salvage local therapy, options include salvage prostatectomy, brachytherapy, stereotactic radiotherapy, HIFU, cryotherapy and salvage electroporation. Local salvage treatments are associated with significant toxicity and	4, C • Case-series (and poor-quality cohort and case-control studies • Level 4 studies or extrapolations from level 2 or 3 studies

Organization and Year Title Methodological Quality	Recommendations	
	an individualized-treatment approach is recommended. Suitable patients should be considered for clinical trials.	

Abbreviations. EANM: European Association of Nuclear Medicine; EAU: European Association of Urologists; EBRT: external beam radiation therapy; ESTRO: European SocieTy for Radiotherapy and Oncology; ESUR: European Society of Urogenital Radiotherapy; ISUP: International Society of Urological Pathology; SBRT: stereotactic body radiation therapy; SIOG: International Society of Geriatric Oncology.

Lung Cancer

Overall, the guidelines indicate there is some evidence for the use of SBRT for lung cancer, although the evidence quality is generally moderate-to-low, and it is usually recommended for patients who refuse or who are at high risk for surgery, lobectomy, or chemotherapy. For patients who are operable, SBRT is still considered a therapy under investigation in the current guidelines (Table 39). [285-289]

Table 39. Excerpted Clinical Practice Recommendations on Stereotactic Body Radiation Therapy for Lung Cancer

Organization and Year Title Methodological Quality	Recommendations	Strength of Recommendation
American Society of Clinical Oncology (ASCO), 2021 Radiation therapy for small-cell lung cancer: ASCO guideline endorsement of an ASTRO guideline[285] Good methodological quality	Recommendation 2.1. For patients with stage I or II node-negative LS-SCLC who are medically inoperable, either SBRT or conventional fractionation is recommended. • Ultracentral tumors (ASCO clarifying comment: meaning those with the planning target volume touching or overlapping the proximal bronchial tree, esophagus, or trachea) may be more appropriately treated with conventional fractionation schema.	Strength of recommendation: strong Quality of evidence: moderate
Society of Interventional Radiology (SIR), 2021 Society of Interventional Radiology multidisciplinary position statement on percutaneous ablation of non-small cell lung cancer and metastatic disease to the lungs: endorsed by the Canadian Association for	In patients with stage IA NSCLC, image-guided thermal ablation is a safe and effective treatment with minimal complications and acceptable long-term oncological and survival outcomes that are comparable to SBRT and sublobar resection.	Level C, moderate quality • Nonrandomized studies • Supported by moderate quality evidence for or against recommendation; new research may be able to

Organization and Year Title Methodological Quality	Recommendations	Strength of Recommendation
Interventional Radiology, the Cardiovascular and Interventional Radiological Society of Europe, and the Society of Interventional Oncology[287] Moderate methodological quality	Thermal ablation should be considered alongside surgical resection and SBRT in patients who require preservation of lung parenchyma function.	provide additional context
European Society for Medical Oncology (ESMO), 2020 (update of 2018) Metastatic non-small cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up[289] and Metastatic Non-Small-Cell Lung Cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up 2020 Update[286] Moderate methodological quality	Stage IV patients with limited synchronous metastases at diagnosis may experience long-term disease-free survival (DFS) following systemic therapy and local consolidative therapy [LCT: high-dose RT including stereotactic ablative body RT (SABR) or surgery]	Level IIIB • Prospective cohort studies • Strong or moderate evidence for efficacy but with a limited clinical benefit, generally recommended
National Institute for Health and Care Excellence (NICE), 2018 Lung cancer: diagnosis and management [NG122][288] Good methodological quality	1.6.5. For people with stage I–IIA (T1a–T2b, N0, M0) NSCLC who decline lobectomy or in whom it is contraindicated, offer radical radiotherapy with stereotactic ablative radiotherapy (SABR) or sublobar resection.	Sublobar resection and SABR […] not clear which is better.
	1.6.8. For people with stage I–IIA (T1a–T2b, N0, M0) NSCLC who decline surgery or in whom any surgery is contraindicated, offer SABR. If SABR is contraindicated, offer either conventional or hyperfractionated radiotherapy.	SABR provides better survival outcomes […] people often prefer it because it involves fewer hospital visits.
	1.6.9. For eligible people with stage IIIA NSCLC who cannot tolerate or who decline chemoradiotherapy (with or without surgery), consider radical radiotherapy (either conventional or hyperfractionated).	Evidence was not strong enough to recommend conventional radiotherapy over hyperfractionated regimens or vice versa.

Abbreviations. LS-SCLC: limited-stage small-cell lung cancer; NSCLC: non-small cell lung cancer; SBRT: stereotactic body radiation therapy.

Colorectal Cancer

Overall, guidelines recommend SBRT as an option for metastases of colorectal cancer, particularly in people who are not considered candidates for surgery (Table 40).[290-292]

Table 40. Excerpted Clinical Practice Recommendations on Stereotactic Body Radiation Therapy for Colorectal Cancer

Organization and Year Title Methodological Quality	Recommendations	Strength of Recommendation
American Society of Clinical Oncology (ASCO), 2022 Treatment of metastatic colorectal cancer: ASCO guideline[290] Good methodological quality	6.1. Stereotactic body radiation therapy may be recommended following systemic therapy for patients with oligometastases of liver who are not considered candidates for resection.	Evidence quality: low Strength of recommendation: weak
European Society for Medical Oncology (ESMO), 2022 Metastatic colorectal cancer: ESMO clinical practice guideline for diagnosis, treatment and follow-up[291] Moderate methodological quality	Treatment of potentially resectable metastatic colorectal cancer: • "Other ablative techniques, such as thermal ablation (TA) or stereotactic body radiotherapy (SBRT), may be added to surgery to achieve a complete treatment or provide an alternative to resection if inoperable due to frailty or poor anatomical location for resection."	III, B • Prospective cohort studies • Strong or moderate evidence for efficacy but with a limited clinical benefit, generally recommended
National Institute for Health and Care Excellence (NICE), 2021 Colorectal cancer [NG151][292] Good methodological quality	1.5.7. Consider metastasectomy, ablation or stereotactic body radiation therapy for people with lung metastases that are suitable for local treatment, after discussion by a multidisciplinary team that includes a thoracic surgeon and a specialist in nonsurgical ablation.	"As there was limited evidence, the committee made recommendations based on their clinical knowledge. There was not enough evidence to recommend one treatment over another even though the current first choice is to perform surgery over stereotactic body radiation therapy or ablation."

Gynecological Cancers

In summary, the eligible guidelines make conditional recommendations for use of SBRT for certain types of patients, specifically those with metastases or who are at high surgical risk (Table 41).[293,294] Evidence quality, when provided, is low. The European Society of Gynaecological Oncology guidelines on cervical cancer are currently being updated and expected to publish in early 2023.[309]

Table 41. Excerpted Clinical Practice Recommendations on Stereotactic Body Radiation Therapy for Gynecologic Cancers

Organization and Year Title Methodological Quality	Recommendations	Strength of Recommendation
European Society of Gynaecological Oncology (ESGO), 2018 European Society of Gynaecological Oncology/European Society for Radiotherapy and Oncology/European Society of Pathology Guidelines for management of patients with cervical cancer[293] Good methodological quality	Pelvic sidewall recurrence after primary surgery • Definitive radiotherapy or chemoradiotherapy followed by a stereotactic ablative boost/image-guided interstitial brachytherapy/particle beam therapy is an emerging option.	Not provided
	Central pelvic or pelvic sidewall recurrence after radiotherapy or chemoradiotherapy • Management of isolated organ metastases (lung, liver, etc.) should be discussed in a multidisciplinary team involved in treatment of specific organ affected by metastasis and should be treated according to preferred method for that organ involving local resection, radiofrequency ablation, interventional brachytherapy, or stereotactic ablative radiotherapy according to size and anatomical position.	Not provided
European Society of Gynaecological Oncology (ESGO), 2020 ESGO/ESTRO/ESP guidelines for management of patients with endometrial carcinoma[294] Good methodological quality	Radiotherapy pretreated patients with locoregional recurrence • If surgery is not feasible, radical re-irradiation options include stereotactic body radiotherapy targeting recurrence, permanent seed implants, or proton therapy. In selected cases, limited volume re-irradiation with EBRT and brachytherapy boost may be an option (especially if longer interval from first irradiation).	IV, C • Retrospective cohort studies or case–control studies • Insufficient evidence for efficacy or benefit does not outweigh risk or disadvantages (adverse events, costs, etc.), optional

Organization and Year Title Methodological Quality	Recommendations	Strength of Recommendation
	Oligometastatic recurrent disease • Treatment options include: surgery, radiation therapy including stereotactic radiotherapy, and local ablating techniques	IV,5 B • Retrospective cohort studies or case–control studies • Insufficient evidence for efficacy or benefit does not outweigh risk or disadvantages (adverse events, costs, etc.), optional

Abbreviations. ESP: European Society of Pathology; ESTRO: European SocieTy for Radiotherapy and Oncology.

Melanoma

For melanoma, the 1 eligible guideline recommends the use of SBRT for locoregional recurrence or single distant metastases, based on low-quality evidence (Table 42).[295]

Table 42. Excerpted Clinical Practice Recommendations on Stereotactic Body Radiation Therapy for Melanoma

Organization and Year Title Methodological Quality	Recommendations	Strength of Recommendation
European Society for Medical Oncology (ESMO), 2019 Cutaneous melanoma: ESMO clinical practice guidelines for diagnosis, treatment and follow-up Approved by the ESMO Guidelines Committee: February 2002, last update September 2019[295] Moderate methodological quality	Surgical removal or stereotactic irradiation of locoregional recurrence or single distant metastasis should be considered in fit patients, as a therapeutic option, offering potential for long-term disease control.	III, C • Prospective cohort studies • Insufficient evidence for efficacy or benefit does not outweigh risk or disadvantages (adverse events, costs, etc.), optional

Renal Cancer

Overall, the guidelines make conditional recommendations on the use of SBRT for certain clinical situations, particularly for metastatic disease or when patients are considered unsuitable for surgery, based on low- to moderate-quality evidence.[296-300] However, guidelines also highlight the need for future clinical trials on the use of SBRT in renal cancer.[296-299]

Table 43. Excerpted Clinical Practice Recommendations on Stereotactic Body Radiation Therapy for Renal Cancer

Organization and Year Title Methodological Quality	Recommendations	Strength of Recommendation
National Comprehensive Cancer Network (NCCN), 2022 Kidney Cancer, Version 3.2022 Moderate methodological quality	Resection is preferred over locally ablative procedures (e.g., image-guided ablation or SBRT However, these local techniques can be considered for liver or lung oligometastases In patients with a limited number of liver or lung metastases, ablative radiotherapy to the metastatic site can be considered in highly selected cases or in the setting of a clinical trial. Radiotherapy should not be used in the place of surgical resection. Radiotherapy should be delivered in a highly conformal manner. The techniques can include 3D conformal radiation therapy, intensity-modulated radiation therapy (IMRT), or SBRT SBRT may be considered for medically inoperable patients with Stage I kidney cancer (category 2B), with Stage II/III kidney cancer (both category 3)	Not reported
European Association of Urology (EAU), 2022 EAU guidelines on renal cell carcinoma[297] Good methodological quality	Local therapy of metastases in metastatic RCC • "Offer stereotactic radiotherapy for clinically relevant bone- or brain metastases for local control and symptom relief." Local ablative therapy • "Although early results of [SBRT] are encouraging, more evidence from randomised trials is needed."	Weak
American Urology Association (AUA), 2021 Renal mass and localized renal cancer: evaluation, management, and follow-up: AUA guideline: Part I[296] and Part II[299]	"Non-extirpative methods, eg, stereotactic-body-radiation-therapy or high-intensity-focused-ultrasound, are still investigational." (Pt 1)	Not applicable

Organization and Year Title Methodological Quality	Recommendations	Strength of Recommendation
Good methodological quality		
European Society for Medical Oncology (ESMO), 2019 Renal cell carcinoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up Approved by ESMO Guidelines Committee: September 2008, last update January 2019. This publication supersedes previously published version—Ann Oncol 2016; 27 (Suppl 5): v58 to v68[298] Moderate methodological quality	Management of advanced/metastatic disease • RT can be used to treat unresectable local or recurrent disease and in patients unsuitable for surgery due to poor PS or unsuitable clinical condition. RT is an alternative if radioablation is not appropriate. Image-guided RT techniques such as VMAT or SBRT are needed to enable a high dose to be delivered.	IV, B • Retrospective cohort studies or case-control studies • Strong or moderate evidence for efficacy but with a limited clinical benefit, generally recommended

Abbreviations. PS: performance status; RCC: renal cell carcinoma; RT: radiation therapy; SBRT: stereotactic body radiotherapy; VMAT: volumetric-modulated arc therapy.

Pancreatic Cancer

The ASTRO guidelines from 2019 make conditional recommendations on the use of SBRT as an option for treating pancreatic cancer, based on very low- to low-quality evidence.[301] However, the guidelines note that following surgical resection, SBRT should only be used in the context of research.[301]

Table 44. Excerpted Clinical Practice Recommendations on Stereotactic Body Radiation Therapy for Pancreatic Cancer

Organization and Year Title Methodological Quality	Recommendations	Strength of Recommendation
American Society for Radiation Oncology (ASTRO), 2019 Radiation Therapy for Pancreatic Cancer: Executive Summary of an ASTRO Clinical Practice Guideline[301] Good methodological quality	a. Following surgical resection of pancreatic cancer, adjuvant SBRT is only recommended on a clinical trial or multi-institutional registry.	Strong recommendation Very low quality of evidence; 100% consensus
	b. For patients with borderline resectable pancreatic cancer and select locally advanced pancreatic cancer appropriate for downstaging prior to surgery, a neoadjuvant therapy regimen of systemic chemotherapy followed by multifraction SBRT is conditionally recommended.	Conditional recommendation Low quality of evidence; 77% consensus

Organization and Year Title Methodological Quality	Recommendations	Strength of Recommendation
	c. For patients with locally advanced pancreatic cancer not appropriate for downstaging to eventual surgery, a definitive therapy regimen of systemic chemotherapy followed by either (1) conventionally fractionated RT with chemotherapy, (2) dose-escalated chemoradiation, or (3) multifraction SBRT without chemotherapy is conditionally recommended.	Conditional recommendation Low quality of evidence; 77% consensus

Abbreviations. RT: radiation therapy; SBRT: stereotactic body radiation therapy.

Liver and Biliary Tract Cancer

For biliary tract cancer, SBRT is conditionally recommended in specific situations, with low-moderate evidence quality.[304] For hepatocellular carcinoma, SBRT is an alternative for treatment of local failure in certain tumors, again with low- to moderate-quality evidence.[302,303,305] American College of Radiology (ACR) appropriateness criteria state SBRT may be appropriate for a range of specific hepatocellular cancer types; however, details of the strength of evidence is not provided.[302]

Table 45. Excerpted Clinical Practice Recommendations on Stereotactic Body Radiation Therapy for Liver and Biliary Tract Cancer

Organization and Year Title Methodological Quality	Recommendations	Strength of Recommendation
American College of Radiology (ACR), 2022 American College of Radiology ACR appropriateness criteria management of liver cancer[302] Good methodological quality	*Note. The recommendations list it as "EBRT" but discussion shows that they mean SBRT.* Hepatocellular cancer • Solitary tumor less than 3 cm, cirrhotic - may be appropriate • Solitary tumor 3 to 5 cm, cirrhotic - may be appropriate • Multifocal, bilobar disease, at least 1 tumor greater than 5 cm, cirrhotic - may be appropriate • Solitary or multifocal disease with vascular invasion, cirrhotic - may be appropriate Intrahepatic cholangiocarcinoma • Peripheral hepatic lobar cholangiocarcinoma, less than 3 cm; no biliary ductal dilatation, macroscopic vascular invasion, regional lymphadenopathy, or distant metastases - may be appropriate	Not provided

Organization and Year Title Methodological Quality	Recommendations	Strength of Recommendation
	Ductal cholangiocarcinoma • Hilar cholangiocarcinoma, greater than 3 cm with poorly defined margins, vascular invasion, and periportal lymphadenopathy - may be appropriate Metastatic liver disease • Multifocal metastatic neuroendocrine tumor (includes carcinoid tumors as well as islet cell tumors of the pancreas) - may be appropriate • Solitary colorectal liver metastasis - may be appropriate • Multifocal bilobar colorectal carcinoma (liver dominant or isolated) - usually not appropriate	
American Society for Radiation Oncology (ASTRO), 2022 External beam radiation therapy for primary liver cancers: an ASTRO clinical practice guideline[303] Good methodological quality	*Note: SBRT is described as ultrahypofractionated EBRT.* a. For patients with HCC who are potential candidates for OLT, ultra- or moderately hypofractionated EBRT is conditionally recommended as a bridge to transplant or as a downstaging intervention.	Strength of recommendation: conditional Quality of evidence: low
	b. For patients with liver-confined HCC, for whom EBRT is recommended, dose-escalated ultra- or moderately hypofractionated EBRT is recommended, with choice of regimen based on tumor location, underlying liver function, and available technology.	Strength of recommendation: strong Quality of evidence: moderate
	c. For patients with unresectable IHC receiving EBRT, dose-escalated ultra- or moderately hypofractionated EBRT is conditionally recommended with fractionation based on tumor location, underlying liver function, and available technology. Implementation remark: Concurrent systemic therapy should not be used with ultrahypofractionated EBRT.	Strength of recommendation: conditional Quality of evidence: low
European Society for Medical Oncology (ESMO), 2022 Biliary tract cancer: ESMO clinical practice guideline for diagnosis, treatment and follow-up[304]	SBRT can be considered for patients with IHC in case of contraindication to surgery for liver-limited disease in palliative setting.	III, C • Prospective cohort studies • Insufficient evidence for efficacy or benefit does not outweigh the risk or the disadvantages

Organization and Year Title Methodological Quality	Recommendations	Strength of Recommendation
Moderate methodological quality		(adverse events, costs, etc.), optional
European Society for Medical Oncology (ESMO), 2018 Hepatocellular carcinoma: ESMO clinical practice guidelines for diagnosis, treatment and follow-up[305] Moderate methodological quality	High conformal HDR radioablation and SBRT may be considered as alternatives for ablation of tumors with a high risk of local failure after thermal ablation due to location.	III, C • Prospective cohort studies • Insufficient evidence for efficacy or benefit does not outweigh risk or disadvantages (adverse events, costs, etc.), optional

Abbreviations. EBRT: external beam radiation therapy; HCC: hepatocellular carcinoma; HDR: high dose rate; IHC: intrahepatic cholangiocarcinoma; OLT: orthotopic liver transplantation; SBRT: stereotactic body radiation therapy.

Bone Cancers

For nonspine bone cancer, SBRT is considered as an option, particularly, again, for localized or metastatic disease. Evidence quality, when provided, is low.

Table 46. Excerpted Clinical Practice Recommendations on Stereotactic Body Radiation Therapy for Bone Cancer

Organization and Year Title Methodological Quality	Recommendations	Strength of Recommendation
European Society for Medical Oncology (ESMO), 2021 Bone sarcomas: ESMO-EURACAN-GENTURIS-ERN PaedCan clinical practice guideline for diagnosis, treatment, and follow-up[306] Moderate methodological quality	a. "For lung metastases, stereotactic RT, radiofrequency ablation (RFA) or cryotherapy might be used as alternative options in patients unfit for surgery [IV, B]. Some groups also consider RFA and stereotactic RT as potentially alternative local treatment options for bone metastases." *Note. Lung metastases from primary bone cancer.*	IV, B • Retrospective cohort studies or case–control studies • Strong or moderate evidence for efficacy but with a limited clinical benefit, generally recommended
	b. "For oligometastatic disease, surgery, RFA, cryotherapy or stereotactic RT can be considered in selected cases."	V, B • Studies without control group, case reports, expert opinions

Organization and Year Title Methodological Quality	Recommendations	Strength of Recommendation
		• Strong or moderate evidence for efficacy but with a limited clinical benefit, generally recommended
	c. "RFA and stereotactic RT are potential alternative local treatment options in patients unfit for surgery and for small lung or bone metastases."	V, B • Studies without control group, case reports, expert opinions • Strong or moderate evidence for efficacy but with a limited clinical benefit, generally recommended
Spanish Society of Radiation Oncology (SEOR), 2022 SEOR SBRT-SG stereotactic body radiation therapy consensus guidelines for nonspine bone metastasis[307] Poor methodological quality	"…it is not possible to clearly differentiate between patients who are candidates for SBRT and those who should undergo prophylactic surgery." "The initial evaluation of patients with NSBM who are potential candidates for SBRT must take into account the performance status of patients" "The use of SBRT in polymetastatic patients in whom not all lesions are susceptible to radical local treatment (SBRT or surgery) has been published but is not the standard of care." "The authors recommended a single fraction as the first treatment option because this scheme requires fewer hospital resources and a shorter hospital stay, an important benefit, especially in the context of the current pandemic. Notwithstanding that recommendation, the most widely accepted fractionation schedules to ensure a BED ≥ 60 Gy are a single fraction of 20–24 Gy, three fractions of 10 Gy each, or five fractions of 7–10 Gy." "Dose de-escalation—defined as more fractions with a lower dose per fraction—should be performed if the lesion has previously been treated with SBRT or EBRT (provided that > 3 months have elapsed between treatments), or if the lesions involve weight-bearing bones, or in	Not provided

Organization and Year Title Methodological Quality	Recommendations	Strength of Recommendation
	patients with moderate-severe (≥ 30%) cortical erosion." "Dose escalation should be considered in metastases with a radiation-resistant histology (e.g., colon, kidney, melanoma, and sarcoma) or if bulky mass or extraosseous involvement is present."	

Abbreviations. BED: biologically equivalent dose; EBRT: external beam radiation therapy; EURACAN: European Reference Network for rare adult solid cancers; GENTURIS ERN: European Reference Network for all patients with one of the rare genetic tumor risk syndromes; NSBM: nonspine bone metastases; RT: radiation therapy.

Testicular Cancer

For testicular cancer, SBRT is considered as an option for salvage treatment; the strength of recommendation was not provided.

Table 47. Excerpted Clinical Practice Recommendations on Stereotactic Body Radiation Therapy for Testicular Cancer

Organization and Year Title Methodological Quality	Recommendations	Strength of Recommendation
European Society for Medical Oncology (ESMO), 2022 Testicular seminoma and non-seminoma: ESMO-EURACAN clinical practice guideline for diagnosis, treatment and follow-up[308] Moderate methodological quality	Salvage treatment • "Principally, all ablative therapies, including stereotactic RT and radiofrequency ablation, should be considered within a multidisciplinary approach with an expert centre."	Not provided

Abbreviations. EURACAN: European Reference Network for rare adult solid cancers; RT: radiation therapy.

Selected Payer Coverage Determinations

We identified no Medicare national coverage determination on the use of SBRT or any local coverage determinations that apply to the state of Washington.

Each of the 3 private payers that we reviewed, Aetna, Cigna, and, Regence, had coverage policies on the use of SBRT.[310]

Aetna considered SBRT as medically necessary in the following clinical conditions[310]:

- Stereotactic body radiation therapy with a CyberKnife, gamma knife, or linear accelerator (LINAC) is considered medically necessary for localized malignant conditions within the body where highly precise application of high-dose radiotherapy is required and clinically appropriate, including:

    - Hepatocellular carcinoma in individuals with unresectable disease considered extensive and not suitable for liver transplantation, or for individuals with local disease only with a good performance status (a score between 80 and 100 on the Karnofsky Performance Scale) but who are not amenable to surgery due to comorbidities
    - Prostate cancer in individuals with organ-confined prostate cancer with Gleason score less than or equal to 8 and prostate-specific antigen (PSA) less than 20
    - Non-small cell lung cancer for inoperable stage I or II tumors
    - Oligometastatic colorectal cancer (1 to 3 metastases to the lung or liver) not amenable to surgery
    - Inoperable primary spinal tumors with compression or intractable pain
    - Recurrent metastatic disease in a previously irradiated area
    - Recurrent localized head and neck cancer
    - Metastatic lesions to the liver when the sole site of disease and cannot be surgically resected or undergo accepted ablation techniques
    - Metastatic disease to the lung when clinically appropriate and on a case-by-case basis
- All other clinical sites or indications are considered experimental and investigational but will be considered on a case-by-case basis.
- Fractionated stereotactic radiotherapy is considered medically necessary when criteria for stereotactic radiosurgery are met. Fractionated stereotactic radiotherapy is useful for treatment of tumors in hard-to-reach locations, tumors with very unusual shapes, or for tumors located in such close proximity to a vital structure (e.g., optic nerve or hypothalamus) that even a very accurate high-dose single fraction of stereotactic radiosurgery could not be tolerated.

Aetna's coverage policy is due to be reviewed in early 2023.[310]

CIGNA has a series of recommendations on the use of the SBRT, reviewed in December of 2022[311]:

- Adrenal cancer
    - SBRT is considered not medically necessary in the adjuvant (post-operative) curative treatment of primary adrenocortical carcinoma.
- Bone metastases
    - SBRT using up to 5 fractions is considered not medically necessary for the treatment of bone metastases except in either of the following clinical scenarios:
        - Treatment to a portion of the spine that has been previously irradiated
        - Treatment of sarcoma, melanoma, and renal cell carcinoma that have metastasized to the spine. SBRT, as a complete course of therapy, must be completed in 5 fractions in a single episode of care.
    - SBRT is considered not to be medically necessary for all other bone metastases.
- Cervical cancer
    - SBRT as an alternative to brachytherapy is considered experimental, investigational, or unproven for the definitive treatment of cervical cancer.
    - SBRT is considered medically necessary based on a history of previous radiation to the same or abutting region and inability to deliver therapeutic doses of radiation with other techniques for locoregional recurrence of cervical cancer in an individual without evidence of distant metastases.

- Head and neck cancer
  - SBRT (up to 5 fractions) may be medically necessary for retreatment in an individual with head and neck cancer who has no evidence of metastatic disease. SBRT, as a complete course of therapy, must be completed in 5 fractions in a single episode of care.
- Liver and hepatobiliary cancer
  - The use of 3 to 5 fractions of SBRT is considered medically necessary to definitely treat concurrently 1 or more tumors in primary hepatocellular carcinoma when there is evidence of the ability to protect an adequate volume of uninvolved liver. SBRT, as a complete course of therapy, must be completed in 5 fractions in a single episode of care.
  - The use of up to 5 fractions of SBRT is considered medically necessary for the definitive treatment of intrahepatic bile duct cancer (cholangiocarcinoma).
  - The use of SBRT is considered not medically necessary for the definitive treatment of extrahepatic bile duct cancer (cholangiocarcinoma).
  - The use of SBRT is considered not medically necessary for adjuvant (postoperative) treatment of extrahepatic bile duct cancer (cholangiocarcinoma).
  - The use of SBRT is considered not medically necessary for definitive treatment of gall bladder cancer.
  - The use of SBRT is considered not medically necessary for adjuvant (postoperative) treatment of gall bladder cancer.
- Renal cell carcinoma
  - The use of 3-dimensional conformal radiation therapy (3DCRT), intensity modulated radiation therapy (IMRT), or SBRT is considered not medically necessary in the definitive treatment of kidney cancer.
- Lung cancer
  - For stage I, node-negative stage IIA or T3N0 (T3 based on size) non-small cell lung cancer (NSCLC), the following regimens are considered medically necessary:
    - Definitive external beam radiation therapy to a dose of 60-70 Gy in 30-35 fractions using 3-dimensional conformal radiation therapy (3DCRT)
    - Up to 5 fractions of stereotactic body radiation therapy (SBRT). SBRT, as a complete course of therapy, must be completed in 5 fractions in a single episode of care
  - For stage I or node-negative stage IIA limited-stage small-cell lung cancer (LSSCLC), the following regimens are considered medically necessary:
    - 3D conformal radiation therapy to a dose of 60-70 Gy in 30-35 fractions or 45 Gy delivered twice daily
    - Up to 5 fractions of stereotactic body radiation therapy (SBRT). SBRT, as a complete course of therapy, must be completed in 5 fractions in a single episode of care.
- Oligometastatic cancer
  - Up to 5 fractions of stereotactic body radiotherapy (SBRT) for extra-cranial oligometastases is considered medically necessary in the following clinical situations:
    - For an individual with non-small cell lung cancer who meets all of the following criteria:
      - Has had or will undergo curative treatment of the primary tumor (based on T and N stage)
      - Has 1 to 3 metastases in the synchronous setting
    - For an individual with colorectal cancer who meets all of the following criteria:

        - Has had or will undergo curative treatment of the primary tumor
        - Presents with 1 to 3 metastases in the lung or liver in the synchronous setting
        - For whom surgical resection is not possible
    - For an individual who meets the following criteria:
        - A clinical presentation of 1 to 3 adrenal gland, lung, liver, or bone metastases in the metachronous setting when ALL of the following criteria are met:
            - Histology is non-small cell lung, colorectal, breast, sarcoma, renal cell, melanoma, or prostate
            - Disease free interval of > 1 year from the initial diagnosis
            - Primary tumor received curative therapy and is controlled
            - No previous evidence of metastatic disease (cranial or extracranial)
            - All metastatic lesions present on imaging will be treated concurrently in a single episode of care
        - SBRT used to stimulate the abscopal effect is considered experimental, investigational, or unproven.
    - For an individual with oligoprogression (progression of a limited number of metastatic sites while other metastatic disease sites remain controlled), SBRT is considered not medically necessary.
    - SBRT, as a complete course of therapy, must be completed in 5 fractions in a single episode of care.
- Pancreatic cancer
    - SBRT using up to 5 fractions is considered medically necessary for curative treatment of unresectable/locally advanced cases and as preoperative treatment in borderlines resectable cases.
    - SBRT is considered not medically necessary in the palliative setting, postoperative setting, or for planned neoadjuvant treatment when the primary tumor is otherwise fully resectable.
- Prostate cancer
    - The following treatments are considered medically necessary for treatment of low-risk prostate cancer:
        - Hypofractionation - 20-28 fractions of IMRT in up to 2 phases
        - Up to 5 fractions of SBRT alone (i.e., not as a boost)
    - The following treatments are considered medically necessary for treatment of intermediate-risk prostate cancer:
        - Hypofractionation - 20-28 fractions of IMRT in up to 2 phases
        - Up to 5 fractions of SBRT alone (i.e., not as a boost)
    - The following treatments are considered medically necessary for treatment of high-risk prostate cancer when not treating the pelvic lymph nodes:
        - Hypofractionation - 20-28 fractions of IMRT in up to 2 phases
        - Up to 5 fractions of SBRT alone (i.e., not as a boost)
- Melanoma
    - The use of SBRT to induce the abscopal effect is considered experimental, investigational, or unproven.
- Soft-tissue sarcoma

- Up to 5 fractions of SBRT is considered medically necessary in the treatment of recurrent soft-tissue sarcoma located within a previously irradiated area.

Regence includes the following in its coverage policy for SBRT[312]:

- SRS and SBRT, also known as SABR, may be considered medically necessary for initial treatment or treatment of recurrence for any of the following indications:
  - Head and neck cancers outside of intracranial, skull base, and orbital sites, when there is documented previous radiation treatment to the planned target volume
  - Hemangioblastoma of the spine
  - Hemangiopericytoma outside of intracranial, skull base, or orbital sites
  - Hepatic tumor (excluding hepatocellular carcinoma; primary or metastatic) as palliative or curative treatment when both of the following are met:
    - Absence or minimal extra hepatic disease; and
    - Karnofsky performance score greater than or equal to 60 or an ECOG score less than or equal to 2
  - Hepatocellular carcinoma (hepatoma) when all of the following criteria are met:
    - 5 or fewer hepatic lesions; and
    - Size of largest lesion is 6 cm diameter or less; and
    - Karnofsky performance score greater than or equal to 60 or an ECOG score less than or equal to 2
  - Lung metastases when both of the following criteria are met:
    - 5 or fewer metastatic lung lesions; and
    - Karnofsky performance score greater than or equal to 60 or an ECOG score less than or equal to 2
  - Non-small cell lung cancer (NSCLC), primary (node negative, tumor stage T1 and T2)
  - Oligometastases when the following criteria are met:
    - 5 or fewer metastatic lesions; and
    - Primary is controlled, stable, or expectation of the same; and
    - Metastases are limited to one to three organs; and
    - Karnofsky performance score greater than or equal to 60 or an ECOG score less than or equal to 2
  - Osteosarcoma, metastatic when all of the following criteria are met:
    - 5 or fewer metastatic lesions; and
    - Karnofsky performance score greater than or equal to 60 or an ECOG score less than or equal to 2
  - Pancreatic adenocarcinoma, locally advanced, borderline resectable, inoperable, or local recurrence after resection
  - Paraganglioma
  - Prostate cancer, very low- to intermediate-risk
  - Renal cell cancer, inoperable primary, when a urological surgeon has documented inoperability
  - Schwannomas
  - Spinal or paraspinal tumors (primary or metastatic)
- SRS and SBRT (also known as SABR) are considered investigational when the first criterion is not met and for all other indications outside of intracranial, skull base, or orbital

- sites, including but not limited to:
  - Tumors, primary, of the cervix, endometrium, esophagus, hemangiomas, large bowel, ovaries, rectum, and small bowel

Ongoing Studies

Details of the eligible ongoing studies can be found in Appendix G. Because of the number of cancer sites of interest, we focused only on ongoing RCTs. In total, we identified 46 ongoing RCTs of SBRT, including for those primary sites where we did not identify any comparative studies for this update review (e.g., breast, ovarian).

Conclusions

The use of SBRT for many cancers remains unsupported with limited or no comparative evidence of effectiveness. However, for other cancer sites, evidence shows SBRT has the potential to be an effective option when compared with cRT. When compared with other forms of RT, the results for SBRT are mixed, depending on the cancer site and the specific type of RT. Some guidelines are more supportive of the use of SBRT, but most note the limited evidence base, highlighting it may be preferred by patients because of the fewer treatment fractions and the favorable safety profile of SBRT.

FDA-reported Harms for Stereotactic Body Radiation Therapy

SBRT appears to be a safe form of RT and adverse events reflect those reported in published studies, but also include device failures and process issues, such as placement errors.

References

1. Cancer.Net. What is radiation therapy? 2022; https://www.cancer.net/navigating-cancer-care/how-cancer-treated/radiation-therapy/what-radiation-therapy. Accessed June 16, 2022.

2. Das IJ, Dawes SL, Dominello MM, et al. Quality and safety considerations in stereotactic radiosurgery and stereotactic body radiation therapy: an ASTRO Safety White Paper update. *Pract Radiat Oncol.* 2022.

3. Paciotti M, Schmidt AL, Ravi P, McKay RR, Trinh QD, Choueiri TK. Temporal trends and predictors in the use of stereotactic body radiotherapy for treatment of metastatic renal cell carcinoma in the US. *Oncologist.* 2021;26(5):e905-e906.

4. McClelland III S, Kim E, Passias PG, Murphy JD, Attia A, Jaboin JJ. Spinal stereotactic body radiotherapy in the United States: a decade-long nationwide analysis of patient demographics, practice patterns, and trends over time. *J Clin Neurosci.* 2017;46:109-112.

5. Mahase SS, D'Angelo D, Kang J, Hu JC, Barbieri CE, Nagar H. Trends in the use of stereotactic body radiotherapy for treatment of prostate cancer in the United States. *JAMA Netw Open.* 2020;3(2):e1920471-e1920471.

6. Gerrity M, Thielke A, Leof A, et al. *Stereotactic radiosurgery and stereotactic body radiation therapy: October 2012 updated evidence report* Portland, OR: Center for Evidence-based Policy, Oregon Health & Science University; 2012.

7. Health Technology Clinical Committee. Stereotactic radiation surgery and stereotactic body radiation therapy. 2013; https://www.hca.wa.gov/assets/program/sbrt_final_findings_decision_041713[1].pdf. Accessed April 13, 2022.

8. Washington State Health Care Authority. Use of stereotactic body radiation therapy. Final key questions and background 2022; https://www.hca.wa.gov/assets/SBRT-final-KQ-20220921.pdf. Accessed January 18, 2023.

9. Mosbaek C, King V, Harrod C. *Stereotactic radiosurgery and stereotactic body radiation therapy: an evidence update* Portland, OR: Center for Evidence-based Policy, Oregon Health & Science University; 2017.

10. Mosbaek C, King V, Harrod C. *Stereotactic radiosurgery and stereotactic body radiation therapy: an evidence update.* Portland, OR: Oregon Health and Science University; 2019.

11. Ruskin M, Shaw B, Robalino S, King V. *Stereotactic radiosurgery and stereotactic body radiation therapy: an evidence update.* Portland, OR: Oregon Health and Science University; 2022.

12. Brouwers MC, Kho ME, Browman GP, et al. AGREE II: advancing guideline development, reporting and evaluation in health care. *CMAJ.* 2010;182(18):E839-842. doi: 10.1503/cmaj.090449.

13. Canadian Agency for Drugs and Technologies in Health. Guidelines for the economic evaluation of health technologies: Canada. 2017; https://www.cadth.ca/sites/default/files/pdf/guidelines_for_the_economic_evaluation_of_health_technologies_canada_4th_ed.pdf. Accessed August 28.

14. Higgins JPT, Green S. Cochrane handbook for systematic reviews of interventions. 2011; http://handbook.cochrane.org/. Accessed April 20, 2017.

15. Scottish Intercollegiate Guidelines Network. Methodology checklist 3: cohort studies. 2012; http://www.sign.ac.uk/checklists-and-notes.html. Accessed May 30, 2018.

16. Scottish Intercollegiate Guidelines Network. Methodology checklist 2: randomised controlled trials. 2015; http://www.sign.ac.uk/checklists-and-notes.html. Accessed May 9, 2017.

17. Guyatt GH, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ.* 2008;336(7650):924-926. doi: 10.1136/bmj.39489.470347.AD.

18. Schünemann H, Brozek J, Guyatt G, Oxman A. GRADE handbook for grading quality of evidence and strength of recommendations. Updated October 2013. The GRADE Working Group, 2013. 2014; http://gdt.guidelinedevelopment.org/app/handbook/handbook.html. Accessed December 15, 2015.

19. Centers for Disease Control and Prevention. US cancer statistics: highlights from 2019 incidence US Cancer Statistics Data Briefs, No. 29. 2022. 2022; https://www.cdc.gov/cancer/uscs/about/data-briefs/no29-USCS-highlights-2019-incidence.htm. Accessed June 17, 2022.

20. United Nations. Human Development Index (HDI). 2021; https://hdr.undp.org/data-center/human-development-index#/indicies/HDI. Accessed January 25, 2023.

21. US Food and Drug Administration. Clinical trial endpoints for the approval of cancer drugs and biologics. Guidance for industry. 2018; https://www.fda.gov/regulatory-information/search-fda-guidance-documents/clinical-trial-endpoints-approval-cancer-drugs-and-biologics. Accessed May 5, 2022.

22. Achard V, Bottero M, Rouzaud M, et al. Radiotherapy treatment volumes for oligorecurrent nodal prostate cancer: a systematic review. *Acta Oncol.* 2020;59(10):1224-1234. doi: 10.1080/0284186X.2020.1775291.

23. Bade BC, Blasberg JD, Mase VJ, Jr., et al. A guide for managing patients with stage I NSCLC: deciding between lobectomy, segmentectomy, wedge, SBRT and ablation-part 3: systematic review of evidence regarding surgery in compromised patients or specific tumors. *J Thorac Dis.* 2022;14(6):2387-2411. doi: 10.21037/jtd-21-1825.

24. Brandao M, Durieux V, Berghmans T. Current and future research efforts in oligometastatic non-small cell lung cancer-a systematic review. *Transl Lung Cancer Res.* 2021;10(7):3473-3485. doi: 10.21037/tlcr-20-964.

25. Cao C, Wang D, Chung C, et al. A systematic review and meta-analysis of stereotactic body radiation therapy versus surgery for patients with non-small cell lung cancer. *J Thorac Cardiovasc Surg.* 2019;157(1):362-373 e368. doi: 10.1016/j.jtcvs.2018.08.075 Accessed 20180915//.

26. Chen D, Zhao M, Xiang X, Liang J. Percutaneous local tumor ablation vs. stereotactic body radiotherapy for early-stage non-small cell lung cancer: a systematic review and meta-analysis. *Chin Med J (Engl).* 2022;135(13):1517-1524. doi: 10.1097/CM9.0000000000002131.

27. Correa RJM, Louie AV, Zaorsky NG, et al. The emerging role of stereotactic ablative radiotherapy for primary renal cell carcinoma: a systematic review and meta-analysis. *Eur Urol Focus.* 2019;5(6):958-969. https://www.eu-focus.europeanurology.com/article/S2405-4569(19)30157-9/fulltext Accessed 20190624//.

28. Dobrzycka M, Spychalski P, Rostkowska O, et al. Stereotactic body radiation therapy for early-stage hepatocellular carcinoma - a systematic review on outcome. *Acta Oncol.* 2019;58(12):1706-1713. doi: 10.1080/0284186X.2019.1657942 Accessed 20190829//.

29. Eastham JA, Auffenberg GB, Barocas DA, et al. Clinically Localized Prostate Cancer: AUA/ASTRO guideline. part III: principles of radiation and future directions. *J Urol.* 2022;208(1):26-33. doi: 10.1097/JU.0000000000002759.

30. Eriguchi T, Takeda A, Nemoto T, et al. Relationship between dose prescription methods and local control rate in stereotactic body radiotherapy for early stage non-small-cell lung cancer: systematic review and meta-analysis. *Cancers (Basel).* 2022;14(15):05. doi: 10.3390/cancers14153815.

31. Facciorusso A, Chierici A, Cincione I, et al. Stereotactic body radiotherapy vs radiofrequency ablation for the treatment of hepatocellular carcinoma: a meta-analysis. *Expert Rev Anticancer Ther.* 2021;21(6):681-688. doi: 10.1080/14737140.2021.1891887 Accessed 20210223//.

32. Foerster R, Zwahlen DR, Buchali A, et al. Stereotactic body radiotherapy for high-risk prostate cancer: a systematic review. *Cancers (Basel).* 2021;13(4):12. doi: 10.3390/cancers13040759.

33. Geng Y, Zhang Q, Feng S, et al. Safety and efficacy of PD-1/PD-L1 inhibitors combined with radiotherapy in patients with non-small-cell lung cancer: a systematic review and meta-analysis. *Cancer Med.* 2021;10(4):1222-1239. doi: 10.1002/cam4.3718.

34. Hunt AA, Choudhury KR, Nukala V, et al. Risk of erectile dysfunction after modern radiotherapy for intact prostate cancer. *Prostate Cancer Prostatic Dis.* 2021;24(1):128-134. doi: 10.1038/s41391-020-0247-x.

35. Ijsseldijk MA, Shoni M, Siegert C, et al. Oncologic outcomes of surgery versus SBRT for non-small-cell lung carcinoma: a systematic review and meta-analysis. *Clin Lung Cancer.* 2021;22(3):e235-e292. doi: 10.1016/j.cllc.2020.04.017 Accessed 20200507//.

36. Jackson WC, Silva J, Hartman HE, et al. Stereotactic body radiation therapy for localized prostate cancer: a systematic review and meta-analysis of over 6,000 patients treated on prospective studies. *Int J Radiat Oncol Biol Phys.* 2019;104(4):778-789. doi: 10.1016/j.ijrobp.2019.03.051.

37. Leaman-Alcibar O, Cigarral C, Deniz C, Romero-Palomar I, Navarro-Martin A. Quality of life after stereotactic body radiation therapy versus video-assisted thoracic surgery in early stage non-small cell lung cancer. Is there enough data to make a recommendation? *J Clin Transl Res.* 2021;7(2):209-220. https://www.ncbi.nlm.nih.gov/pubmed/34104823.

38. Lee J, Shin I-S, Yoon WS, Koom WS, Rim CH. Comparisons between radiofrequency ablation and stereotactic body radiotherapy for liver malignancies: meta-analyses and a systematic review. *Radiother Oncol.* 2020;145:63-70. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med18&NEWS=N&AN=31923711 Accessed 20200107//.

39. Leeman JE, Chen YH, Catalano P, et al. Radiation dose to the intraprostatic urethra correlates strongly with urinary toxicity after prostate stereotactic body radiation therapy: a combined analysis of 23 prospective clinical trials. *Int J Radiat Oncol Biol Phys.* 2022;112(1):75-82. doi: 10.1016/j.ijrobp.2021.06.037.

40. Lehrer EJ, Singh R, Wang M, et al. Safety and survival rates associated with ablative stereotactic radiotherapy for patients with oligometastatic cancer: a systematic review and meta-analysis. *JAMA Oncol.* 2021;7(1):92-106. doi: 10.1001/jamaoncol.2020.6146.

41. Londero F, Grossi W, Morelli A, et al. Surgery versus stereotactic radiotherapy for treatment of pulmonary metastases. A systematic review of literature. *Future Sci OA.* 2020;6(5):FSO471. doi: 10.2144/fsoa-2019-0120.

42. Miura N, Pradere B, Mori K, et al. Metastasis-directed therapy and prostate-targeted therapy in oligometastatic prostate cancer: a systematic review. *Minerva Urol Nefrol.* 2020;72(5):531-542. doi: 10.23736/S0393-2249.20.03779-0.

43. Mortezaee K, Motallebzadeh E, Milajerdi A, Farhood B, Najafi M, Sahebkar A. The effect of prostate cancer radiotherapy on testosterone level: a systematic review and meta-analysis. *Anticancer Agents Med Chem.* 2020;20(6):636-642. doi: 10.2174/1871520620666200128112558.

44. Munoz F, Fiorica F, Caravatta L, et al. Outcomes and toxicities of re-irradiation for prostate cancer: a systematic review on behalf of the Re-Irradiation Working Group of the Italian Association of Radiotherapy and Clinical Oncology (AIRO). *Cancer Treat Rev.* 2021;95:102176. doi: 10.1016/j.ctrv.2021.102176.

45. Park HS, Detterbeck FC, Madoff DC, et al. A guide for managing patients with stage I NSCLC: deciding between lobectomy, segmentectomy, wedge, SBRT and ablation-part 4: systematic review of evidence involving SBRT and ablation. *J Thorac Dis.* 2022;14(6):2412-2436. doi: 10.21037/jtd-21-1826.

46. Peng L, Deng HY, Liu ZK, et al. Wedge resection vs. stereotactic body radiation therapy for clinical stage I non-small cell lung cancer: a systematic review and meta-analysis. *Front Surg.* 2022;9:850276. doi: 10.3389/fsurg.2022.850276.

47. Peyraga G, Lizee T, Khalifa J, et al. Brachytherapy boost (BT-boost) or stereotactic body radiation therapy boost (SBRT-boost) for high-risk prostate cancer (HR-PCa). *Cancer Radiother.* 2021;25(4):400-409. doi: 10.1016/j.canrad.2020.11.004.

48. Rim CH, Kim HJ, Seong J. Clinical feasibility and efficacy of stereotactic body radiotherapy for hepatocellular carcinoma: A systematic review and meta-analysis of observational studies. *Radiother Oncol.* 2019;131:135-144. doi: 10.1016/j.radonc.2018.12.005 Accessed 20181231//.

49. Rim CH, Shin IS, Yoon WS, Park S. Dose-response relationship of stereotactic body radiotherapy for ultracentral tumor and comparison of efficacy with central tumor: a meta-analysis. *Transl Lung Cancer Res.* 2020;9(4):1268-1284. doi: 10.21037/tlcr-20-503.

50. Rodriguez Pla M, Dualde Beltran D, Ferrer Albiach E. Immune checkpoints inhibitors and SRS/SBRT synergy in metastatic non-small-cell lung cancer and melanoma: a systematic review. *Int J Mol Sci.* 2021;22(21):27. doi: 10.3390/ijms222111621.

51. Royce TJ, Mavroidis P, Wang K, et al. Tumor control probability modeling and systematic review of the literature of stereotactic body radiation therapy for prostate cancer. *Int J Radiat Oncol Biol Phys.* 2021;110(1):227-236. doi: 10.1016/j.ijrobp.2020.08.014.

52. Saha A, Dickinson P, Shrimali RK, Salem A, Agarwal S. Is thoracic radiotherapy an absolute contraindication for treatment of lung cancer patients with interstitial lung disease? A systematic review. *Clin Oncol (R Coll Radiol).* 2022;34(12):e493-e504. doi: 10.1016/j.clon.2022.01.043.

53. Schroder C, Tang H, Windisch P, et al. Stereotactic radiotherapy after radical prostatectomy in patients with prostate cancer in the adjuvant or salvage setting: a systematic review. *Cancers (Basel).* 2022;14(3):29. doi: 10.3390/cancers14030696.

54. Shanker MD, Moodaley P, Soon W, Liu HY, Lee YY, Pryor DI. Stereotactic ablative radiotherapy for hepatocellular carcinoma: a systematic review and meta-analysis of local control, survival and toxicity outcomes. *J Med Imaging Radiat Oncol.* 2021;65(7):956-968. doi: 10.1111/1754-9485.13309 Accessed 20210815//.

55. Sun H, Jin C, Wang H, Hu S, Chen Y, Wang H. Cost-effectiveness of stereotactic body radiotherapy in the treatment of non-small-cell lung cancer (NSCLC): a systematic review. *Expert Rev Pharmacoecon Outcomes Res.* 2022;22(5):723-734. doi: 10.1080/14737167.2022.2050217.

56. Tchelebi LT, Lehrer EJ, Trifiletti DM, et al. Conventionally fractionated radiation therapy versus stereotactic body radiation therapy for locally advanced pancreatic cancer (CRiSP): An international systematic review and meta-analysis. *Cancer.* 2020;126(10):2120-2131. doi: 10.1002/cncr.32756.

57. Tetta C, Carpenzano M, Algargoush ATJ, et al. Non-surgical treatments for lung metastases in patients with soft tissue sarcoma: stereotactic body radiation therapy (SBRT) and radiofrequency ablation (RFA). *Curr Med Imaging.* 2021;17(2):261-275. doi: 10.2174/1573405616999200819165709.

58. Tetta C, Londero F, Micali LR, et al. Stereotactic body radiotherapy versus metastasectomy in patients with pulmonary metastases from soft tissue sarcoma. *Clin Oncol (R Coll Radiol).* 2020;32(5):303-315. doi: 10.1016/j.clon.2020.01.005.

59. Valle LF, Lehrer EJ, Markovic D, et al. A systematic review and meta-analysis of local salvage therapies after radiotherapy for prostate cancer (MASTER). *Eur Urol.* 2021;80(3):280-292. doi: 10.1016/j.eururo.2020.11.010.

60. Verma V, Yegya-Raman N, Sprave T, et al. A systematic review of cost-effectiveness studies of stereotactic radiotherapy for cancer oligometastases. *Int J Radiat Oncol Biol Phys.* 2022.

61. Viani GA, Arruda CV, De Fendi LI. Effectiveness and safety of reirradiation with stereotactic ablative radiotherapy of lung cancer after a first course of thoracic radiation: a meta-analysis. *Am J Clin Oncol.* 2020;43(8):575-581. doi: 10.1097/COC.0000000000000709.

62. Viani GA, Arruda CV, Hamamura AC, Faustino AC, Freitas Bendo Danelichen A, Guimaraes FS. Stereotactic body radiotherapy for oligometastatic prostate cancer recurrence: a meta-analysis. *Am J Clin Oncol.* 2020;43(2):73-81. doi: 10.1097/COC.0000000000000635.

63. Viani GA, Gouveia AG, Yan M, Matsuura FK, Moraes FY. Stereotactic body radiotherapy versus surgery for early-stage non-small cell lung cancer: an updated meta-analysis involving 29,511 patients included in comparative studies. *J Bras Pneumol.* 2022;48(3):e20210390. doi: 10.36416/1806-3756/e20210390.

64. Virbel G, Le Fevre C, Noel G, Antoni D. Stereotactic body radiotherapy for patients with lung oligometastatic disease: a five-year systematic review. *Cancers (Basel).* 2021;13(14):20. doi: 10.3390/cancers13143623.

65. Wang BC, Kuang BH, Lin GH. Immunotherapy alone or in combination with stereotactic body radiotherapy in advanced lung cancer: a pooled analysis of randomized clinical trials. *J Oncol.* 2022;2022:7506300. doi: 10.1155/2022/7506300.

66. Wang K, Mavroidis P, Royce TJ, et al. Prostate stereotactic body radiation therapy: an overview of toxicity and dose response. *Int J Radiat Oncol Biol Phys.* 2021;110(1):237-248. doi: 10.1016/j.ijrobp.2020.09.054.

67. Wilt TJ, Ullman KE, Linskens EJ, et al. Therapies for clinically localized prostate cancer: a comparative effectiveness review. *J Urol.* 2021;205(4):967-976. doi: 10.1097/JU.0000000000001578.

68. Yan M, Moideen N, Bratti VF, Moraes FY. Stereotactic body radiotherapy (SBRT) in metachronous oligometastatic prostate cancer: a systematic review and meta-analysis on the current prospective evidence. *Br J Radiol.* 2020;93(1116):20200496. doi: 10.1259/bjr.20200496.

69. Yegya-Raman N, Cao CD, Hathout L, et al. Stereotactic body radiation therapy for oligometastatic gynecologic malignancies: A systematic review. *Gynecol Oncol.* 2020;159(2):573-580. doi: 10.1016/j.ygyno.2020.08.010 Accessed 20200909//.

70. Zaorsky NG, Lehrer EJ, Kothari G, Louie AV, Siva S. Stereotactic ablative radiation therapy for oligometastatic renal cell carcinoma (SABR ORCA): a meta-analysis of 28 studies. *Eur Urol Oncol.* 2019;2(5):515-523. doi: 10.1016/j.euo.2019.05.007 Accessed 20190711//.

71. Zhang B, Leech M. A review of stereotactic body radiation therapy in the management of oligometastatic prostate cancer. *Anticancer Res.* 2020;40(5):2419-2428. doi: 10.21873/anticanres.14211.

72. Zhong J, Slevin F, Scarsbrook AF, et al. Salvage reirradiation options for locally recurrent prostate cancer: a systematic review. *Front Oncol.* 2021;11:681448. doi: 10.3389/fonc.2021.681448.

73. Friedland JL, Freeman DE, Masterson-McGary ME, Spellberg DM. Stereotactic body radiotherapy: an emerging treatment approach for localized prostate cancer. *Technol Cancer Res Treat.* 2009;8(5):387-392. doi: 10.1177/153303460900800509.

74. Katz AJ, Santoro M, Ashley R, Diblasio F, Witten M. Stereotactic body radiotherapy as boost for organ-confined prostate cancer. *Technol Cancer Res Treat.* 2010;9(6):575-582. doi: 10.1177/153303461000900605.

75. King CR, Brooks JD, Gill H, Presti JC, Jr. Long-term outcomes from a prospective trial of stereotactic body radiotherapy for low-risk prostate cancer. *Int J Radiat Oncol Biol Phys.* 2012;82(2):877-882. doi: 10.1016/j.ijrobp.2010.11.054.

76. Townsend NC, Huth BJ, Ding W, et al. Acute toxicity after cyberknife-delivered hypofractionated radiotherapy for treatment of prostate cancer. *Am J Clin Oncol.* 2011;34(1):6-10. doi: 10.1097/COC.0b013e3181c4c7c4.

77. Brand DH, Tree AC, Ostler P, et al. Intensity-modulated fractionated radiotherapy versus stereotactic body radiotherapy for prostate cancer (PACE-B): acute toxicity findings from an international, randomised, open-label, phase 3, non-inferiority trial. *Lancet Oncol.* 2019;20(11):1531-1543. doi: 10.1016/S1470-2045(19)30569-8.

78. Lukka HR, Pugh SL, Bruner DW, et al. Patient reported outcomes in NRG Oncology RTOG 0938, evaluating two ultrahypofractionated regimens for prostate cancer. *Int J Radiat Oncol Biol Phys.* 2018;102(2):287-295. doi: 10.1016/j.ijrobp.2018.06.008.

79. Widmark A, Gunnlaugsson A, Beckman L, et al. Ultra-hypofractionated versus conventionally fractionated radiotherapy for prostate cancer: 5-year outcomes of the HYPO-RT-PC randomised, non-inferiority, phase 3 trial. *Lancet.* 2019;394(10196):385-395. doi: 10.1016/S0140-6736(19)31131-6.

80. Kwan W, Bahl G, Kim D, Ye A, Gagne I, Alexander A. Acute toxicity of ultrahypofractionation compared with moderate hypofractionation in prostate cancer treatment: a randomized trial. *Int J Radiat Oncol Biol Phys.* 2022;113(5):1036-1043. doi: 10.1016/j.ijrobp.2022.04.006.

81. Tree AC, Ostler P, van der Voet H, et al. Intensity-modulated radiotherapy versus stereotactic body radiotherapy for prostate cancer (PACE-B): 2-year toxicity results from an open-label, randomised, phase 3, non-inferiority trial. *Lancet Oncol.* 2022;23(10):1308-1320. doi: 10.1016/S1470-2045(22)00517-4.

82. Fransson P, Nilsson P, Gunnlaugsson A, et al. Ultra-hypofractionated versus conventionally fractionated radiotherapy for prostate cancer (HYPO-RT-PC): patient-reported quality-of-life outcomes of a randomised, controlled, non-inferiority, phase 3 trial. *Lancet Oncol.* 2021;22(2):235-245. doi: 10.1016/S1470-2045(20)30581-7.

83. Andruska N, Fischer-Valuck BW, Agabalogun T, et al. Propensity-weighted survival analysis of SBRT vs. conventional radiotherapy in unfavorable intermediate-risk prostate cancer. *Clin Genitourin Cancer.* 2022;20(2):123-131. doi: 10.1016/j.clgc.2021.11.012.

84. Bernetich M, Oliai C, Lanciano R, et al. SBRT for the primary treatment of localized prostate cancer: The effect of gleason score, dose and heterogeneity of intermediate risk on outcome utilizing 2.2014 NCCN risk stratification guidelines. *Front Oncol.* 2014;4:312. doi: 10.3389/fonc.2014.00312.

85. Glowacki G, Majewski W, Wojcieszek P, Grabinska K, Wozniak G, Miszczyk L. Ultrahypofractionated CyberKnife based stereotactic radiotherapy versus conventional radiotherapy in patients with prostate cancer - acute toxicity evaluation in two phase II prospective studies. *Neoplasma.* 2017;64(4):599-604. doi: 10.4149/neo_2017_421.

86. Halpern JA, Sedrakyan A, Hsu WC, et al. Use, complications, and costs of stereotactic body radiotherapy for localized prostate cancer. *Cancer.* 2016;122(16):2496-2504. doi: 10.1002/cncr.30101.

87. Katz A, Ferrer M, Suarez JF, Multicentric Spanish Group of Clinically Localized Prostate C. Comparison of quality of life after stereotactic body radiotherapy and surgery for early-stage prostate cancer. *Radiat Oncol.* 2012;7:194. doi: 10.1186/1748-717X-7-194.

88. Lee SH, Kim HJ, Kim WC. Prostate-specific antigen kinetics following hypofractionated stereotactic body radiotherapy versus conventionally fractionated external beam radiotherapy for low- and intermediate-risk prostate cancer. *Asia Pac J Clin Oncol.* 2016;12(4):388-395. doi: 10.1111/ajco.12566.

89. Loblaw A, Pickles T, Crook J, et al. Stereotactic ablative radiotherapy versus low dose rate brachytherapy or external beam radiotherapy: propensity score matched analyses of Canadian data. *Clin Oncol (R Coll Radiol).* 2017;29(3):161-170. doi: 10.1016/j.clon.2016.10.001.

90. Monaco A, Sommer J, Akerman M, et al. Four-year quality-of-life outcomes in low- to intermediate-risk prostate cancer patients following definitive stereotactic body radiotherapy versus management with active surveillance. *World J Urol.* 2022;40(9):2213-2219. doi: 10.1007/s00345-022-04084-2.

91. Oliai C, Bernetich M, Brady L, et al. Propensity score matched comparison of SBRT versus IMRT for the treatment of localized prostate cancer. *J Radiat Oncol.* 2016;5:187-195. doi: 10.1007/s13566-015-0237-0.

92. Pan HY, Jiang J, Hoffman KE, et al. Comparative toxicities and cost of intensity-modulated radiotherapy, proton radiation, and stereotactic body radiotherapy among younger men with prostate cancer. *J Clin Oncol.* 2018;36(18):1823. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6008105/pdf/JCO.2017.75.5371.pdf.

93. Patel SA, Switchenko JM, Fischer-Valuck B, et al. Stereotactic body radiotherapy versus conventional/moderate fractionated radiation therapy with androgen deprivation therapy for unfavorable risk prostate cancer. *Radiat Oncol.* 2020;15(1):217. doi: 10.1186/s13014-020-01658-5.

94. Ricco A, Hanlon A, Lanciano R. Propensity score matched comparison of intensity modulated radiation therapy vs stereotactic body radiation therapy for localized prostate cancer: a survival analysis from the National Cancer Database. *Front Oncol.* 2017;7:185. doi: 10.3389/fonc.2017.00185.

95. Ricco A, Manahan G, Lanciano R, et al. The comparison of stereotactic body radiation therapy and intensity-modulated radiation therapy for prostate cancer by NCCN risk groups. *Front Oncol.* 2016;6:184. doi: 10.3389/fonc.2016.00184.

96. Tsang YM, Tharmalingam H, Belessiotis-Richards K, et al. Ultra-hypofractionated radiotherapy for low- and intermediate risk prostate cancer: High-dose-rate brachytherapy vs stereotactic ablative radiotherapy. *Radiother Oncol.* 2021;158:184-190. doi: 10.1016/j.radonc.2021.02.028.

97. Werneburg GT, Kongnyuy M, Halpern DM, et al. Patient-reported quality of life progression in men with prostate cancer following primary cryotherapy, cyberknife, or active holistic surveillance. *Prostate Cancer Prostatic Dis.* 2018;21(3):355-363. doi: 10.1038/s41391-017-0004-y.

98. Yu JB, Cramer LD, Herrin J, Soulos PR, Potosky AL, Gross CP. Stereotactic body radiation therapy versus intensity-modulated radiation therapy for prostate cancer: comparison of toxicity. *J Clin Oncol.* 2014;32(12):1195-1201. doi: 10.1200/JCO.2013.53.8652.

99. Bolzicco G, Favretto MS, Satariano N, Scremin E, Tambone C, Tasca A. A single-center study of 100 consecutive patients with localized prostate cancer treated with stereotactic body radiotherapy. *BMC Urol.* 2013;13:49. doi: 10.1186/1471-2490-13-49.

100. Chen LN, Suy S, Uhm S, et al. Stereotactic body radiation therapy (SBRT) for clinically localized prostate cancer: the Georgetown University experience. *Radiat Oncol.* 2013;8(1):58. doi: 10.1186/1748-717X-8-58.

101. Davis J, Sharma S, Shumway R, et al. Stereotactic body radiotherapy for clinically localized prostate cancer: Toxicity and biochemical disease-free outcomes from a multi-institutional patient registry. *Cureus.* 2015;7(12):e395. doi: 10.7759/cureus.395.

102. Freeman D, Dickerson G, Perman M. Multi-institutional registry for prostate cancer radiosurgery: a prospective observational clinical trial. *Front Oncol.* 2014;4:369. doi: 10.3389/fonc.2014.00369.

103. Fuller DB, Crabtree T, Kane BL, et al. High dose "HDR-Like" prostate SBRT: PSA 10-year results from a mature, multi-institutional clinical trial. *Front Oncol.* 2022;12:935310. doi: 10.3389/fonc.2022.935310.

104. Fuller DB, Falchook AD, Crabtree T, et al. Phase 2 multicenter trial of heterogeneous-dosing stereotactic body radiotherapy for low- and intermediate-risk prostate cancer: 5-year outcomes. *Eur Urol Oncol.* 2018;1(6):540-547. doi: 10.1016/j.euo.2018.06.013.

105. Glowacki G, Majewski W, Wojcieszek P, et al. Acute toxicity of robotic ultrahypofractionated radiotherapy CyberKnifeTM in prostate cancer patients. *Neoplasma.* 2015;62(4):674-682. doi: 10.4149/neo_2015_081.

106. Gurka MK, Chen LN, Bhagat A, et al. Hematuria following stereotactic body radiation therapy (SBRT) for clinically localized prostate cancer. *Radiat Oncol.* 2015;10:44. doi: 10.1186/s13014-015-0351-6.

107. Joh DY, Chen LN, Porter G, et al. Proctitis following stereotactic body radiation therapy for prostate cancer. *Radiat Oncol.* 2014;9(1):277. doi: 10.1186/s13014-014-0277-4.

108. Johansson S, Isacsson U, Sandin F, Turesson I. High efficacy of hypofractionated proton therapy with 4 fractions of 5 Gy as a boost to 50 Gy photon therapy for localized prostate cancer. *Radiat Oncol.* 2019;141:164-173.

109. Katz A. Stereotactic body radiotherapy for low-risk prostate cancer: a ten-year analysis. *Cureus.* 2017;9(9):e1668. doi: 10.7759/cureus.1668.

110. Katz AJ, Kang J. Quality of life and toxicity after SBRT for organ-confined prostate cancer, a 7-year study. *Front Oncol.* 2014;4:301. doi: 10.3389/fonc.2014.00301.

111. Katz AJ, Kang J. Stereotactic body radiotherapy as treatment for organ confined low- and intermediate-risk prostate carcinoma, a 7-year study. *Front Oncol.* 2014;4:240. doi: 10.3389/fonc.2014.00240.

112. Katz AJ, Santoro M, Ashley R, Diblasio F, Witten M. Stereotactic body radiotherapy for organ-confined prostate cancer. *BMC urology.* 2010;10(1):1-10.

113. Katz AJ, Santoro M, Diblasio F, Ashley R. Stereotactic body radiotherapy for localized prostate cancer: disease control and quality of life at 6 years. *Radiation oncology.* 2013;8(1):1-8.

114. Koskela K, Palmgren JE, Heikkila J, et al. Hypofractionated stereotactic body radiotherapy for localized prostate cancer - first Nordic clinical experience. *Acta Oncol.* 2017;56(7):978-983. doi: 10.1080/0284186X.2017.1288923.

115. Ma TM, Ballas LK, Wilhalme H, et al. Quality-of-life outcomes and toxicity profile among patients with localized prostate cancer after radical prostatectomy treated with stereotactic body radiation: the SCIMITAR multicenter phase 2 trial. *Int J Radiat Oncol Biol Phys.* 2023;115(1):142-152. doi: 10.1016/j.ijrobp.2022.08.041.

116. Mantz C. A phase II trial of stereotactic ablative body radiotherapy for low-risk prostate cancer using a non-robotic linear accelerator and real-time target tracking: report of toxicity, quality of life, and disease control outcomes with 5-year minimum follow-up. *Front Oncol.* 2014;4:279. doi: 10.3389/fonc.2014.00279.

117. Meier RM, Bloch DA, Cotrutz C, et al. Multicenter trial of stereotactic body radiation therapy for low- and intermediate-risk prostate cancer: survival and toxicity endpoints. *Int J Radiat Oncol Biol Phys.* 2018;102(2):296-303. doi: 10.1016/j.ijrobp.2018.05.040.

118. Miszczyk L, Namysl Kaletka A, Napieralska A, et al. Cyberknife radioablation of prostate cancer - preliminary results for 400 patients. *Asian Pac J Cancer Prev.* 2017;18(4):1007-1013. doi: 10.22034/APJCP.2017.18.4.1007.

119. Miszczyk L, Napieralska A, Namysł-Kaletka A, et al. CyberKnife-based prostate cancer patient radioablation–early results of irradiation in 200 patients. *Cent European J Urol.* 2015;68(3):289. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4643703/pdf/CEJU-68-00582.pdf.

120. Pasquier D, Martinage G, Janoray G, et al. Salvage stereotactic body radiation therapy for local prostate cancer recurrence after radiation therapy: a retrospective multicenter study of the GETUG. *Int J Radiat Oncol Biol Phys.* 2019;105(4):727-734. doi: 10.1016/j.ijrobp.2019.07.012.

121. Paydar I, Cyr RA, Yung TM, et al. Proctitis 1 week after stereotactic body radiation therapy for prostate cancer: implications for clinical trial design. *Front Oncol.* 2016;6:167. doi: 10.3389/fonc.2016.00167.

122. Pryor D, Sidhom M, Arumugam S, et al. Phase 2 multicenter study of gantry-based stereotactic radiotherapy boost for intermediate and high risk prostate cancer (PROMETHEUS). *Front Oncol.* 2019;9:217. doi: 10.3389/fonc.2019.00217.

123. Rana Z, Hong RL, Abugideiri M, et al. Sexual, irritative, and voiding outcomes, following stereotactic body radiation therapy for prostate cancer. *Radiat Oncol.* 2015;10(1):182. doi: 10.1186/s13014-015-0488-3.

124. Woo JA, Chen LN, Bhagat A, et al. Clinical characteristics and management of late urinary symptom flare following stereotactic body radiation therapy for prostate cancer. *Front Oncol.* 2014;4:122. doi: 10.3389/fonc.2014.00122.

125. Andolino DL, Forquer JA, Henderson MA, et al. Chest wall toxicity after stereotactic body radiotherapy for malignant lesions of the lung and liver. *Int J Radiat Oncol Biol Phys.* 2011;80(3):692-697. doi: 10.1016/j.ijrobp.2010.03.020.

126. Brown WT, Wu X, Wen BC, et al. Early results of CyberKnife image-guided robotic stereotactic radiosurgery for treatment of lung tumors. *Comput Aided Surg.* 2007;12(5):253-261. doi: 10.3109/10929080701684754.

127. Casamassima F, Masi L, Bonucci I, et al. Relevance of biologically equivalent dose values in outcome evaluation of stereotactic radiotherapy for lung nodules. *Int J Radiat Oncol Biol Phys.* 2008;71(1):145-151. doi: 10.1016/j.ijrobp.2007.09.036.

128. Coon D, Gokhale AS, Burton SA, Heron DE, Ozhasoglu C, Christie N. Fractionated stereotactic body radiation therapy in the treatment of primary, recurrent, and metastatic lung tumors: the role of positron emission tomography/computed tomography-based treatment planning. *Clin Lung Cancer.* 2008;9(4):217-221. doi: 10.3816/CLC.2008.n.032.

129. Dunlap NE, Cai J, Biedermann GB, et al. Chest wall volume receiving >30 Gy predicts risk of severe pain and/or rib fracture after lung stereotactic body radiotherapy. *Int J Radiat Oncol Biol Phys.* 2010;76(3):796-801. doi: 10.1016/j.ijrobp.2009.02.027.

130. Fritz P, Kraus HJ, Muhlnickel W, et al. Stereotactic, single-dose irradiation of stage I non-small cell lung cancer and lung metastases. *Radiat Oncol.* 2006;1:30. doi: 10.1186/1748-717X-1-30.

131. Guckenberger M, Baier K, Polat B, et al. Dose-response relationship for radiation-induced pneumonitis after pulmonary stereotactic body radiotherapy. *Radiother Oncol.* 2010;97(1):65-70. doi: 10.1016/j.radonc.2010.04.027.

132. Hiraoka M, Matsuo Y, Nagata Y. Stereotactic body radiation therapy (SBRT) for early-stage lung cancer. *Cancer Radiother.* 2007;11(1-2):32-35. doi: 10.1016/j.canrad.2006.11.001.

133. Milano MT, Chen Y, Katz AW, Philip A, Schell MC, Okunieff P. Central thoracic lesions treated with hypofractionated stereotactic body radiotherapy. *Radiother Oncol.* 2009;91(3):301-306. doi: 10.1016/j.radonc.2009.03.005.

134. Nambu A, Onishi H, Aoki S, et al. Rib fracture after stereotactic radiotherapy on follow-up thin-section computed tomography in 177 primary lung cancer patients. *Radiat Oncol.* 2011;6:137. doi: 10.1186/1748-717X-6-137.

135. Olsen JR, Robinson CG, El Naqa I, et al. Dose-response for stereotactic body radiotherapy in early-stage non-small-cell lung cancer. *Int J Radiat Oncol Biol Phys.* 2011;81(4):e299-303. doi: 10.1016/j.ijrobp.2011.01.038.

136. Pennathur A, Luketich JD, Burton S, et al. Stereotactic radiosurgery for the treatment of lung neoplasm: initial experience. *Ann Thorac Surg.* 2007;83(5):1820-1824; discussion 1824-1825. doi: 10.1016/j.athoracsur.2006.11.077.

137. Peulen H, Karlsson K, Lindberg K, et al. Toxicity after reirradiation of pulmonary tumours with stereotactic body radiotherapy. *Radiother Oncol.* 2011;101(2):260-266. doi: 10.1016/j.radonc.2011.09.012.

138. Ricardi U, Filippi AR, Guarneri A, et al. Dosimetric predictors of radiation-induced lung injury in stereotactic body radiation therapy. *Acta Oncol.* 2009;48(4):571-577. doi: 10.1080/02841860802520821.

139. Takeda A, Kunieda E, Ohashi T, Aoki Y, Koike N, Takeda T. Stereotactic body radiotherapy (SBRT) for oligometastatic lung tumors from colorectal cancer and other primary cancers in comparison with primary lung cancer. *Radiother Oncol.* 2011;101(2):255-259. doi: 10.1016/j.radonc.2011.05.033.

140. Takeda A, Ohashi T, Kunieda E, et al. Early graphical appearance of radiation pneumonitis correlates with the severity of radiation pneumonitis after stereotactic body radiotherapy (SBRT) in patients with lung tumors. *Int J Radiat Oncol Biol Phys.* 2010;77(3):685-690. doi: 10.1016/j.ijrobp.2009.06.001.

141. Welsh J, Thomas J, Shah D, et al. Obesity increases the risk of chest wall pain from thoracic stereotactic body radiation therapy. *Int J Radiat Oncol Biol Phys.* 2011;81(1):91-96. doi: 10.1016/j.ijrobp.2010.04.022.

142. Yamashita H, Kobayashi-Shibata S, Terahara A, et al. Prescreening based on the presence of CT-scan abnormalities and biomarkers (KL-6 and SP-D) may reduce severe radiation pneumonitis after stereotactic radiotherapy. *Radiat Oncol.* 2010;5:32. doi: 10.1186/1748-717X-5-32.

143. Verstegen NE, Lagerwaard FJ, Haasbeek CJ, Slotman BJ, Senan S. Outcomes of stereotactic ablative radiotherapy following a clinical diagnosis of stage I NSCLC: comparison with a contemporaneous cohort with pathologically proven disease. *Radiother Oncol.* 2011;101(2):250-254. doi: 10.1016/j.radonc.2011.09.017.

144. Trovo M, Linda A, El Naqa I, Javidan-Nejad C, Bradley J. Early and late lung radiographic injury following stereotactic body radiation therapy (SBRT). *Lung Cancer.* 2010;69(1):77-85.

145. Altorki NK, McGraw TE, Borczuk AC, et al. Neoadjuvant durvalumab with or without stereotactic body radiotherapy in patients with early-stage non-small-cell lung cancer: a single-centre, randomised phase 2 trial. *Lancet Oncol.* 2021;22(6):824-835. doi: 10.1016/S1470-2045(21)00149-2.

146. Lee B, Mynard N, Nasar A, et al. Surgical resection after neoadjuvant durvalumab and radiation is feasible and safe in non-small cell lung cancer: Results from a randomized trial. *J Thorac Cardiovasc Surg.* 2023;165(1):327-334 e322. doi: 10.1016/j.jtcvs.2022.07.017.

147. Theelen W, Peulen HMU, Lalezari F, et al. Effect of pembrolizumab after stereotactic body radiotherapy vs pembrolizumab alone on tumor response in patients with advanced non-small cell lung cancer: Results of the PEMBRO-RT phase 2 randomized clinical trial. *JAMA Oncol.* 2019;5(9):1276-1282. doi: 10.1001/jamaoncol.2019.1478.

148. Filippi AR, Guerrera F, Badellino S, et al. Exploratory analysis on overall survival after either surgery or stereotactic radiotherapy for lung oligometastases from colorectal cancer. *Clin Oncol (R Coll Radiol).* 2016;28(8):505-512. doi: 10.1016/j.clon.2016.02.001.

149. Fleming C, Rimner A, Foster A, Woo KM, Zhang Z, Wu AJ. Palliative efficacy and local control of conventional radiotherapy for lung metastases. *Ann Palliat Med.* 2017;6(Suppl 1):S21-S27. doi: 10.21037/apm.2017.03.08.

150. Jacobs CD, Gao J, Wang X, et al. Definitive radiotherapy for inoperable stage IIb non-small-cell lung cancer: patterns of care and comparative effectiveness. *Clin Lung Cancer.* 2020;21(3):238-246. doi: 10.1016/j.cllc.2019.10.005.

151. Kanzaki R, Suzuki O, Kanou T, et al. The short-term outcomes of pulmonary metastasectomy or stereotactic body radiation therapy for pulmonary metastasis from epithelial tumors. *J Cardiothorac Surg.* 2020;15(1):43. doi: 10.1186/s13019-020-1079-4 Accessed 20200227//.

152. Lee YH, Kang KM, Choi HS, et al. Comparison of stereotactic body radiotherapy versus metastasectomy outcomes in patients with pulmonary metastases. *Thorac Cancer.* 2018;9(12):1671-1679. doi: 10.1111/1759-7714.12880.

153. Littau MJ, Freeman R, Vigneswaran WT, et al. Comparative effectiveness of stereotactic body radiation therapy versus surgery for stage I lung cancer in otherwise healthy patients: an instrumental variable analysis. *JTCVS Open.* 2022;9:249-261. doi: 10.1016/j.xjon.2021.09.052.

154. Lo H, Abel S, Finley G, Weksler B, Colonias A, Wegner RE. Surgical resection versus stereotactic body radiation therapy in early stage bronchopulmonary large cell neuroendocrine carcinoma. *Thorac Cancer.* 2020;11(2):305-310. doi: 10.1111/1759-7714.13260 Accessed 20191220//.

155. Nelson DB, Tayob N, Nguyen QN, et al. Local failure after stereotactic body radiation therapy or wedge resection for colorectal pulmonary metastases. *J Thorac Cardiovasc Surg.* 2019;158(4):1234-1241 e1216. doi: 10.1016/j.jtcvs.2019.02.133 Accessed 20190511//.

156. Rosen JE, Salazar MC, Wang Z, et al. Lobectomy versus stereotactic body radiotherapy in healthy patients with stage I lung cancer. *J Thorac Cardiovasc Surg.* 2016;152(1):44-54 e49. doi: 10.1016/j.jtcvs.2016.03.060.

157. Scotti V, Bruni A, Francolini G, et al. Stereotactic ablative radiotherapy as an alternative to lobectomy in patients with medically operable stage I NSCLC: a retrospective, multicenter analysis. *Clin Lung Cancer.* 2019;20(1):e53-e61. doi: 10.1016/j.cllc.2018.09.003.

158. Wegner RE, Abel S, Colonias A. Stereotactic ablative body radiotherapy versus conventionally fractionated radiotherapy for early stage large cell neuroendocrine carcinoma of the lung. *Lung Cancer Manag.* 2020;9(3):LMT32. doi: 10.2217/lmt-2020-0004 Accessed 20200421//.

159. Berkovic P, Gulyban A, Defraene G, et al. Stereotactic robotic body radiotherapy for patients with oligorecurrent pulmonary metastases. *BMC Cancer.* 2020;20(1):402. doi: 10.1186/s12885-020-06906-1 Accessed 20200508//.

160. Davis JN, Medbery C, Sharma S, et al. Stereotactic body radiotherapy for centrally located early-stage non-small cell lung cancer or lung metastases from the RSSearch patient registry. *Radiat Oncol.* 2015;10:113. doi: 10.1186/s13014-015-0417-5.

161. Duijm M, Tekatli H, Oomen-de Hoop E, et al. Esophagus toxicity after stereotactic and hypofractionated radiotherapy for central lung tumors: normal tissue complication probability modeling. *Radiother Oncol.* 2018;127(2):233-238. doi: 10.1016/j.radonc.2018.02.004.

162. Guckenberger M, Wulf J, Mueller G, et al. Dose-response relationship for image-guided stereotactic body radiotherapy of pulmonary tumors: relevance of 4D dose calculation. *Int J Radiat Oncol Biol Phys.* 2009;74(1):47-54. doi: 10.1016/j.ijrobp.2008.06.1939.

163. Helou J, Thibault I, Poon I, et al. Stereotactic ablative radiation therapy for pulmonary metastases: histology, dose, and indication matter. *Int J Radiat Oncol Biol Phys.* 2017;98(2):419-427. doi: 10.1016/j.ijrobp.2017.02.093.

164. Lagerwaard FJ, Verstegen NE, Haasbeek CJ, et al. Outcomes of stereotactic ablative radiotherapy in patients with potentially operable stage I non-small cell lung cancer. *Int J Radiat Oncol Biol Phys.* 2012;83(1):348-353. doi: 10.1016/j.ijrobp.2011.06.2003.

165. Lee TH, Kim DY, Wu HG, Lee JH, Kim HJ. Treatment outcomes of re-irradiation using stereotactic ablative radiotherapy to lung: a propensity score matching analysis. *Radiat Oncol.* 2021;16(1):222. doi: 10.1186/s13014-021-01948-6.

166. Osti MF, Agolli L, Valeriani M, et al. 30 Gy single dose stereotactic body radiation therapy (SBRT): report on outcome in a large series of patients with lung oligometastatic disease. *Lung Cancer.* 2018;122:165-170. doi: 10.1016/j.lungcan.2018.06.018.

167. Sharma A, Duijm M, Oomen-de Hoop E, et al. Factors affecting local control of pulmonary oligometastases treated with stereotactic body radiotherapy. *Acta Oncol.* 2018;57(8):1031-1037. doi: 10.1080/0284186X.2018.1445285.

168. Yamamoto T, Niibe Y, Aoki M, et al. Analyses of the local control of pulmonary oligometastases after stereotactic body radiotherapy and the impact of local control on survival. *BMC Cancer.* 2020;20(1):997. doi: 10.1186/s12885-020-07514-9 Accessed 20201014//.

169. Sharma A, Duijm M, Oomen-de Hoop E, et al. Survival and prognostic factors of pulmonary oligometastases treated with stereotactic body radiotherapy. *Acta oncologica (Stockholm, Sweden).* 2019;58(1):74-80. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med16&NEWS=N&AN=30280633 Accessed 20181003//.

170. Hoyer M, Roed H, Traberg Hansen A, et al. Phase II study on stereotactic body radiotherapy of colorectal metastases. *Acta Oncol.* 2006;45(7):823-830. doi: 10.1080/02841860600904854.

171. Kang JK, Kim MS, Kim JH, et al. Oligometastases confined one organ from colorectal cancer treated by SBRT. *Clin Exp Metastasis.* 2010;27(4):273-278. doi: 10.1007/s10585-010-9325-0.

172. Al-Wassia R, Dal Pra A, Shun K, et al. Stereotactic fractionated radiotherapy in the treatment of juxtapapillary choroidal melanoma: the McGill University experience. *Int J Radiat Oncol Biol Phys.* 2011;81(4):e455-462. doi: 10.1016/j.ijrobp.2011.05.012.

173. Dieckmann K, Georg D, Zehetmayer M, Rottenfusser A, Potter R. Stereotactic photon beam irradiation of uveal melanoma: indications and experience at the University of Vienna since 1997. *Strahlenther Onkol.* 2007;183 Spec No 2:11-13. doi: 10.1007/s00066-007-2005-6.

174. Emara K, Weisbrod DJ, Sahgal A, et al. Stereotactic radiotherapy in the treatment of juxtapapillary choroidal melanoma: preliminary results. *Int J Radiat Oncol Biol Phys.* 2004;59(1):94-100. doi: 10.1016/j.ijrobp.2003.10.007.

175. Krema H, Somani S, Sahgal A, et al. Stereotactic radiotherapy for treatment of juxtapapillary choroidal melanoma: 3-year follow-up. *Br J Ophthalmol.* 2009;93(9):1172-1176. doi: 10.1136/bjo.2008.153429.

176. Modorati G, Miserocchi E, Galli L, Picozzi P, Rama P. Gamma knife radiosurgery for uveal melanoma: 12 years of experience. *Br J Ophthalmol.* 2009;93(1):40-44. doi: 10.1136/bjo.2008.142208.

177. Muller K, Nowak PJ, Naus N, et al. Lacrimal gland radiosensitivity in uveal melanoma patients. *Int J Radiat Oncol Biol Phys.* 2009;74(2):497-502. doi: 10.1016/j.ijrobp.2008.08.010.

178. Somani S, Sahgal A, Krema H, et al. Stereotactic radiotherapy in the treatment of juxtapapillary choroidal melanoma: 2-year follow-up. *Can J Ophthalmol.* 2009;44(1):61-65. doi: 10.3129/i08-177.

179. Kim S, Wuthrick E, Blakaj D, et al. Combined nivolumab and ipilimumab with or without stereotactic body radiation therapy for advanced Merkel cell carcinoma: a randomised, open label, phase 2 trial. *Lancet.* 2022;400(10357):1008-1019. doi: 10.1016/S0140-6736(22)01659-2.

180. Uhlig A, Uhlig J, Trojan L, Kim HS. Stereotactic body radiotherapy for stage I renal cell carcinoma: national treatment trends and outcomes compared to partial nephrectomy and thermal ablation. *J Vasc Interv Radiol.* 2020;31(4):564-571. doi: 10.1016/j.jvir.2019.11.009 Accessed 20200229//.

181. Siva S, Ali M, Correa RJM, et al. 5-year outcomes after stereotactic ablative body radiotherapy for primary renal cell carcinoma: an individual patient data meta-analysis from IROCK (the International Radiosurgery Consortium of the Kidney). *Lancet Oncol.* 2022;23(12):1508-1516. doi: 10.1016/S1470-2045(22)00656-8.

182. Chang DT, Schellenberg D, Shen J, et al. Stereotactic radiotherapy for unresectable adenocarcinoma of the pancreas. *Cancer.* 2009;115(3):665-672. doi: 10.1002/cncr.24059.

183. Didolkar MS, Coleman CW, Brenner MJ, et al. Image-guided stereotactic radiosurgery for locally advanced pancreatic adenocarcinoma results of first 85 patients. *J Gastrointest Surg.* 2010;14(10):1547-1559. doi: 10.1007/s11605-010-1323-7.

184. Seo Y, Kim MS, Yoo S, et al. Stereotactic body radiation therapy boost in locally advanced pancreatic cancer. *Int J Radiat Oncol Biol Phys.* 2009;75(5):1456-1461. doi: 10.1016/j.ijrobp.2009.01.042.

185. Zamboglou C, Messmer MB, Becker G, Momm F. Stereotactic radiotherapy in the liver hilum. Basis for future studies. *Strahlenther Onkol.* 2012;188(1):35-41. doi: 10.1007/s00066-011-0002-2.

186. Rwigema JC, Parikh SD, Heron DE, et al. Stereotactic body radiotherapy in the treatment of advanced adenocarcinoma of the pancreas. *Am J Clin Oncol.* 2011;34(1):63-69. doi: 10.1097/COC.0b013e3181d270b4.

187. Murphy JD, Chang DT, Abelson J, et al. Cost-effectiveness of modern radiotherapy techniques in locally advanced pancreatic cancer. *Cancer.* 2012;118(4):1119-1129. doi: 10.1002/cncr.26365.

188. de Geus SWL, Eskander MF, Kasumova GG, et al. Stereotactic body radiotherapy for unresected pancreatic cancer: a nationwide review. *Cancer.* 2017;123(21):4158-4167. doi: 10.1002/cncr.30856.

189. Moningi S, Lei X, Fang P, et al. Contemporary use and outcomes of radiation and chemotherapy for unresectable pancreatic cancer. *Clin Transl Radiat Oncol.* 2022;35:9-16. doi: 10.1016/j.ctro.2022.04.007.

190. Zhong J, Patel K, Switchenko J, et al. Outcomes for patients with locally advanced pancreatic adenocarcinoma treated with stereotactic body radiation therapy versus conventionally fractionated radiation. *Cancer.* 2017;123(18):3486-3493. doi: 10.1002/cncr.30706.

191. Guss ZD, Batra S, Limb CJ, et al. Radiosurgery of glomus jugulare tumors: a meta-analysis. *Int J Radiat Oncol Biol Phys.* 2011;81(4):e497-502. doi: 10.1016/j.ijrobp.2011.05.006.

192. Yamazaki H, Demizu Y, Okimoto T, et al. Reirradiation for recurrent head and neck cancers using charged particle or photon radiotherapy. *Strahlenther Onkol.* 2017;193(7):525-533. doi: 10.1007/s00066-017-1129-6.

193. Yamazaki H, Demizu Y, Okimoto T, et al. Comparison of re-irradiation outcomes for charged particle radiotherapy and robotic stereotactic radiotherapy using cyberknife for recurrent head and neck cancers: a multi-institutional matched-cohort analysis. *Anticancer Res.* 2016;36(10):5507-5514. doi: 10.21873/anticanres.11132.

194. McBride S, Sherman E, Tsai CJ, et al. Randomized phase II trial of nivolumab with stereotactic body radiotherapy versus nivolumab alone in metastatic head and neck squamous cell carcinoma. *J Clin Oncol.* 2021;39(1):30-37. doi: 10.1200/JCO.20.00290.

195. Al-Mamgani A, Van Rooij P, Sewnaik A, et al. Brachytherapy or stereotactic body radiotherapy boost for early-stage oropharyngeal cancer: comparable outcomes of two different approaches. *Oral Oncol.* 2013;49(10):1018-1024. doi: 10.1016/j.oraloncology.2013.07.007.

196. Vargo JA, Ward MC, Caudell JJ, et al. A multi-institutional comparison of SBRT and IMRT for definitive reirradiation of recurrent or second primary head and neck cancer. *Int J Radiat Oncol Biol Phys.* 2018;100(3):595-605. doi: 10.1016/j.ijrobp.2017.04.017.

197. Ozyigit G, Cengiz M, Yazici G, et al. A retrospective comparison of robotic stereotactic body radiotherapy and three-dimensional conformal radiotherapy for the reirradiation of locally recurrent nasopharyngeal carcinoma. *Int J Radiat Oncol Biol Phys.* 2011;81(4):e263-268. doi: 10.1016/j.ijrobp.2011.02.054.

198. Tao C, Yang LX. Improved radiotherapy for primary and secondary liver cancer: stereotactic body radiation therapy. *Anticancer Res.* 2012;32(2):649-655. https://www.ncbi.nlm.nih.gov/pubmed/22287758.

199. Andolino DL, Johnson CS, Maluccio M, et al. Stereotactic body radiotherapy for primary hepatocellular carcinoma. *Int J Radiat Oncol Biol Phys.* 2011;81(4):e447-453. doi: 10.1016/j.ijrobp.2011.04.011.

200. Chang DT, Swaminath A, Kozak M, et al. Stereotactic body radiotherapy for colorectal liver metastases: a pooled analysis. *Cancer.* 2011;117(17):4060-4069. doi: 10.1002/cncr.25997.

201. Katz AW, Carey-Sampson M, Muhs AG, Milano MT, Schell MC, Okunieff P. Hypofractionated stereotactic body radiation therapy (SBRT) for limited hepatic metastases. *Int J Radiat Oncol Biol Phys.* 2007;67(3):793-798. doi: 10.1016/j.ijrobp.2006.10.025.

202. Lee WY, Cho DY, Lee HC, et al. Outcomes and cost-effectiveness of gamma knife radiosurgery and whole brain radiotherapy for multiple metastatic brain tumors. *J Clin Neurosci.* 2009;16(5):630-634. doi: 10.1016/j.jocn.2008.06.021.

203. Rusthoven KE, Kavanagh BD, Cardenes H, et al. Multi-institutional phase I/II trial of stereotactic body radiation therapy for liver metastases. *J Clin Oncol.* 2009;27(10):1572-1578. doi: 10.1200/JCO.2008.19.6329.

204. Shun SC, Chiou JF, Lai YH, et al. Changes in quality of life and its related factors in liver cancer patients receiving stereotactic radiation therapy. *Support Care Cancer.* 2008;16(9):1059-1065. doi: 10.1007/s00520-007-0384-y.

205. Tse RV, Hawkins M, Lockwood G, et al. Phase I study of individualized stereotactic body radiotherapy for hepatocellular carcinoma and intrahepatic cholangiocarcinoma. *J Clin Oncol.* 2008;26(4):657-664. doi: 10.1200/JCO.2007.14.3529.

206. Bettinger D, Pinato DJ, Schultheiss M, et al. Stereotactic body radiation therapy as an alternative treatment for patients with hepatocellular carcinoma compared to sorafenib: a propensity score analysis. *Liver Cancer.* 2019;8(4):281-294. doi: 10.1159/000490260.

207. Hara K, Takeda A, Tsurugai Y, et al. Radiotherapy for hepatocellular carcinoma results in comparable survival to radiofrequency ablation: a propensity score analysis. *Hepatology.* 2019;69(6):2533-2545. doi: 10.1002/hep.30591.

208. Honda Y, Kimura T, Aikata H, et al. Stereotactic body radiation therapy combined with transcatheter arterial chemoembolization for small hepatocellular carcinoma. *J Gastroenterol Hepatol.* 2013;28(3):530-536. doi: 10.1111/jgh.12087.

209. Jacob R, Turley F, Redden DT, et al. Adjuvant stereotactic body radiotherapy following transarterial chemoembolization in patients with non-resectable hepatocellular carcinoma tumours of >/= 3 cm. *HPB (Oxford).* 2015;17(2):140-149. doi: 10.1111/hpb.12331.

210. Jeong Y, Lee KJ, Lee SJ, et al. Radiofrequency ablation versus stereotactic body radiation therapy for small (</= 3 cm) hepatocellular carcinoma: a retrospective comparison analysis. *J Gastroenterol Hepatol.* 2021;36(7):1962-1970. doi: 10.1111/jgh.15442 Accessed 20210305//.

211. Ji R, Ng KK, Chen W, et al. Comparison of clinical outcome between stereotactic body radiotherapy and radiofrequency ablation for unresectable hepatocellular carcinoma. *Medicine (Baltimore).* 2022;101(4):e28545. doi: 10.1097/MD.0000000000028545.

212. Jun BG, Kim SG, Kim YD, et al. Combined therapy of transarterial chemoembolization and stereotactic body radiation therapy versus transarterial chemoembolization for </=5cm hepatocellular carcinoma: propensity score matching analysis. *PLoS One.* 2018;13(10):e0206381. doi: 10.1371/journal.pone.0206381 Accessed 20181031//.

213. Kim N, Cheng J, Jung I, et al. Stereotactic body radiation therapy vs. radiofrequency ablation in Asian patients with hepatocellular carcinoma. *J Hepatol.* 2020;73(1):121-129. doi: 10.1016/j.jhep.2020.03.005.

214. Kimura T, Aikata H, Doi Y, et al. Comparison of stereotactic body radiation therapy combined with or without transcatheter arterial chemoembolization for patients with small hepatocellular carcinoma ineligible for resection or ablation therapies. *Technol Cancer Res Treat.* 2018;17:1533033818783450. doi: 10.1177/1533033818783450.

215. Nabavizadeh N, Jahangiri Y, Rahmani R, et al. Thermal ablation versus stereotactic body radiotherapy after transarterial chemoembolization for inoperable hepatocellular carcinoma: a propensity score-weighted analysis. *AJR Am J Roentgenol.* 2021;217(3):691-698. doi: 10.2214/AJR.20.24117 Accessed 20200930//.

216. Nieuwenhuizen S, Dijkstra M, Puijk RS, et al. Thermal ablation versus stereotactic ablative body radiotherapy to treat unresectable colorectal liver metastases: a comparative analysis from the prospective Amsterdam CORE registry. *Cancers (Basel).* 2021;13(17):26. doi: 10.3390/cancers13174303.

217. Oladeru OT, Miccio JA, Yang J, Xue Y, Ryu S, Stessin AM. Conformal external beam radiation or selective internal radiation therapy-a comparison of treatment outcomes for hepatocellular carcinoma. *J Gastrointest Oncol.* 2016;7(3):433-440. doi: 10.21037/jgo.2015.10.04.

218. Parikh ND, Marshall VD, Green M, et al. Effectiveness and cost of radiofrequency ablation and stereotactic body radiotherapy for treatment of early-stage hepatocellular carcinoma: An analysis of SEER-medicare. *J Med Imaging Radiat Oncol.* 2018;62(5):673-681. doi: 10.1111/1754-9485.12754.

219. Rajyaguru DJ, Borgert AJ, Smith AL, et al. Radiofrequency ablation versus stereotactic body radiotherapy for localized hepatocellular carcinoma in nonsurgically managed patients: analysis of the National Cancer Database. *J Clin Oncol.* 2018;36(6):600-608. doi: 10.1200/JCO.2017.75.3228.

220. Sapisochin G, Barry A, Doherty M, et al. Stereotactic body radiotherapy vs. TACE or RFA as a bridge to transplant in patients with hepatocellular carcinoma. an intention-to-treat analysis. *J Hepatol.* 2017;67(1):92-99. doi: 10.1016/j.jhep.2017.02.022.

221. Sebastian NT, Tan Y, Miller ED, Williams TM, Alexandra Diaz D. Stereotactic body radiation therapy is associated with improved overall survival compared to chemoradiation or radioembolization in the treatment of unresectable intrahepatic cholangiocarcinoma. *Clin Transl Radiat Oncol.* 2019;19:66-71. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=pmnm4&NEWS=N&AN=31517072 Accessed 20190726//.

222. Wahl DR, Stenmark MH, Tao Y, et al. Outcomes after stereotactic body radiotherapy or radiofrequency ablation for hepatocellular carcinoma. *J Clin Oncol.* 2016;34(5):452-459. doi: 10.1200/JCO.2015.61.4925.

223. Wang F, Numata K, Takeda A, et al. Safety and efficacy study: short-term application of radiofrequency ablation and stereotactic body radiotherapy for Barcelona Clinical Liver Cancer stage 0-B1 hepatocellular carcinoma. *PLoS One.* 2021;16(1):e0245076. doi: 10.1371/journal.pone.0245076 Accessed 20210105//.

224. Wong TC, Chiang CL, Lee AS, et al. Better survival after stereotactic body radiation therapy following transarterial chemoembolization in nonresectable hepatocellular carcinoma: a propensity score matched analysis. *Surg Oncol.* 2019;28:228-235. doi: 10.1016/j.suronc.2019.01.006 Accessed 20190129//.

225. Wong TC, Lee VH, Law AL, et al. Prospective study of stereotactic body radiation therapy for hepatocellular carcinoma on waitlist for liver transplant. *Hepatology.* 2021;74(5):2580-2594. doi: 10.1002/hep.31992 Accessed 20210930//.

226. Park S, Jung J, Cho B, et al. Clinical outcomes of stereotactic body radiation therapy for small hepatocellular carcinoma. *J Gastroenterol Hepatol.* 2020;35(11):1953-1959. doi: 10.1111/jgh.15011 Accessed 20200220//.

227. Kibe Y, Takeda A, Tsurugai Y, et al. Feasibility of marker-less stereotactic body radiotherapy for hepatocellular carcinoma. *Acta Oncol.* 2022;61(1):104-110. doi: 10.1080/0284186X.2021.2001566 Accessed 20211117//.

228. Loi M, Comito T, Franzese C, et al. Stereotactic body radiotherapy in hepatocellular carcinoma: patient selection and predictors of outcome and toxicity. *J Cancer Res Clin Oncol.* 2021;147(3):927-936. doi: 10.1007/s00432-020-03389-2 Accessed 20200918//.

229. Voglhuber T, Eitz KA, Oechsner M, Vogel MME, Combs SE. Analysis of using high-precision radiotherapy in the treatment of liver metastases regarding toxicity and survival. *BMC cancer.* 2021;21(1):780. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=medl&NEWS=N&AN=34229642 Accessed 20210706//.

230. Mathew AS, Atenafu EG, Owen D, et al. Long term outcomes of stereotactic body radiation therapy for hepatocellular carcinoma without macrovascular invasion. *Eur J Cancer.* 2020;134:41-51. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med17&NEWS=N&AN=32460180 Accessed 20200524//.

231. Bujold A, Massey CA, Kim JJ, et al. Sequential phase I and II trials of stereotactic body radiotherapy for locally advanced hepatocellular carcinoma. *J Clin Oncol.* 2013;31(13):1631-1639. doi: 10.1200/JCO.2012.44.1659.

232. Stintzing S, Einem JV, Fueweger C, Haidenberger A, Fedorov M, Muavcevic A. Long-term survival in patients treated with a robotic radiosurgical device for liver metastases. *Cancer Res Treat.* 2019;51(1):187-193. doi: 10.4143/crt.2017.594.

233. Mahadevan A, Blanck O, Lanciano R, et al. Stereotactic body radiotherapy (SBRT) for liver metastasis - clinical outcomes from the international multi-institutional RSSearch patient registry. *Radiat Oncol.* 2018;13(1):26. doi: 10.1186/s13014-018-0969-2.

234. Lock M, Chow R, Jayatilaka A, et al. Does stereotactic body radiation improve outcomes compared to conventional radiation for liver cancer patients? *Clin Transl Radiat Oncol.* 2022;35:17-20. doi: 10.1016/j.ctro.2022.04.002.

235. Munoz-Schuffenegger P, Barry A, Atenafu EG, et al. Stereotactic body radiation therapy for hepatocellular carcinoma with macrovascular invasion. *Radiother Oncol.* 2021;156:120-126. doi: 10.1016/j.radonc.2020.11.033.

236. Andratschke N, Alheid H, Allgauer M, et al. The SBRT database initiative of the German Society for Radiation Oncology (DEGRO): patterns of care and outcome analysis of stereotactic body radiotherapy (SBRT) for liver oligometastases in 474 patients with 623 metastases. *BMC Cancer.* 2018;18(1):283. doi: 10.1186/s12885-018-4191-2.

237. Berber B, Ibarra R, Snyder L, et al. Multicentre results of stereotactic body radiotherapy for secondary liver tumours. *HPB (Oxford).* 2013;15(11):851-857. doi: 10.1111/hpb.12044.

238. Mendez Romero A, Schillemans W, van Os R, et al. The Dutch-Belgian registry of stereotactic body radiation therapy for liver metastases: clinical outcomes of 515 patients and 668 metastases. *Int J Radiat Oncol Biol Phys.* 2021;109(5):1377-1386. doi: 10.1016/j.ijrobp.2020.11.045.

239. Murray LJ, Sykes J, Brierley J, et al. Baseline albumin-bilirubin (albi) score in Western patients with hepatocellular carcinoma treated with stereotactic body radiation therapy (SBRT). *Int J Radiat Oncol Biol Phys.* 2018;101(4):900-909. doi: 10.1016/j.ijrobp.2018.04.011.

240. Milano MT, Katz AW, Muhs AG, et al. A prospective pilot study of curative-intent stereotactic body radiation therapy in patients with 5 or fewer oligometastatic lesions. *Cancer.* 2008;112(3):650-658. doi: 10.1002/cncr.23209.

241. Milano MT, Katz AW, Okunieff P. Patterns of recurrence after curative-intent radiation for oligometastases confined to one organ. *Am J Clin Oncol.* 2010;33(2):157-163. doi: 10.1097/COC.0b013e3181979238.

242. Ost P, Reynders D, Decaestecker K, et al. Surveillance or metastasis-directed therapy for oligometastatic prostate cancer recurrence: a prospective, randomized, multicenter phase II trial. *J Clin Oncol.* 2018;36(5):446-453. doi: 10.1200/JCO.2017.75.4853 Accessed 2022/11/21.

243. Phillips R, Shi WY, Deek M, et al. Outcomes of observation vs stereotactic ablative radiation for oligometastatic prostate cancer: the ORIOLE phase 2 randomized clinical trial. *JAMA Oncol.* 2020;6(5):650-659. doi: 10.1001/jamaoncol.2020.0147.

244. Palma DA, Olson R, Harrow S, et al. Stereotactic ablative radiotherapy versus standard of care palliative treatment in patients with oligometastatic cancers (SABR-COMET): a randomised, phase 2, open-label trial. *Lancet.* 2019;393(10185):2051-2058. doi: 10.1016/S0140-6736(18)32487-5.

245. Bouman-Wammes EW, van Dodewaard-De Jong JM, Dahele M, et al. Benefits of using stereotactic body radiotherapy in patients with metachronous oligometastases of hormone-sensitive prostate cancer detected by [18F]fluoromethylcholine PET/CT. *Clin Genitourin Cancer.* 2017;15(5):e773-e782. doi: 10.1016/j.clgc.2017.03.009.

246. De Bleser E, Jereczek-Fossa BA, Pasquier D, et al. Metastasis-directed therapy in treating nodal oligorecurrent prostate cancer: a multi-institutional analysis comparing the outcome and toxicity of stereotactic body radiotherapy and elective nodal radiotherapy. *Eur Urol.* 2019. https://www.cochranelibrary.com/central/doi/10.1002/central/CN-01964903/full.

247. Hurmuz P, Onal C, Ozyigit G, et al. Treatment outcomes of metastasis-directed treatment using (68)Ga-PSMA-PET/CT for oligometastatic or oligorecurrent prostate cancer: Turkish Society for Radiation Oncology group study (TROD 09-002). *Strahlenther Onkol.* 2020;196(11):1034-1043. doi: 10.1007/s00066-020-01660-6.

248. Deek MP, Van der Eecken K, Sutera P, et al. Long-term outcomes and genetic predictors of response to metastasis-directed therapy versus observation in oligometastatic prostate cancer: analysis of STOMP and ORIOLE Trials. *J Clin Oncol.* 2022;40(29):3377-3382. doi: 10.1200/JCO.22.00644.

249. Palma DA, Olson R, Harrow S, et al. Stereotactic ablative radiotherapy for the comprehensive treatment of oligometastatic cancers: long-term results of the SABR-COMET phase II randomized trial. *J Clin Oncol.* 2020;38(25):2830-2838. doi: 10.1200/JCO.20.00818 Accessed 20200602//.

250. Olson R, Senan S, Harrow S, et al. Quality of life outcomes after stereotactic ablative radiation therapy (SABR) versus standard of care treatments in the oligometastatic setting: a secondary analysis of the SABR-COMET Randomized Trial. *Int J Radiat Oncol Biol Phys.* 2019;105(5):943-947. doi: 10.1016/j.ijrobp.2019.08.041 Accessed 20190827//.

251. Palma DA, Haasbeek CJ, Rodrigues GB, et al. Stereotactic ablative radiotherapy for comprehensive treatment of oligometastatic tumors (SABR-COMET): study protocol for a randomized phase II trial. *BMC Cancer.* 2012;12:305. doi: 10.1186/1471-2407-12-305.

252. Van Oirschot M, Bergman A, Verbakel W, et al. Determining planning priorities for SABR for oligometastatic disease: a secondary analysis of the SABR-COMET phase II randomized trial. *Int J Radiat Oncol Biol Phys.* 2022;114(5):1016-1021. doi: 10.1016/j.ijrobp.2022.01.002.

253. Radwan N, Phillips R, Ross A, et al. A phase II randomized trial of observation versus stereotactic ablative radiation for oligometastatic prostate cancer (ORIOLE). *BMC Cancer.* 2017;17(1):453. doi: 10.1186/s12885-017-3455-6.

254. Bowden P, See AW, Frydenberg M, et al. Fractionated stereotactic body radiotherapy for up to five prostate cancer oligometastases: interim outcomes of a prospective clinical trial. *Int J Cancer.* 2020;146(1):161-168. doi: 10.1002/ijc.32509.

255. Chalkidou A, Macmillan T, Grzeda MT, et al. Stereotactic ablative body radiotherapy in patients with oligometastatic cancers: a prospective, registry-based, single-arm, observational, evaluation study. *Lancet Oncol.* 2021;22(1):98-106. doi: 10.1016/S1470-2045(20)30537-4.

256. Franzese C, Marvaso G, Francolini G, et al. The role of stereotactic body radiation therapy and its integration with systemic therapies in metastatic kidney cancer: a multicenter study on behalf of the AIRO (Italian Association of Radiotherapy and Clinical Oncology) genitourinary study group. *Clin Exp Metastasis.* 2021;38(6):527-537. doi: 10.1007/s10585-021-10131-w Accessed 20211108//.

257. Macchia G, Lazzari R, Colombo N, et al. A large, multicenter, retrospective study on efficacy and safety of stereotactic body radiotherapy (SBRT) in oligometastatic ovarian cancer (MITO RT1 Study): a collaboration of MITO, AIRO GYN, and MaNGO groups. *Oncologist.* 2020;25(2):e311-e320. doi: 10.1634/theoncologist.2019-0309.

258. Nicosia L, Franzese C, Mazzola R, et al. Recurrence pattern of stereotactic body radiotherapy in oligometastatic prostate cancer: a multi-institutional analysis. *Strahlenther Onkol.* 2020;196(3):213-221. doi: 10.1007/s00066-019-01523-9.

259. Olson R, Jiang W, Liu M, et al. Treatment with stereotactic ablative radiotherapy for up to 5 oligometastases in patients with cancer: primary toxic effect results of the nonrandomized phase 2 SABR-5 clinical trial. *JAMA Oncol.* 2022;8(11):1644-1650. doi: 10.1001/jamaoncol.2022.4394.

260. Ost P, Jereczek-Fossa BA, As NV, et al. Progression-free survival following stereotactic body radiotherapy for oligometastatic prostate cancer treatment-naive recurrence: a multi-institutional analysis. *Eur Urol.* 2016;69(1):9-12. doi: 10.1016/j.eururo.2015.07.004.

261. Poon I, Erler D, Dagan R, et al. Evaluation of definitive stereotactic body radiotherapy and outcomes in adults with extracranial oligometastasis. *JAMA Netw Open.* 2020;3(11):e2026312. doi: 10.1001/jamanetworkopen.2020.26312.

262. Sogono P, Bressel M, David S, et al. Safety, efficacy, and patterns of failure after single-fraction stereotactic body radiation therapy (SBRT) for oligometastases. *Int J Radiat Oncol Biol Phys.* 2021;109(3):756-763. doi: 10.1016/j.ijrobp.2020.10.011 Accessed 20201015//.

263. Sutera P, Clump DA, Kalash R, et al. Initial results of a multicenter phase 2 trial of stereotactic ablative radiation therapy for oligometastatic cancer. *Int J Radiat Oncol Biol Phys.* 2019;103(1):116-122. doi: 10.1016/j.ijrobp.2018.08.027 Accessed 20180825//.

264. Triggiani L, Alongi F, Buglione M, et al. Efficacy of stereotactic body radiotherapy in oligorecurrent and in oligoprogressive prostate cancer: new evidence from a multicentric study. *Br J Cancer.* 2017;116(12):1520-1525. doi: 10.1038/bjc.2017.103.

265. Milano MT, Katz AW, Zhang H, Okunieff P. Oligometastases treated with stereotactic body radiotherapy: long-term follow-up of prospective study. *Int J Radiat Oncol Biol Phys.* 2012;83(3):878-886. doi: 10.1016/j.ijrobp.2011.08.036.

266. Casamassima F, Livi L, Masciullo S, et al. Stereotactic radiotherapy for adrenal gland metastases: university of Florence experience. *Int J Radiat Oncol Biol Phys.* 2012;82(2):919-923. doi: 10.1016/j.ijrobp.2010.11.060.

267. Chawla S, Chen Y, Katz AW, et al. Stereotactic body radiotherapy for treatment of adrenal metastases. *Int J Radiat Oncol Biol Phys.* 2009;75(1):71-75. doi: 10.1016/j.ijrobp.2008.10.079.

268. Franzese C, Nicosia L, Facondo G, et al. Stereotactic body radiation therapy for adrenal gland metastases: outcome and predictive factors from a multicenter analysis. *Clin Exp Metastasis.* 2021;38(6):511-518. doi: 10.1007/s10585-021-10124-9.

269. Grozman V, Onjukka E, Wersall P, et al. Extending hypofractionated stereotactic body radiotherapy to tumours larger than 70cc - effects and side effects. *Acta oncologica (Stockholm, Sweden).* 2021;60(3):305-311. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=medl&NEWS=N&AN=33448899 Accessed 20210115//.

270. Levine AM, Coleman C, Horasek S. Stereotactic radiosurgery for the treatment of primary sarcomas and sarcoma metastases of the spine. *Neurosurgery.* 2009;64(2 Suppl):A54-59. doi: 10.1227/01.NEU.0000339131.28485.4A.

271. McCammon R, Schefter TE, Gaspar LE, Zaemisch R, Gravdahl D, Kavanagh B. Observation of a dose-control relationship for lung and liver tumors after stereotactic body radiation therapy. *Int J Radiat Oncol Biol Phys.* 2009;73(1):112-118. doi: 10.1016/j.ijrobp.2008.03.062.

272. Scorsetti M, Bignardi M, Alongi F, et al. Stereotactic body radiation therapy for abdominal targets using volumetric intensity modulated arc therapy with RapidArc: feasibility and clinical preliminary results. *Acta Oncol.* 2011;50(4):528-538. doi: 10.3109/0284186X.2011.558522.

273. Yoon SM, Luterstein E, Chu FI, et al. Clinical outcomes of stereotactic magnetic resonance image-guided adaptive radiotherapy for primary and metastatic tumors in the abdomen and pelvis. *Cancer Med.* 2021;10(17):5897-5906. doi: 10.1002/cam4.4139.

274. Nguyen QN, Chun SG, Chow E, et al. Single-Fraction Stereotactic vs Conventional Multifraction Radiotherapy for Pain Relief in Patients With Predominantly Nonspine Bone Metastases: A Randomized Phase 2 Trial. *JAMA Oncol.* 2019;5(6):872-878. doi: 10.1001/jamaoncol.2019.0192.

275. Kim H, Vargo JA, Beriwal S, et al. Cost-effectiveness analysis of salvage therapies in locoregional previously irradiated head and neck cancer. *Head Neck.* 2018;40(8):1743-1751. doi: 10.1002/hed.25142.

276. Kim H, Vargo JA, Ling DC, Beriwal S, Smith KJ. Cost-effectiveness analysis of upfront SBRT for oligometastatic stage IV non-small cell lung cancer based on mutational status. *Am J Clin Oncol.* 2019;42(11):837-844. doi: 10.1097/COC.0000000000000608.

277. Kumar A, Straka C, Courtney PT, Vitzthum L, Riviere P, Murphy JD. Cost-effectiveness analysis of stereotactic ablative radiation therapy in patients with oligometastatic cancer. *Int J Radiat Oncol Biol Phys.* 2021;109(5):1185-1194. doi: 10.1016/j.ijrobp.2020.09.045.

278. Mehrens D, Unterrainer M, Corradini S, et al. Cost-effectiveness analysis of local treatment in oligometastatic disease. *Front Oncol.* 2021;11:667993. doi: 10.3389/fonc.2021.667993 Accessed 20210615//.

279. Santos PMG, Lapen K, Zhang Z, et al. Trends in radiation therapy for bone metastases, 2015 to 2017: Choosing Wisely in the era of complex radiation. *Int J Radiat Oncol Biol Phys.* 2021;109(4):923-931. doi: 10.1016/j.ijrobp.2020.11.016.

280. Parikh NR, Chang EM, Nickols NG, et al. Cost-Effectiveness of Metastasis-Directed Therapy in Oligorecurrent Hormone-Sensitive Prostate Cancer. *Int J Radiat Oncol Biol Phys.* 2020;108(4):917-926. doi: 10.1016/j.ijrobp.2020.06.009.

281. Eastham JA, Auffenberg GB, Barocas DA, et al. Clinically localized prostate cancer: AUA/ASTRO guideline, part I: introduction, risk assessment, staging, and risk-based management. *J Urol.* 2022;208(1):10-18. doi: 10.1097/JU.0000000000002757.

282. Eastham JA, Auffenberg GB, Barocas DA, et al. Clinically Localized Prostate Cancer: AUA/ASTRO guideline, part II: principles of active surveillance, principles of surgery, and follow-up. *J Urol.* 2022;208(1):19-25. doi: 10.1097/JU.0000000000002758.

283. European Association of Urology Prostate Cancer Guidelines Panel. EAU - EANM - ESTRO - ESUR - ISUP - SIOG guidelines on prostate cancer. 2022; https://uroweb.org/guidelines/prostate-cancer. Accessed December 29, 2022.

284. Lieng H, Hayden AJ, Christie DRH, et al. Radiotherapy for recurrent prostate cancer: 2018 recommendations of the Australian and New Zealand radiation oncology genito-urinary group. *Radiother Oncol.* 2018;129(2):377-386. doi: 10.1016/j.radonc.2018.06.027.

285. Daly ME, Ismaila N, Decker RH, et al. Radiation therapy for small-cell lung cancer: ASCO guideline endorsement of an ASTRO guideline. *J Clin Oncol.* 2021;39(8):931-939. doi: 10.1200/JCO.20.03364 Accessed 2022/12/29.

286. European Society for Medical Oncology. Metastatic non-small-cell lung cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up 2020 update. 2020; https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer. Accessed December 29, 2020.

287. Genshaft SJ, Suh RD, Abtin F, et al. Society of Interventional Radiology multidisciplinary position statement on percutaneous ablation of non-small cell lung cancer and metastatic disease to the lungs: endorsed by the Canadian Association for Interventional Radiology, the Cardiovascular and Interventional Radiological Society of Europe, and the Society of Interventional Oncology. *J Vasc Interv Radiol.* 2021;32(8):1241 e1241-1241 e1212. doi: 10.1016/j.jvir.2021.04.024 Accessed 2022/12/29.

288. National Institute for Health and Care Excellence. Lung cancer: diagnosis and management [NG122]. *NICE guideline [NG122]* 2018; https://www.nice.org.uk/guidance/ng122/resources/lung-cancer-diagnosis-and-management-pdf-66141655525573. Accessed December 29, 2022.

289. Planchard D, Popat S, Kerr K, et al. Metastatic non-small cell lung cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Ann Oncol.* 2018;29(Suppl 4):iv192-iv237. doi: 10.1093/annonc/mdy275.

290. Morris VK, Kennedy EB, Baxter NN, et al. Treatment of metastatic colorectal cancer: ASCO guideline. *J Clin Oncol.* 2023;41(3):678-700. doi: 10.1200/JCO.22.01690 Accessed 2022/12/29.

291. Cervantes A, Adam R, Rosello S, et al. Metastatic colorectal cancer: ESMO clinical practice guideline for diagnosis, treatment and follow-up. *Ann Oncol.* 2023;34(1):10-32. doi: 10.1016/j.annonc.2022.10.003 Accessed 2022/12/29.

292. National Institute for Health and Care Excellence. Colorectal cancer [NG151]. *NICE Guideline [NG151]* 2021; https://www.nice.org.uk/guidance/ng151/resources/colorectal-cancer-pdf-66141835244485. Accessed December 29, 2022.

293. Cibula D, Potter R, Planchamp F, et al. The European Society of Gynaecological Oncology/European Society for Radiotherapy and Oncology/European Society of Pathology guidelines for the management of patients with cervical cancer. *Virchows Arch.* 2018;472(6):919-936. doi: 10.1007/s00428-018-2362-9.

294. Concin N, Matias-Guiu X, Vergote I, et al. ESGO/ESTRO/ESP guidelines for the management of patients with endometrial carcinoma. *Int J Gynecol Cancer.* 2021;31(1):12-39. doi: 10.1136/ijgc-2020-002230.

295. Michielin O, van Akkooi ACJ, Ascierto PA, Dummer R, Keilholz U, Esmo Guidelines Committee. Cutaneous melanoma: ESMO clinical practice guidelines for diagnosis,

treatment and follow-up. *Ann Oncol.* 2019;30(12):1884-1901. doi: 10.1093/annonc/mdz411.

296. Campbell SC, Clark PE, Chang SS, Karam JA, Souter L, Uzzo RG. Renal mass and localized renal cancer: evaluation, management, and follow-up: AUA guideline: part I. *J Urol.* 2021;206(2):199-208. doi: 10.1097/JU.0000000000001911.

297. European Association of Urology Renal Cell Cancer Guidelines Panel. EAU guidelines on renal cell carcinoma. 2022; https://uroweb.org/guidelines/renal-cell-carcinoma. Accessed December 29, 2022.

298. Escudier B, Porta C, Schmidinger M, et al. Renal cell carcinoma: ESMO clinical practice guidelines for diagnosis, treatment and follow-updagger. *Ann Oncol.* 2019;30(5):706-720. doi: 10.1093/annonc/mdz056.

299. Campbell SC, Uzzo RG, Karam JA, Chang SS, Clark PE, Souter L. Renal mass and localized renal cancer: evaluation, management, and follow-up: AUA guideline: part II. *J Urol.* 2021;206(2):209-218. doi: 10.1097/JU.0000000000001912.

300. Motzer RJ, Jonasch E, Agarwal N, et al. Kidney cancer, version 3.2022, NCCN clinical practice guidelines in oncology. *J Natl Compr Canc Netw.* 2022;20(1):71-90. doi: 10.6004/jnccn.2022.0001.

301. Palta M, Godfrey D, Goodman KA, et al. Radiation therapy for pancreatic cancer: executive summary of an ASTRO clinical practice guideline. *Pract Radiat Oncol.* 2019;9(5):322-332. doi: 10.1016/j.prro.2019.06.016.

302. American College of Radiology. American College of Radiology ACR appropriateness criteria management of liver cancer. 2022; https://acsearch.acr.org/docs/69379/Narrative/. Accessed December 29, 2022.

303. Apisarnthanarax S, Barry A, Cao M, et al. External beam radiation therapy for primary liver cancers: an ASTRO clinical practice guideline. *Pract Radiat Oncol.* 2022;12(1):28-51. doi: 10.1016/j.prro.2021.09.004 Accessed 2022/12/29.

304. Vogel A, Bridgewater J, Edeline J, et al. Biliary tract cancer: ESMO clinical practice guideline for diagnosis, treatment and follow-up. *Ann Oncol.* 2022. doi: 10.1016/j.annonc.2022.10.506 Accessed 2022/12/29.

305. Vogel A, Cervantes A, Chau I, et al. Hepatocellular carcinoma: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Ann Oncol.* 2018;29(Suppl 4):iv238-iv255. doi: 10.1093/annonc/mdy308.

306. Strauss SJ, Frezza AM, Abecassis N, et al. Bone sarcomas: ESMO-EURACAN-GENTURIS-ERN PaedCan clinical practice guideline for diagnosis, treatment and follow-up. *Ann Oncol.* 2021;32(12):1520-1536. doi: 10.1016/j.annonc.2021.08.1995.

307. Lopez-Campos F, Cacicedo J, Counago F, et al. SEOR SBRT-SG stereotactic body radiation therapy consensus guidelines for non-spine bone metastasis. *Clin Transl Oncol.* 2022;24(2):215-226. doi: 10.1007/s12094-021-02695-6.

308. Oldenburg J, Berney DM, Bokemeyer C, et al. Testicular seminoma and non-seminoma: ESMO-EURACAN clinical practice guideline for diagnosis, treatment and follow-up. *Ann Oncol.* 2022;33(4):362-375. doi: 10.1016/j.annonc.2022.01.002 Accessed 2022/12/29.

309. European Society of Gynaecological Oncology. ESGO-ESTRO-ESP 2022 update of the cervical cancer guidelines. 2023; https://guidelines.esgo.org/cervical-cancer/guidelines/recommendations/. Accessed Janury 21, 2023.

310. Aetna. Stereotactic radiosurgery. 2022; https://www.aetna.com/cpb/medical/data/1_99/0083.html. Accessed January 23, 2023.

311. Cigna. Radiation oncology guidelines. 2022; https://www.evicore.com/-/media/files/evicore/provider/network-standard/cigna_radiation_oncology_guidelines_v102022_eff12152022_pub09052022.pdf.

312. Regence. Stereotactic radiosurgery and stereotactic body radiation therapy for tumors outside of intracranial, skull base, or orbital sites. 2022; https://blue.regence.com/trgmedpol/surgery/sur214.pdf. Accessed January 25, 2023.

Appendix A. Search Strategy

Databases

- Ovid MEDLINE(R) All: from 1946 to October 21, 2022
- Cochrane Library databases (Cochrane Database of Systematic Reviews and Cochrane Central Register of Controlled Trials): from database inception to October 31, 2022

Database search strategies designed and executed by Shannon Robalino.

Search Terms for Ovid MEDLINE

Ovid MEDLINE(R) ALL <1946 to October 21, 2022>

Search date: October 24, 2022

1. (SBRT or SABR).ti,ab,kw.

2. (("stereotactic body" or stereotactic-body) adj1 (radiotherap* or "radio therap*" or RT or radiation or irradi* or ablati* or radioablati* or "radio ablat*")).ti,ab,kw.

3. ((stereotactic ablati* or stereotactic-ablati*) adj1 (radiotherap* or "radio therap*" or RT or radiation or irradi*)).ti,ab,kw.

4. (stereotactic radioablati* or stereotactic-radioablati*).ti,ab,kw.

5. or/1-4

6. (cyberknife* or cyber knife* or gammaknife* or gamma knife*).ti,ab,kw.

7. 6 and 5

8. ((cyberknife* or cyber knife* or gammaknife* or gamma knife*) and (SBRT or SABR)).ti,ab,kw.

9. ((cyberknife* or cyber knife* or gammaknife* or gamma knife*) adj2 (radiotherap* or "radio therap*" or RT or radiation or irradi* or ablati* or radioablati* or "radio ablat*")).ti,ab,kw.

10. or/7-9

11. 5 or 10

12. limit 11 to english language

13. (case reports or clinical conference or comment or congress or consensus development conference or consensus development conference, nih or editorial or interactive tutorial or letter or observational study, veterinary or randomized controlled trial, veterinary).pt.

14. ((phase 1* or phase i or phase ii or phase 2*) not (phase iii* or phase iv)).ti.

15. (exp Animals/ not Humans/) or (animal$1 or bovine$1 or canine$1 or cat$1 or chimpanzee$1 or cow$1 or dog$1 or feline$1 or goat$1 or hens or mice or monkey$1 or mouse

or murine$1 or ovine or pig$1 or porcine or primate$1 or sheep or rabbit$1 or rat or rats or rattus or rhesus or rodent*).ti.

16. ((spine or spinal or brain or CNS or central nervous system or ventricular) not (non-spine or non-brain or non-CNS)).ti.

17. or/13-16

18. 12 not 17

19. "Africa South of Sahara"/ or Africa, Central/ or Africa, Eastern/ or Africa, Northern/ or Africa, Southern/ or Africa, Western/ or Indochina/ or Melanesia/ or Sub-Saharan.ti. or Central Africa.ti. or East$3 Africa.ti. or North$3 Africa.ti. or Southern Africa.ti. or West$3 Africa.ti.

20. Afghanistan.ti. or Afghanistan/ or Albania.ti. or Albania/ or Algeria.ti. or Algeria/ or Angola.ti. or Angola/ or Antigua.ti. or Barbuda.ti. or "Antigua and Barbuda"/ or Armenia.ti. or Aremenia/ or Azerbaijan.ti. or Azerbaijan/ or Bangladesh.ti. or Bangladesh/ or Barbados.ti. or Barbados/ or Belize.ti. or Belize/ or Benin.ti. or Benin/ or Bhutan.ti. or Bhutan/ or Bolivia.ti. or Bolivia/ or "Bosnia and Herzegovina".ti. or "Bosnia and Herzegovina"/ or Botswana.ti. or Botswana/ or Brazil.ti. or Brasil.ti. or Brazil/ or Bulgaria.ti. or Bulgaria/ or Burkina Faso.ti. or Burkina Faso/ or Burundi.ti. or Burundi/

21. Cabo Verde.ti. or Cabo Verde/ or Cambodia.ti. or Cambodia/ or Cameroon.ti. or Cameroon/ or "Central African Republic".ti. or Central African Republic/ or Chad.ti. or Chad/ or China.ti. or China/ or Colombia.ti. or Colombia/ or Comoros.ti. or Comoros/ or Congo.ti. or Congo/ or Cote d'Ivoire.ti. or Ivory Coast.mp. or Cote d'Ivoire/ or Cuba.ti. or Cuba/ or "Democratic Republic of Congo"/ or Djibouti.ti. or Djibouti/ or Dominica.ti. or Dominica/ or Dominican Republic.ti. or Dominican Republic/ [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

22. Ecuador.ti. or Ecuador/ or Egypt.ti. or Egypt/ or El Salvador.ti. or El Salvador/ or Equatorial Guinea.ti. or Equatorial Guinea/ or Eritrea.ti. or Eritrea/ or Eswatini.ti. or Eswatini/ or Ethiopia.ti. or Ethiopia/ or Fiji.ti. or Fiji/ or Gabon.ti. or Gabon/ or Gambia.ti. or Gambia/ or Ghana.ti. or Ghana/ or Grenada.ti. or Grenada/ or Guatemala.ti. or Guatemala/ or Guinea.ti. or Guinea/ or Guinea-Bissau.ti. or Guinea-Bissau/ or Guyana.ti. or Guyana/ or Haiti.ti. or Haiti/ or Honduras.ti. or Honduras/

23. India.ti. or India/ or Indonesia.ti. or Indonesia/ or Iran.ti. or Iran/ or Iraq.ti. or Iraq/ or Jamaica.ti. or Jamaica/ or Jordan.ti. or Jordan/ or Kenya.ti. or Kenya/ or Kiribati.ti. or Kyrgyzstan.ti. or Kyrgyzstan/ or Laos.ti. or Laos/ or Lebanon.ti. or Lebanon/ or Lesotho.ti. or Lesotho/ or Liberia.ti. or Liberia/ or Libya.ti. or Libya/

24. Madagascar.ti. or Madagascar/ or Malawi.ti. or Malawi/ or Maldives.ti. or Mali.ti. or Mali/ or Marshall Islands.ti. or Mauritania.ti. or Mauritania/ or ((Mexico.ti. or Mexico/) not "New Mexico".ti.) or Micronesia.ti. or Moldova.ti. or Moldova/ or Mongolia.ti. or Mongolia/ or Morocco.ti. or Morocco/ or Mozambique.ti. or Mozambique/ or Myanmar.ti. or Myanmar/ or

Namibia.ti. or Namibia/ or Nauru.ti. or Nepal.ti. or Nepal/ or Nicaragua.ti. or Nicaragua/ or Niger.ti. or Niger/ or Nigeria.ti. or Nigeria/ or North Korea.ti. or "Democratic People's Republic of Korea"/ or North Macedonia.ti. or "Republic of North Macedonia"/

25. Pakistan.ti. or Pakistan/ or Palau.ti. or Palau/ or Palestine.ti. or Papua New Guinea.ti. or Papua New Guinea/ or Paraguay.ti. or Paraguay/ or Peru.ti. or Peru/ or Philippines.ti. or Philippines/ or Rwanda.ti. or Rwanda/ or "Saint Kitts and Nevis".ti. or "Saint Kitts and Nevis"/ or Saint Lucia.ti. or Saint Lucia/ or "Saint Vincent and Grenadines".ti. or "Saint Vincent and Grenadines"/ or Samoa.ti. or Samoa/ or "Sao Tome and Principe".ti. or "Sao Tome and Principe"/ or Senegal.ti. or Senegal/ or Seychelles.ti. or Seychelles/ or Sierra Leone.ti. or Sierra Leone/ or Solomon Islands.ti. or Somalia.ti. or Somalia/ or South Africa.ti. or South Africa/ or South Sudan.ti. or South Sudan/ or Sri Lanka.ti. or Sri Lanka/ or Sudan.ti. or Sudan/ or Suriname.ti. or Suriname/ or "Syrian Arab Republic".ti. or Syria.ti. or Syria/

26. Tajikistan.ti. or Tajikistan/ or Tanzania.ti. or Tanzania/ or Timor-Leste.ti. or Timor-Leste/ or Togo.ti. or Togo/ or Tonga.ti. or Tonga/ or Tunisia.ti. or Tunisia/ or Turkmenistan.ti. or Turmenistan/ or Tuvalu.ti. or Uganda.ti. or Uganda/ or Ukraine.ti. or Ukraine/ or Uzbekistan.ti. or Uzbekistan/ or Vanuatu.ti. or Vanuatu/ or Venezuela.ti. or Venezuela/ or Viet Nam.ti. or Vietnam.ti. or Vietnam/ or Yemen.ti. or Yemen/ or Zambia.ti. or Zambia/ or Zimbabwe.ti. or Zimbabwe/

27. or/19-26

28. 18 not 27

29. (random* adj3 assign*).ab.

30. ("clinical trial" or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or "multicenter study" or "randomized controlled trial").pt. or double-blind method/ or clinical trials as topic/ or clinical trials, phase iii as topic/ or clinical trials, phase iv as topic/ or controlled clinical trials as topic/ or randomized controlled trials as topic/ or early termination of clinical trials as topic/ or multicenter studies as topic/ or ((randomi?ed adj7 trial*) or (controlled adj3 trial*) or (clinical adj2 trial*) or ((single* or doubl* or tripl* or treb* or quad*) adj1 (blind* or mask*))).ti,ab,kw. or ("2 arm" or "two arm" or "3 arm" or "three arm" or "4 arm" or "four arm" or "5 arm" or "five arm").ti,ab,kw. or quasi*.ti,ab.

31. (phase 3* or phase iii* or phase 4* or phase iv*).ti,ab.

32. (placebo* or head-to-head or (compar* adj3 (effectiveness or efficacy))).ti,ab,kw. or Comparative Effectiveness Research/

33. (active adj1 (comparator* or control$1 or treatment*)).ti,ab.

34. or/29-33

35. 28 and 34

36. cohort studies/ or longitudinal studies/ or follow-up studies/ or prospective studies/ or retrospective studies/ or cohort.ti,ab. or longitudinal.ti,ab. or prospective.ti,ab. or retrospective.ti,ab.

37. (28 and 36) not 35

38. (((comprehensive* or integrative or systematic*) adj3 (bibliographic* or review* or literature)) or (meta-analy* or metaanaly* or "research synthesis" or ((information or data) adj3 synthesis) or (data adj2 extract*))).ti,ab. or (cinahl or (cochrane adj3 trial*) or embase or medline or psyclit or (psycinfo not "psycinfo database") or pubmed or scopus or "sociological abstracts" or "web of science").ab. or ("cochrane database of systematic reviews" or evidence report technology assessment or evidence report technology assessment summary).jn. or Evidence Report: Technology Assessment*.jn. or ((review adj5 (rationale or evidence)).ti,ab. and review.pt.) or meta-analysis as topic/ or Meta-Analysis.pt.

39. psychinfo.ab. or heath technology assessment.ti,ab. or ((review or umbrella or evidence) adj2 (review* or synthesis)).ti,ab.

40. or/38-39

41. (28 and 40) not (35 or 37)

42. 28 not (35 or 37 or 41)

Cochrane Central Register of Controlled Trials (via CochraneLibrary.com)

Issue 10 of 12, October 2022

Search date: October 31, 2022

1 SBRT or SABR

2 (("stereotactic body" or stereotactic-body) near/1 (radiotherap* or "radio therap*" or RT or radiation or irradi* or ablati* or radioablati* or "radio ablat*"))

3 ((stereotactic ablati* or stereotactic-ablati*) near/1 (radiotherap* or "radio therap*" or RT or radiation or irradi*))

4 stereotactic radioablati* or stereotactic-radioablati*

5 (or 1-4)

6 ((cyberknife* or cyber knife* or gammaknife* or gamma knife*) and (SBRT or SABR)):ti,ab

7 ((cyberknife* or cyber knife* or gammaknife* or gamma knife*) near/2 (radiotherap* or "radio therap*" or RT or radiation or irradi* or ablati* or radioablati* or "radio ablat*")):ti,ab

8 (or 6-7)

9 5 or 8

10 ((spine or spinal or brain or CNS or central nervous system or ventricular) not (non-spine or non-brain or non-CNS)):ti

11 9 NOT 10

12 11 in Trials

Clinical Practice Guidelines

We also searched following sources on November 28, 2022, for cancer guidelines containing information on SBRT using terms stereotactic, SBRT, SABR, ultrahypofractionated, and radiotherapy:

- NICE (National Institute for Health and Care Excellence)
- SIGN (Scottish Intercollegiate Guidelines Network)
- GIN (Guidelines International Network)
- AHRQ (Agency for Healthcare Research and Quality)
- VA EBS (Veteran's Administration Evidence-Based Synthesis Program
- ASCO (American Society of Clinical Oncology)
- ESMO (European Society for Medical Oncology)
- ASCRS (American Society of Colon and Rectal Surgeons)
- SIOP (International Society of Paediatric Oncology)
- ACP (Association of Cancer Physicians)
- SGO (Society of Gynecologic Oncology)
- IASLC (International Association for Study of Lung Cancer)
- ESGO (European Society of Gynaecological Oncology)
- COSA (Clinical Oncology Society of Australia). The
- ACR (American College of Radiology)
- ASTRO (American Society for Radiation Oncology)
- RSNA (Radiological Society of North America)
- SIR (Society of Interventional Radiology)
- RANZCR (Royal Australian and New Zealand College of Radiologists)
- AUA (American Urological Association)
- EAU (European Association of Urology)

We also conducted a search for guidelines using Duck Duck Go web browser. Only guidelines published in past 5 years were considered. Guideline searches designed and executed by Jennifer Lyon.

Safety Searches

We searched the US FDA Manufacturer and User Facility Device Experience (MAUDE) and Medical Device Recall databases using the keyword *stereotactic*.

Ongoing Studies

We searched the ClinicalTrials.gov for ongoing randomized controlled trials using the keyword *stereotactic*.

Appendix B. Additional Methods

Table B1. Risk-of-Bias Assessment: Randomized Controlled Trials

Domain	Domain Elements The elements included in each domain are assessed and rated as *Yes*, *No*, *Unclear*, or *Not Applicable* based on performance and documentation of individual elements in each domain. The overall risk-of-bias for study is assessed as *High*, *Moderate*, or *Low* based on assessment of how well overall study methods and processes were performed to limit bias and ensure validity.
Randomization	• An appropriate method of randomization is used to allocate participants or clusters to groups, such as a computer random number generator • Baseline characteristics between groups or clusters are similar
Allocation Concealment	• An adequate concealment method is used to prevent investigators and participants from influencing enrollment or intervention allocation
Intervention	• Intervention and comparator intervention applied equally to groups • Co-interventions appropriate and applied equally to groups • Control selected is an appropriate intervention
Outcomes	• Outcomes are measured using valid and reliable measures • Investigators use single outcome measures and do not rely on composite outcomes, or outcome of interest can be calculated from composite outcome • The trial has an appropriate length of follow-up and groups are assessed at same time points • Outcome reporting of entire group or subgroups is not selective
Masking (Blinding) of Investigators and Participants	• Investigators and participants are unaware (masked or blinded) of intervention status
Masking (Blinding) of Outcome Assessors	• Outcome assessors are unaware (masked or blinded) of intervention status
Intention to Treat Analysis	• Participants are analyzed based on random assignment (intention-to-treat analysis)
Statistical Analysis	• Participants lost to follow-up unlikely to significantly bias results (i.e., complete follow-up of ≥ 80% of participants overall and nondifferential, ≤ 10% difference between groups) • The most appropriate summary estimate (e.g., risk ratio, hazard ratio) is used • Paired or conditional analysis used for crossover RCT • Clustering appropriately accounted for in a cluster-randomized trial (e.g., use of an intraclass correlation coefficient)

Other Biases (as appropriate)	• List others in table footnote and describe, such as:
	  ○ Sample size adequacy
	  ○ Interim analysis or early stopping
	  ○ Recruitment bias, including run-in period used inappropriately
	  ○ Use of unsuitable crossover intervention in a crossover RCT

Interest Disclosure	• Disclosures of interest are provided for authors/funders/commissioners of study • Interests are unlikely to significantly affect study validity
Funding	• There is a description of source(s) of funding • Funding source is unlikely to have a significant impact on study validity

Abbreviation. RCT: randomized controlled trial.

Table B2. Risk-of-Bias Assessment: Nonrandomized Studies

Domain	Domain Elements The elements included in each domain are assessed and rated as *Yes*, *No*, *Unclear*, or *Not Applicable* based on performance and documentation of individual elements in each domain. The overall risk-of-bias for study is assessed as *High*, *Moderate*, or *Low*, based on assessment of how well overall study methods and processes were performed to limit bias and ensure validity.
Participant Selection	For cohort studies: • The 2 groups being studied are selected from source populations comparable in all respects other than factor under investigation, or statistical adjustment is used appropriately to achieve this • The study indicates how many of people asked to take part did so in each of groups being studied • The likelihood some eligible participants might have outcome at time of enrolment is assessed and considered in analysis • Fewer than 20% of individuals or clusters in each arm of study dropped out before study was completed For case-control studies: • Cases and controls are clearly specified and defined, with inclusion and exclusion criteria applied appropriately • Cases may be selected by meeting inclusion criteria, controls may be selected by meeting inclusion criteria and then being matched to cases • Sampling selection (ratio of cases to control) is justified • Cases and controls selected from same population and same timeframe; when not all cases and controls are selected from same population, these are randomly selected • Among cases, investigators confirm that exposure occurred before development of disease being studied and/or likelihood that some eligible participants might have outcome at time of enrolment is assessed and considered in analysis
Intervention	• The assessment of exposure to intervention is reliable • Exposure level or prognostic factors are assessed at multiple times across length of study, if appropriate • For case-control studies assessors of (intervention) exposure status are unaware (masked or blinded) to case or control status of participants there is a method to limit effects of recall bias on assessment of exposure to intervention
Control	• Control condition represents an appropriate comparator
Outcome	• There is a precise definition of outcomes used • Outcomes are measured using valid and reliable measures, evidence from other sources is used to demonstrate method of outcome assessment is valid and reliable • Investigators use single outcome measures and do not rely on composite outcomes, or outcome of interest can be calculated from composite outcome • The study has an appropriate length of follow-up for outcome reported and groups are assessed at same time points • Outcome reporting of entire group or subgroups is not selective • When patient-reported outcomes are used, there is a method for validating measure

Domain	Domain Elements The elements included in each domain are assessed and rated as *Yes*, *No*, *Unclear*, or *Not Applicable* based on performance and documentation of individual elements in each domain. The overall risk-of-bias for study is assessed as *High*, *Moderate*, or *Low*, based on assessment of how well overall study methods and processes were performed to limit bias and ensure validity.
Masked Outcome Assessment	• The assessment of outcome(s) is made blind to exposure status. Where outcome assessment blinding was not possible, there is recognition that knowledge of exposure status could have influenced assessment of outcome • For case-control study: assessors of exposure status are unaware (masked or blinded) of case or control status of participant)
Confounding	• The main potential confounders are identified and considered in design and analysis of study
Statistical Analysis	• Comparison is made between full participants and those who dropped out or were lost to follow-up, by exposure status • If groups were not followed for an equal length of time, analysis was adjusted for differences in length of follow-up • All major confounders are adjusted for using multiple variable logistic regression or other appropriate statistical methods • Confidence intervals (or information used to calculate them) are provided • For case-control studies that use matching, conditional analysis is conducted or matching factors are adjusted for in analysis
Other Biases (as appropriate)	• List others in table footnote and describe • Sample size adequacy
Interest Disclosure	• Disclosures of interest are provided for authors/funders/commissioners of study • Interests are unlikely to significantly affect study validity
Funding Source	• There is a description of source(s) of funding • Funding source is unlikely to have a significant impact on study validity

Table B3. Risk-of-Bias Assessment: Economic Modeling Studies

Domain	Domain Elements The elements included in each domain are assessed and rated as *Yes*, *No*, *Unclear*, or *Not Applicable* based on performance and documentation of individual elements in each domain. The overall risk-of-bias for study is assessed as *High*, *Moderate*, or *Low* based on assessment of how well overall study methods and processes were performed to limit bias and ensure validity.
Target Population	• Target population and care setting described • Describe and justify basis for any target population stratification, identify any a previousi identifiable subgroups • If no subgroup analyses were performed, justify why these were not required
Perspective	• State and justify analytic perspective (e.g., societal, payer, etc.)
Time Horizon	• Describe and justify time horizon(s) used in analysis
Discount Rate	• State and justify discount rate used for costs and outcomes
Comparators	• Describe and justify selected comparators • Competing alternatives appropriate and clearly described
Modelling	• Model structure (e.g., scope, assumptions made) is described and justified • Model diagram provided, if appropriate • Model validation is described (may involve validation of different aspects such as structure, data, assumptions, and coding and different validation models such as comparison with other models) • Data sources listed and assumptions for use justified • Statistical analyses are described
Effectiveness	• Estimates of efficacy/effectiveness of interventions are described and justified • The factors likely to have an impact on effectiveness (e.g., adherence, diagnostic accuracy, values, and preferences) are described and an explanation of how these were factored into analysis is included • The quality of evidence for relationship between intervention and outcomes, and any necessary links, is described
Outcomes	• All relevant outcomes are identified, measured, and valued appropriately (including harms/adverse events) for each intervention, and justification for information/assumptions is given • Any quality of life measures used in modelling are described and use justified • Any other outcomes that were considered but rejected are described with rationale for rejection • Ethical and equity-related outcomes are considered and included when appropriate
Resource Use/Costs	• All resources used are identified, valued appropriately, and included in analyses • Methods for costing are reporting (e.g., patient level) • Resource quantities and unit costs are both reported • Methods for costing time (e.g., lost time, productivity losses) are appropriate and a justification is provided if time costs are not considered
Uncertainty	• Sources of uncertainty in analyses are identified and justification for probability distributions used in probabilistic analyses are given • For scenario analyses, values and assumptions tested are provided and justified
Results	• All results are presented in a disaggregated fashion, by component, in addition to an aggregated manner

Domain	Domain Elements The elements included in each domain are assessed and rated as *Yes*, *No*, *Unclear*, or *Not Applicable* based on performance and documentation of individual elements in each domain. The overall risk-of-bias for study is assessed as *High*, *Moderate*, or *Low* based on assessment of how well overall study methods and processes were performed to limit bias and ensure validity.
	• All results are presented with undiscounted totals before discounting and aggregation • Natural units are presented along with alternative units (e.g., QALYs) • The components of incremental cost-effectiveness ratio (ICER) are shown (e.g., mean costs of each intervention in numerator and mean outcomes of each intervention in denominator) • Results of scenario analyses, including variability in factors such as practice patterns and costs, are reported and described in relation to reference (base) case
Interest Disclosure	• Disclosures of interest are provided for authors/funders/commissioners of study • Interests are unlikely to significantly affect study validity
Funding Source	• There is a description of source(s) of funding • Funding source is unlikely to have a significant impact on study validity

Abbreviations. ICER: incremental cost-effectiveness ratio; QALY: quality-adjusted life year.

Table B4. Risk-of-Bias Assessment: Clinical Practice Guidelines

Domain	Domain Elements Assessment indicates how well guideline methodology and development process were performed to limit bias and ensure validity for elements in domain (each domain rated as *Good*, *Fair*, or *Poor* overall based on performance and documentation of elements)
Rigor of Development: Evidence	• Systematic literature search meets quality standards for a systematic review (i.e., comprehensive search strategy with, at a minimum, 2 or more electronic databases) • The criteria used to select evidence for inclusion is clear and appropriate • The strengths and limitations of individual evidence sources is assessed and overall quality of body of evidence assessed
Rigor of Development: Recommendations	• Methods for developing recommendations clearly described and appropriate • There is an explicit link between recommendations and supporting evidence • The balance of benefits and harms is considered in formulating recommendations • The guideline has been reviewed by external expert peer reviewers • The updating procedure for guideline is specified in guideline or related materials (e.g., specialty society website)
Editorial Independence	• There is a description of source(s) of funding and views of funder(s) are unlikely to have influenced content or validity of guideline • Disclosures of interests for guideline panel members are provided and are unlikely to have a significant impact on overall validity of guideline (e.g., a process for members to recuse themselves from participating on recommendations for which a significant conflict is provided)
Scope and Purpose	• Objectives specifically described • Health question(s) specifically described • Target population(s) for guideline recommendations is specified (e.g., patients in primary care) and target users for guideline (e.g., primary care clinicians)
Stakeholder Involvement	• Relevant professional groups represented • Views and preferences of target population(s) sought (e.g. clinicians and patients)
Clarity and Presentation	• Recommendations are specific and unambiguous • Different management options are clearly presented • Key recommendations are easily identifiable
Applicability	• Provides advice and/or tools on how recommendation(s) can be put into practice • Description of facilitators and barriers to its application • Potential resource implications considered • Criteria for implementation monitoring, audit, and/or performance measures based on guideline are presented

Appendix C. Evidence Tables

Study Characteristics of Included Randomized Controlled Trials

Breast Cancer

No RCTs identified.

Prostate Cancer

Table C1. Study Characteristics for Randomized Controlled Trials

Citation Setting NCT or Other Trial ID or Study Name	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Intervention	Comparator(s)	Relevant Outcomes Measured
Brand et al, 2019[1,2] 37 centers in UK, Ireland, and Canada NCT01584258 PACE-B	To compare conventionally fractionated or moderately hypofractionated RT with 5-fraction SBRT for low-risk to intermediate-risk localized prostate cancer Randomized noninferiority trial Followed up to 24 months	Inclusion criteria (must meet all): aged at least 18 years; WHO performance status of 0 to 2; life expectancy of ≥ 5 years; histologically confirmed prostate adenocarcinoma; NCCN low-risk or intermediate-risk disease; Gleason score ≤ 3 + 4 Exclusion criteria (excluded if any criteria met): previous malignancy within past 2 years (except basal cell carcinoma or	Total N = 874, comprising 433 in SBRT group and 441 in control group Toxicity analysis included 847 patients (415 in SBRT group and 432 in control group) Sex: men only Race/ethnicity: 35 (8%) Black, 4 (1%) East Asian, 2 (< 1%) Mixed heritage, 19 5%) South Asian, 352 (85%) White, 3 (1%) other, SBRT; 25 (6%)	• SBRT ○ 36.25 Gy in 5 fractions over 1 to 2 weeks (i.e., daily or alternate days, at center discretion), with an additional secondary CTV dose target of 40 Gy	• cRT or moderately hypofractionated radiotherapy ○ PTV dose was 78 Gy in 39 daily fractions or, following an approved protocol amendment, 62 Gy in 20 daily fractions	• Progression • Safety

Citation Setting NCT or Other Trial ID or Study Name	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Intervention	Comparator(s)	Relevant Outcomes Measured
		squamous cell carcinoma of skin), or if previous malignancy is expected to significantly compromise 5-year survival; previous pelvic RT; previous ADT	Black, 3 (1%) East Asian, 2 (< 1%) Mixed heritage, 9 (2%) South Asian, 386 (89%) White, 7 (2%) other, control Mean age (SD): 69.6 years (65.3 to 73.8), SBRT; 69.7 years (65.6 to 73.9), control No family history of prostate cancer: 300 (72%), SBRT; 321 (74%), control WHO performance status: 372 (90%), SBRT; 382 (88%), control NCCN risk score: 30 (7%) low, 385 (93%) intermediate, SBRT; 38 (9%) low, 394 (91%)			

Citation Setting NCT or Other Trial ID or Study Name	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Intervention	Comparator(s)	Relevant Outcomes Measured
			intermediate, control Active surveillance before enrollment: 146 (35%) SBRT; 160 (37%), control			
Kwan et al., 2022[3] 2 sites in Canada NCT02594072 ASSERT	To compare moderate hypofractionation with SBRT in men with high-risk localized prostate cancer RCT At least 6 months	Inclusion criteria (must meet all): men with intermediate- or high-risk prostate cancer Exclusion criteria (excluded if any criteria met): high-risk disease with metastases; hip prosthesis; prostate volume > 90 mL In general, patients were not candidates for brachytherapy or were unwilling to undergo brachytherapy	Total N = 80, comprising 42 in SBRT group and 36 in control group Sex: men only Race/ethnicity: NR Median age (range): 73.2 years (64.7 to 83.5) SBRT; 74.2 years (61.8 to 86.6) control High-risk: 15 (36%) SBRT; 10 (28%) control Previous TURP: 4 (9%) SBRT; 4 (11%) control	• SBRT ○ 36.25 Gy in 5 fractions weekly ○ ADT (6 months in intermediate risk and 18 months in high-risk) by either luteinizing hormone-releasing hormone agonists or antagonists	• Moderate hypofractionation RT ○ 70 Gy in 28 fractions 5 times a week • ADT (6 months in intermediate risk and 18 months in high risk) by either luteinizing hormone-releasing hormone agonists or antagonists	• Quality of life • Safety

Citation Setting NCT or Other Trial ID or Study Name	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Intervention	Comparator(s)	Relevant Outcomes Measured
Lukka et al., 2018[4] 37 sites, including academic centers, in US and Canada NCT01434290	To assess QoL in patients treated with SBRT or UHRT RCT (along with comparison against historical controls) Median follow-up of 3.8 years	Inclusion criteria (must meet all): prostate adenocarcinoma; Gleason scores of 2 to 6; cT1-2a; PSA < 10 ng/mL; undergoing active surveillance if rebiopsied and confirmed still to have low-risk disease eligible for enrollment within 1 year of repeat biopsy Exclusion criteria (excluded if any criteria met): previous or concurrent invasive malignancy; lymphomatous or hematogenous malignancy, unless continually disease-free for a minimum of 5 years; distant metastases; regional lymph node involvement;	Total N = 255, comprising 127 in SBRT group and 128 in UHRT group Sex: men only Race/ethnicity: 1 (1%) Asian, 11 (9%) Black, 106 (89%) White, 1 (1%) unknown, 4 (3%) Hispanic or Latino, SBRT; 3 (3%) Asian, 10 (8%) Black, 105 (87%) White, 3 (3%) unknown, 3 (3%) Hispanic or Latino, UHRT Median age (range): 64 years (48 to 77) SBRT; 66 years (50 to 79) UHRT Zubrod performance status of 0: 112 (94%) SBRT; 117 (97%) UHRT	• SBRT ◦ 36.25 Gy in 5 fractions of 7.25 Gy ◦ More than 2 weeks	• UHRT ◦ 51.6 Gy in 12 fractions of 4.3 Gy • More than 2.5 weeks	• Quality of life • Safety

Citation Setting NCT or Other Trial ID or Study Name	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Intervention	Comparator(s)	Relevant Outcomes Measured
		previous prostatectomy; cryosurgery; high-intensity focused ultrasound treatment; pelvic irradiation; prostate BT; bilateral orchiectomy or hormonal therapy; previous or concurrent cytotoxic chemotherapy; used finasteride or dutasteride within 30 to 90 days; severe active comorbidities	Clinical T-stage: 2 (2%) T1a, 96 (81%) T1c; 1 (1%) T2, 20 (17%) T2a, SBRT; 0 T1a, 100 (83%) T1c; 0 T2, 21 (17%) T2a, UHRT Median PSA (range): 5.6 ng/mL (0.71 to 9.9) SBRT; 5.5 ng/mL (1.69 to 9.99) UHRT			
Widmark et al., 2019[5,6] 12 centers in Sweden and Denmark ISRCTN45905321 HYPO-RT-PC	To show noninferiority of UHRT compared with conventional fractionation Randomized noninferiority trial Followed up to 10 years	Inclusion criteria (must meet all): men aged up to 75 years; histologically verified intermediate-to-high-risk prostate cancer (T1c to T3a with no evidence of lymph node involvement or distant metastases with 1 or 2 of	Total N = 1,200, comprising 598 in SBRT group and 602 in cRT group PP analysis included 1,180 (589 in SBRT group and 591 in cRT group) Sex: men only	• SBRT ◦ 42.7 Gy in 7 fractions ◦ 3 days over 2.4 weeks	• cRT ◦ 78.0 Gy in 39 fractions ◦ 5 days per week for 8 weeks	• Survival rate • Progression • Quality of life • Safety

Citation Setting NCT or Other Trial ID or Study Name	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Intervention	Comparator(s)	Relevant Outcomes Measured
		following risk factors: stage T3a, Gleason score of at least 7, or PSA of at least 10 ng/mL); WHO performance status of 0 to 2 Exclusion criteria (excluded if any criteria met): PSA > 20 ng/mL; ADT	Race/ethnicity: NR Median age (IQR): 68 years (64 to 72), SBRT; 69 years (64 to 72), cRT Risk group: 527 (89%), intermediate, 62 (11%) high, SBRT; 527 (89%), intermediate, 64 (11%) high, cRT Median time from randomization to start of RT: 3 weeks (1 to 6), SBRT; 3 weeks (1 to 6), cRT Median time of total RT: 16 weeks (15 to 17), SBRT; 57 days (55 to 59), cRT			

Abbreviations. ADT: androgen deprivation therapy; cRT: conventional radiation therapy; CTV: clinical target volume; ECOG: Eastern Cooperative Oncology Group; GI: gastrointestinal; GU: genitourinary; Gy: Gray; IQR: interquartile range; ITT: intention-to-treat; MFR: multifraction radiotherapy; MRI: magnetic

resonance imaging; NCCN: National Comprehensive Cancer Network; NCT: US National Clinical Trial; NR: not reported; OS: overall survival; PFS: progression-free survival; PP: per-protocol; PSA: prostate-specific antigen; PSADT: PSA doubling time; PTV: planning target volume; QoL: quality of life; RCT: randomized controlled trial; RT: radiotherapy; SABR: stereotactic ablative radiotherapy; SBRT: stereotactic body radiation therapy; SD: standard deviation; TURP: transurethral resection of prostate; UHRT: ultrahypofractionated radiation therapy; WHO: World Health Organization.

Lung Cancer

Table C2. Study Characteristics for Randomized Controlled Trials

Citation Setting NCT or Other Trial ID or Study Name	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Intervention	Comparator(s)	Relevant Outcomes Measured
Altorki et al., 2021[7,8] Single center in US NCT02904954	To evaluate use of SBRT in patients with early-stage NSCLC as an immunomodulator to enhance anti-tumor immune response associated with durvalumab previous to surgery RCT Followed up to 2 years	Inclusion criteria (must meet all): biopsy-proven NSCLC with clinical stages I to IIIA; deemed surgically resectable with curative intent; aged 18 years or older; ECOG performance status of 0 or 1; adequate cardiopulmonary, hematological, and other end organ function Exclusion criteria (excluded if any criteria met): concurrent invasive malignancy; history of another invasive cancer within past 3 years; active	Total N = 60, comprising 30 in durvalumab plus SBRT group and 30 in durvalumab in group Sex: 15 (50%) female, SBRT; 14 (47%) control Race/ethnicity: NR Median age (IQR): 70 years (64 to 74) SBRT; 71 years (65 to 75) control ECOG performance status: 23 (77%) 0, 7 (23%) 1, SBRT; 21 (70%) 0, 9 (30%) 1, control	• SBRT plus durvalumab ○ 3 consecutive daily fractions of 8 Gy ○ 2 cycles of durvalumab 3 weeks apart at a dose of 1·12 g by intravenous infusion over 60 min	• Durvalumab ○ 2 cycles of durvalumab 3 weeks apart at a dose of 1·12 g by intravenous infusion over 60 min	• Duration of symptom-free remission • Quality of life • Safety

Citation Setting NCT or Other Trial ID or Study Name	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Intervention	Comparator(s)	Relevant Outcomes Measured
		autoimmune disease; systemic immune suppression; radiographic evidence of interstitial lung disease	Smoking status: 10 (33%) current, 16 (53%) former, SBRT; 7 (23%) current, 17 (57%) former, control Clinical stage: 1 (3%) IA, 7 (23%) IB, 6 (20%) IIA, 4 (13%) IIB, 12 (40%) IIIA, SBRT; 3 (10%) IA, 8 (27%) IB, 1 (3%) IIA, 4 (13%) IIB, 14 (47%) IIIA, control Invasive mediastinal staging: 13 (43%) SBRT; 12 (40%) control Cell type: 18 (60%) adenocarcinoma, 12 (40%) squamous, 0 sarcomatoid, 0 not otherwise specified, SBRT; 16 (53%) adenocarcinoma,			

Citation Setting NCT or Other Trial ID or Study Name	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Intervention	Comparator(s)	Relevant Outcomes Measured
			11 (37%) squamous, 1 (3%) sarcomatoid, 2 (7%) not otherwise specified, control EGFR mutation positive: 7 (23%) SBRT; 5 (17%) control			
Theelen et al., 2019[9] 3 centers in Netherlands NCT02492568 PEMBRO-RT	To assess whether stereotactic body radiotherapy on a single tumor site preceding pembrolizumab treatment enhances tumor response in patients with metastatic NSCLC RCT Median follow-up of 24 months	Inclusion criteria (must meet all): 18 years or older; histological or cytological confirmed metastatic NSCLC that progressed after at least 1 regimen of chemotherapy; immunotherapy naïve; ECOG performance status of 1 or lower Exclusion criteria (excluded if any criteria met): RT to any tumor site within 6 months before	Total N = 78, comprising 38 in SBRT group and 40 in control group Sex: 16 (44%) female, SBRT; 17 (43%) female, control Race/ethnicity: NR Median age (range): 62 years (35 to 78) SBRT; 62 years (38 to 78) control ECOG performance score: 17 (47%) 0, 19 (53%) 1, 0 0,	• SBRT plus pembrolizumab ○ 3 doses of 8 Gy delivered on alternate days to a single tumor site that did not overlap with biopsy site and was deemed most safe or convenient for patient ○ Pembrolizumab administered intravenously at 200 mg every 3 weeks	• Pembrolizumab ○ Pembrolizumab administered intravenously at 200 mg every 3 weeks	• Survival rate • Duration of symptom-free remission • Safety

Citation Setting NCT or Other Trial ID or Study Name	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Intervention	Comparator(s)	Relevant Outcomes Measured
		randomization; known, active CNS metastases; carcinomatous meningitis; untreated driver alterations of epidermal growth factor receptor or anaplastic lymphomakinase; active autoimmune or interstitial lung disease.	SBRT; 22 (55%) 0, 17 (43%) 1, 1 (3%) 2, control Histology: 31 (86%) nonsquamous, SBRT; 36 (90%) nonsquamous, control Previous RT: 15 (42%) SBRT; 17 (43%) control Number of lines of previous systemic treatment: 26 (72%) 1, 6 (17%) 2, 4 (11%) 3, SBRT; 31 (78%) 1, 8 (20%) 2, 1 (3%) 3, control			

Abbreviations. CNS: central nervous system; Gy: Gray; ECOG: Eastern Cooperative Oncology Group; IQR: interquartile range; NR: not reported; SBRT: stereotactic body radiation therapy; SD: standard deviation.

Colorectal Cancer

No RCTs identified.

Uterine Cancer

No RCTs identified.

Melanoma

Table C3. Study Characteristics for Randomized Controlled Trials

Citation Setting NCT or Other Trial ID or Study Name	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Intervention	Comparator(s)	Relevant Outcomes Measured
Melanoma						
Kim et al., 2022[10] 2 centers, 1 academic, in US NCT03071406	To assess treatment with combined nivolumab plus ipilimumab, with or without SBRT in patients with advanced Merkel cell carcinoma as a first-line therapy or following previous treatment with anti-PD-1 and PD-L1 monotherapy RCT Median follow-up of 15 months	Inclusion criteria (must meet all): aged at least 18 years with unresectable, recurrent, or stage IV Merkel cell carcinoma; any stage if unresectable or recurrent; ECOG performance status of 0 or 1; minimum of 2 histologically proven measurable tumors lesions measurable by CT, MRI, or clinical exam Exclusion criteria (excluded if any criteria met): history of grade 3 toxicity; of infliximab with previous immunotherapy; active brain metastasis; autoimmune disease or other conditions requiring systemic treatment with corticosteroids or other immunosuppressive medications; history of non-Merkel cell carcinoma malignancies	Total N = 50, comprising 25 in SBRT group and 25 in control group Sex: 6 (24%) female, SBRT; 5 (20%) female, control Race/ethnicity: 25 (100%) White, SBRT; 25 (100%) White, control Median age (IQR): 73 years (68 to 76) SBRT; 74 years (66 to 81) control ECOG status 0: 12 (48%) SBRT; 11 (44%) control Disease stage: 8 (32%) IIIB, 17 (68%) IV SBRT; 4 (16%) IIIB, 21 (84%) IV control Primary site: 5 (20%) head and neck, 1 (4%) trunk., 15 (60%) extremities, 4 (16%)	• SBRT ○ 24 Gy in 3 fractions ○ To at least 1 tumor site • Nivolumab and ipilimumab	• Nivolumab and ipilimumab	• OS and PFS • Disease control • Safety

Citation Setting NCT or Other Trial ID or Study Name	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Intervention	Comparator(s)	Relevant Outcomes Measured
			unknown SBRT; 11 (44%) head and neck, 1 (4%) trunk., 11 (44%) extremities, 2 (8%) unknown No metastatic sites: 8 (32%) SBRT; 4 (16%) control Elevated lactate dehydrogenase concentration: 9 (36%) SBRT; 15 (60%) control Previous immunotherapy: 14 (56%) SBRT; 12 (48%) control Previous chemotherapy: 3 (12% SBRT; 2 (8%) control			

Abbreviations. CT: computed tomography; ECOG: Eastern Cooperative Oncology Group; Gy: Gray; IQR: interquartile range; MRI: magnetic resonance imaging; NCT: OS: overall survival; PFS: progression-free survival; US National Clinical Trial; PD: programmed death; SBRT: stereotactic body radiation therapy.

Renal Cancer

No RCTs identified.

Pancreatic Cancer

No RCTs identified.

Head and Neck Cancer

Table C4. Study Characteristics for Randomized Controlled Trials

Citation Setting NCT or Other Trial ID or Study Name	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Intervention	Comparator(s)	Relevant Outcomes Measured
McBride et al., 2021[11] Single center in US NCT02684253	To test whether RT may act synergistically with anti-PD-1 therapy to improve response through abscopal effect RCT Median follow-up of 20 months	Inclusion criteria (must meet all): adults with histologically confirmed metastatic head and neck squamous cell carcinoma or WHO type I-III nasopharyngeal carcinoma; presence of at least 2 metastatic lesions; ECOG performance status ≤ 2l sufficient biopsy material for PD-L1 staining Exclusion criteria (excluded if any criteria met): previous immunotherapy	Total N = 62, comprising 32 in SBRT group and 30 in control group Sex: NR Race/ethnicity: NR Median age (range): 66 years (35 to 83) SBRT; 61 years (29 to 77) control Median lines of chemotherapy (range): 1 (0 to 3) SBRT; 1 (0 to 2) control Viral status positive: 16 (50%) SBRT; 15 (50%) control Primary disease: 6 (19%) nasopharynx, 12 (37%) oropharynx, 14 (44%) other, SBRT; 4 (13%) nasopharynx, 11 (37%) oropharynx,	• SBRT in combination with nivolumab ○ 9 Gy in 3 fractions delivered every other day	• Nivolumab	• Survival • Disease control • Safety

Citation Setting NCT or Other Trial ID or Study Name	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Intervention	Comparator(s)	Relevant Outcomes Measured
			15 (50%) other, control Previous chemotherapy: 26 (81%) SBRT; 29 (97%) control			

Abbreviations. ECOG: Eastern Cooperative Oncology Group; Gy: Gray; PD: programmed death; RCT: randomized controlled trial; RT: radiation therapy; SBRT: stereotactic body radiation therapy; WHO: World Health Organization.

Ovarian Cancer

No RCTs identified.

Liver Cancer

No RCTs identified.

Cervical Cancer

No RCTs identified.

Esophageal Cancer

No RCTs identified.

Oligometastatic Cancer

Table C5. Study Characteristics for Randomized Controlled Trials

Citation Setting NCT or Other Trial ID or Study Name	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Intervention	Comparator(s)	Relevant Outcomes Measured

Ost et al., 2017[12,13]
 	
6 centers, including academic centers, in Belgium
 	
NCT01558427
 	
STOMP
	To assess benefit of metastatic-directed therapy
	
	RCT
	
	Median follow-up of 3 years
		Inclusion criteria (must meet all): pathologically confirmed prostate cancer treated with curative intent; PSA; up to 3 extracranial metastases; treated and controlled primary tumor; WHO performance status 0 to 1
		
		Exclusion criteria (excluded if any criteria met): testosterone levels < 50 ng/mL; symptomatic metastases; previous metastatic-directed treatment; PSA relapse while receiving an active systemic treatment; previous treatment with a cytotoxic agent for prostate cancer; treatment during past month with products known
			Total N = 62, comprising 31 in treatment arm (majority received SBRT; remainder underwent surgery) and 31 in active surveillance arm
			
			Sex: men only
			
			Race/ethnicity: NR
			
			Mean age (range): 61 years (43 to 75) SBRT; 63 years (47 to 79) surveillance
			
			Mean PSA at diagnosis (range): 22.0 ng/ml (3.5 to 11.40) SBRT; 12.1 ng/ml (2.5 to 36.2) surveillance
			
			Primary tumor: 2 (7%) T1, 9 (29%) T2, 20 (65%) T3
				• SBRT
				  ○ Total dose of 30 Gy (80%of maximal dose) delivered in 3 fractions
				  ○ 25 (81%)
				• Metastectomy
				  ○ 6 (19%)
					• Surveillance	• PFS
						• Disease control
						• Toxicity

Citation Setting NCT or Other Trial ID or Study Name	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Intervention	Comparator(s)	Relevant Outcomes Measured
		to influence PSA levels	or T4 SBRT; 4 (13%) T1, 13 (42% T2, 14 (45%) T3 or T4, surveillance Primary treatment: 2 (7%) surgery, 7 (22%) RT, 22 (71%) both, SBRT; 5 (16%) surgery, 8 (26%) RT, 18 (58%) both, surveillance ADT: 12 (39%) SBRT; 15 (48%) surveillance Number of metastases: 18 (58%) 1, 6 (19%) 2, 7 (23%) 3 SBRT; 9 (29%) 1, 10 (32%) 2, 12 (39%) 3 surveillance Location of metastases: 17 (55%) nodal, 14 (45%) non-nodal SBRT; 17 (55%) nodal, 14 (45%)			

Citation Setting NCT or Other Trial ID or Study Name	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Intervention	Comparator(s)	Relevant Outcomes Measured
			non-nodal, surveillance			
Palma et al., 2019[14-18] 10 hospitals in Canada, Netherlands, Scotland, and Australia NCT01446744 SABR-COMET	To assess effect of SBRT in patients with a controlled primary tumor and 1 to 5 oligometastatic lesions RCT Followed up to 10 years	Inclusion criteria (must meet all): aged 18 years or older; ECOG score 0 to 1; life expectancy ≥ 6 months; primary tumor treated definitively ≥ 3 months before enrolment, with no progression at that site since treatment; to be discussed at a tumor board or quality-assurance rounds with consensus opinion that entry into study was appropriate; metastatic lesions had to be amenable to SBRT, and a maximum of 3 metastases in any one organ with no more than 5 metastases in total Exclusion criteria (excluded if any criteria met): serious	Total N = 99, comprising 66 in SBRT group and 33 in control group Sex: 26 (%) SBRT, female; 14 (42%) control, female Race/ethnicity: NR Median age (IQR): 67 (59 to 73) years, SBRT; 69 (64 to 75) years, control Median time from diagnosis to randomization (IQR): 2.4 (1.6 to 5.3) years, SBRT; 2.3 (1.3 to 4.5) years, control No, of metastases: 1 46%, 2 29%, 3 18%, 4 3%, 5 5%, SBRT; 1 36%, 2	• SBRT ◦ Doses ranged from 30 to 60 Gy in 3 to 8 fractions, depending on target size and location ◦ Single fractions of 16 to 24 Gy permitted for targets in brain and vertebrae ◦ Concurrent chemotherapy or targeted therapy was not permitted within 4 weeks before SBRT • Standard of care, tailored to individual clinical circumstance	• Standard of care, tailored to individual clinical circumstance • Radiotherapy delivered according to standard principles of palliative radiation, with goal of alleviating symptoms or preventing anticipated complications of progression	• OS • PFS • Lesion control • QoL • Safety

Citation Setting NCT or Other Trial ID or Study Name	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Intervention	Comparator(s)	Relevant Outcomes Measured
		medical comorbidities precluding radiotherapy; bone metastasis in a femoral bone; 1 to 3 brain metastases with no disease elsewhere; previous radiotherapy to a site requiring treatment; malignant pleural effusion, tumor within 3 mm of spinal cord on MRI; dominant brain metastasis requiring surgical decompression, pregnancy, or lactation	40%, 3 18%, 4 6%, 5 0, control Location of metastases: adrenal 6%, bone 35%, liver 13%, lung 43%, other 3%, SBRT; adrenal 3%, bone 31%, liver 5%, lung 53%, other 8%, control			
Phillips et al., 2020[13,19,20] 3 academic centers in US NCT02680587 ORIOLE	To determine if SABR improves oncologic outcomes in men with oligometastatic prostate cancer RCT Followed up to 24 months	Inclusion criteria (must meet all): 18 and older; ECOG ≤ 2; 1 to 3 asymptomatic metastases arisen within previous 6 months; no larger than 5.0 cm in largest axis or 250 cm^2; previous definitive treatment of primary	Total N = 54, comprising 36 in group and 18 in observation group Sex: men only Race/ethnicity: NR Median age (range): 68 years	• SBRT ○ Dose and fractionation based on size and location of each lesion, with prescription doses ranging from 19.5 to 48.0 Gy in 3 to 5 fractions	• Observation ○ Salvage RT was allowed ○ Patients were allowed to have received ADT or other systemic therapy during initial management	• Progression • Local control • Quality of life • Safety

Citation Setting NCT or Other Trial ID or Study Name	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Intervention	Comparator(s)	Relevant Outcomes Measured
		tumor with surgery or radiotherapy; PSA values ≥ 0.5 ng/mL but ≤ 50 ng/mL with testosterone ≥ 125 ng/dL and ADT < 15 months Exclusion criteria (excluded if any criteria met): previously received more than 3 years of ADT; received ADT in previous 6 months; developed castration-resistant disease; suspected pulmonary or liver metastases greater > 10 mm in largest axis; spinal cord compression or impending spinal cord compression; abnormal liver or renal test results	(61 to 70), SBRT; 68 years (64 to 76), control Initial N stage: 31 (86%) N0, 2 (6%) N1, 3 (8%) NX, SBRT; 16 (89%) N0, 1 (6%) N1, 1 (6%) NX, control Initial management: 30 (83%) surgery, 6 (17%) RT, SBRT; 15 (83%) surgery, 3 (17%) RT, control Median time to first recurrence (range): 22 months (9 to 42), SBRT; 22 months (9 to 51), control Received previous ADT: 15 (42%) SBRT; 5 (28%) control	○ Salvage RT was allowed ○ Patients were allowed to have received ADT or other systemic therapy during initial management or salvage treatment but not within 6 months of enrollment	or salvage treatment but not within 6 months of enrollment	

Abbreviations. ADT: androgen deprivation therapy; ECOG: Eastern Cooperative Oncology Group; Gy: Gray; IQR: interquartile range; MRI: magnetic resonance imaging; NCT: US National Clinical Trial; NR: not reported; OS: overall survival; PFS: progression-free survival; PSA: prostate-specific antigen; QoL: quality of life; RCT: randomized controlled trial; RT: radiation therapy; SBRT: stereotactic body radiation therapy; WHO : World Health Organization.

Other Cancers

Table C6. Study Characteristics for Randomized Controlled Trials

Citation Setting NCT or Other Trial ID or Study Name	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Intervention	Comparator(s)	Relevant Outcomes Measured
Other cancers						
Bone cancer						
Nguyen et al., 2019[21] Single academic center in US NCT02163226	To compare pain relief from high-dose single-fraction SBRT with conventional MFRT Randomized noninferiority trial Followed up to 24 months	Inclusion criteria (must meet all): pathologic diagnosis of cancer; painful bone metastases; aged 18 years or older; life expectancy of more than 3 months Exclusion criteria (excluded if any criteria met): previous radiation to site being evaluated; untreated spinal cord compression; pathologic fracture at evaluated site; previous radioactive isotope therapy within 30 days of randomization	Total N = 160, comprising 81 in SBRT group and 79 in control group Sex: 32 (39%) female, SBRT; 32 (40%) female control Race/ethnicity: 68 (84%) Caucasian, 2 (2%) African American, 7 (9%) Hispanic, 3 (4%) Asian, 1 (1%) other, SBRT; 59 (75%) Caucasian, 8 (10%) African American, 4 (5%) Hispanic, 2 (2%) Asian, 6 (8%) other, control Mean age (SD): 62.0 years (10.1), SBRT; 62.7 years (10.9), control Disease stage IV: 81 (100%) female,	• SBRT ○ Single-fraction 12 Gy for lesions >4 cm or 16 Gy for lesions ≤4 cm ○ Standard concurrent chemotherapy, immunotherapy, or targeted therapy was allowed	• Standard MFRT ○ 30 Gy delivered in 10 3-Gy fractions ○ Standard concurrent chemotherapy, immunotherapy, or targeted therapy was allowed	• OS • Local control • QoL • Safety

Citation Setting NCT or Other Trial ID or Study Name	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Intervention	Comparator(s)	Relevant Outcomes Measured
			SBRT; 79 (100%) female control More than 4 lesions: 39 (48%) female, SBRT; 38 (48%) female control Site of bony metastases: 3 (4%) abdomen, 10 (12%) thorax, 15 (18%) extremities, 4 (5%) head and neck, 46 (57%) pelvis, 3 (4%) spine, SBRT; 4 (5%) abdomen, 9 (11%) thorax, 13 (17%) extremities, 2 (2%) head and neck, 48 (61%) pelvis, 3 (4%) spine, control			

Abbreviations. Gy: Gray; MFRT: moderately-fractionated radiation therapy; NCT: US National Clinical Trial; NR: not reported; OS: overall survival; QoL: quality of life; RCT: randomized controlled trial; SBRT: stereotactic body radiation therapy; SD: standard deviation.

Study Findings of Included Randomized Controlled Trials

Breast Cancer

No RCTs identified.

Prostate Cancer

Table C7. Evidence Tables for Randomized Controlled Trials[a]

Citation Setting NCT or Other Trial ID or Study Name	Survival and Disease Control	Other Outcomes	Safety
Brand et al, 2019[1,2] 37 centers in UK, Ireland, and Canada NCT01584258 PACE-B	OS NR Progression and PFS Data not mature at time of publication	QoL and symptom control No difference between groups in QoL No other outcomes of interest reported	No deaths due to AEs were observed at 12 weeks or 24 months Grade 2 or higher GI AEs at 12 weeks: 43 (10%), SBRT; 53 (12%), control; difference of 1.9% points (95% CI, -6.2 to 2.4); *P* = .38 Grade 2 or higher GU AEs at 12 weeks: 96 (23%), SBRT; 118 (27%), control; difference of 4.2% points (95% CI, -10.0 to 1.7); *P* = .16 Grade 2 or higher GI AEs at 24 months: 6 (2%), SBRT; 11 (3%) control; difference of 1.3% points (95% CI, -3.9 to 1.1); *P* = .32 Grade 2 or higher GU AEs at 24 months: 13 (3%), SBRT; 8 (2%), control; difference of 1.3% points (95% CI, -1.3 to 4.0); *P* = .39 Cumulative rate of grade 2 or higher GI AEs over 24 months: 7.8% SBRT; 8.1%, control: HR, 1.02 (95% CI, 0.70 to 1.51); *P* = .91 **Cumulative rate of grade 2 or higher GU AEs over 24 months: 18.3% SBRT; 10.6%, control: HR, 1.80 (95% CI, 1.25 to 2.61); *P* = .001**

Citation Setting NCT or Other Trial ID or Study Name	Survival and Disease Control	Other Outcomes	Safety
			No difference between groups for a grade 3 or higher GI worst event (< 1% SBRT; 1% control; difference of -0.7 percentage points; *P* = .37) or GU worst event (2% SBRT; 2% control; difference of 0.8 percentage points; *P* = .47)
Kwan et al., 2022[3] 2 sites in Canada NCT02594072 ASSERT	NR	Remission and local control NR QoL and symptom control Overall improvement in symptoms, measured by IPSS (defined as a rise ≥ 5): 51.2% SBRT; 64.5% control; *P* = .35 Improvement in incontinence domain, measured by EPIC: 33% SBRT; 36% control; *P* = .75 Improvement in irritative/ obstructive domain, measured by EPIC: 74% SBRT; 56% control; *P* = .07 Improvement in bowel domain, measured by EPIC: 74% SBRT; 56% control; *P* = .51 Costs and cost effectiveness NR	No AEs higher than grade 3 At least 1 grade 3 GU or GI AE: 2% SBRT; 8% control At least 1 grade 2 and higher GU or GI AE: 24% SBRT; 36% control At least 1 grade 3 GU AE: 2% SBRT; 6% control At least 1 grade 2 and higher GU AE: 19% SBRT; 25% control At least 1 grade 3 GI AE: 0 SBRT; 3% control At least 1 grade 2 and higher GI AE: 7% SBRT; 14% control No statistically significant differences between groups
Lukka et al., 2018[4] 37 sites, including academic centers, in US and Canada NCT01434290	NR	QoL Only reported comparison with baseline and not between groups	Mortality not reported Acute grade 3 GI: 1 (< 1%) SBRT; 2 (1.6%) UHRT Acute grade 3 renal and urinary: 1 (< 1%) SBRT; 0 UHRT

Citation Setting NCT or Other Trial ID or Study Name	Survival and Disease Control	Other Outcomes	Safety
			No acute grade 4 or 5 toxicities in either group Late grade 3 GI: 1 (< 1%) SBRT; 1 (< 1%) UHRT Late grade 3 renal and urinary1 (< 1%) SBRT; 1 (< 1%) UHRT No late grade 4 or 5 toxicities in either group
Widmark et al., 2019[5,6] 12 centers in Sweden and Denmark ISRCTN45905321 HYPO-RT-PC	OS At 5 years, overall survival: 543 (94%), SBRT; 548 (96%), cRT; HR, 1.11 (95% CI, 0.73 to 1.69); *P* = .95 At 5 years, prostate-cancer specific survival: 578 (98.0%), SBRT; 583 (99.8%), cRT; HR, 1.40 (95% CI, 0.56 to 3.49); *P* = .46 Progression and PFS At 5 years, failure-free survival (biochemical or clinical failure): 84% SBRT; 84% cRT; aHR, 1.00 (95% CI, 0.76 to 1.33) At 5 years, biochemical failure: 84% SBRT; 84% cRT; HR, 1.00 (95% CI, 0.76 to 1.33) At 5 years, local failure: 99% SBRT; 98% cRT; HR, 0.94 (95% CI, 0.40 to 2.22)	QoL and symptom control At end of RT treatment, significantly more people in SBRT group reported a clinically meaningful deterioration in stool frequency, rush to toilet in morning because of bowel movements, flatulence, bowel cramp, mucus, blood in stool, limitations in ADL due to bowel symptoms, role function, emotional function, QoL overall, pain and diarrhea Meaningful deterioration in overall bother from all urinary symptoms at 6 years: mean difference, 5.1% (95% CI, -4.4 to 14.6); *P* = .38 Meaningful deterioration in QoL at 6 years: mean difference, 5.0% (95% CI, -5.0 to 15.0); *P* = .41 Meaningful deterioration in overall bother from bowel symptoms at 6 years: mean difference, 5.7% (95% CI, -3.8 to 15.2); *P* = .33 Meaningful deterioration in overall bother from sexual function at 6 years: mean difference, 9.1% (95% CI, -1.4 to 19.6); *P* = .15	No deaths related to treatment were observed Patients in SBRT group had significantly more physician-assessed urinary toxicity at 1 year, but not at other timepoints, including at treatment end Patients in SBRT group reported significantly higher urinary problem severity at treatment end and at 1 year, but not at other timepoints; however, patients in SBRT reported significantly lower urinary problem severity at 3 months Patients in SBRT group had similar physician-assessed bowel toxicity at all timepoints, including at treatment end Patients in SBRT group reported significantly higher urinary problem

Citation Setting NCT or Other Trial ID or Study Name	Survival and Disease Control	Other Outcomes	Safety
	At 5 years, distant failure: 94% SBRT; 95% cRT; HR, 0.99 (95% CI, 0.63 to 1.54) At 5 years, ADT after primary failure: 89% SBRT; 92% cRT; HR, 1.12 (95% CI, 0.79 to 1.59) Post-hoc subgroup analyses of failure-free survival showed no significant interactions between clinical factors (age, Gleason score, T stage, PSA, and risk group) and treatment group	Overall QoL: mean difference, 5.0% (95% CI, -5.0 to 15.0); *P* = .41 At 6 years, significantly more people reported a clinically meaningful deterioration in weak stream, emptying bladder, and insomnia with cRT when compared with SBRT Costs and cost effectiveness NR	severity at treatment end but not at other timepoints Grade 2 and higher urinary toxicity at 5 years: 18%, SBRT; 17%, cRT; HR, 1.07 (95% CI, 0.81 to 1.41); *P* = .63 Grade 2 and higher bowel toxicity at 5 years: 9%, SBRT; 10%, cRT; HR, 1.00 (95% CI, 0.68 to 2.71); *P* = 1.00 No differences were seen between groups for any measure of erectile function at any time point, including end of treatment

Note. [a] *Bold text indicates statistically significant findings.*
Abbreviations. ADL: activities of daily living; ADT: androgen deprivation therapy; AE: adverse event; aHR: adjusted hazard ratio; CI: confidence interval; cRT: conventional radiotherapy; CT: computed tomography; EPIC: Expanded Prostate Inventory Composite; FACT-G: Functional Assessment of Cancer Therapy: General; HR: hazard ratio; IPSS: International Prostate Symptom Score; IQR: interquartile range; MRI: magnetic resonance imaging; NCT: US National Clinical Trial; NR: not reported; OS: overall survival; PFS: progression-free survival; PSA: prostate-specific antigen; QoL: quality of life; RT: radiotherapy; SBRT; stereotactic body radiation therapy; UHRT: ultrahypofractionated radiation therapy.

Lung Cancer

Table C8. Evidence Tables for Randomized Controlled Trials[a]

Citation Setting NCT or Other Trial ID or Study Name	Survival and Disease Control	Other Outcomes	Safety
Altorki et al., 2021[7,8]	OS NR	Remission and local control **Major pathological response: 16 (53.3%) SBRT;**	No treatment-related deaths or deaths within 30 and 90 days of surgery

Citation Setting NCT or Other Trial ID or Study Name	Survival and Disease Control	Other Outcomes	Safety
Single center in US NCT02904954	Progression and PFS NR	**2 (6.7%) control; OR, 16.0 (95% CI, 3.2 to 79.6)** **Partial radiographic response: 14 (46.7%) SBRT; 1 (3.3%) control; *P* = .001** QoL and symptom control NR Costs and cost effectiveness NR	SAEs occurred in 2 (7%) patients in each group (pancreatitis and fatigue in SBRT group and pulmonary embolism and stroke in control group) Grade 3 and higher AEs in SBRT group: • Grade 3 fatigue, 1 (3%) • Grade 3 hyponatremia, 3 (10%) • Grade 3 adrenal insufficiency, 1 (3%) • Grade 3 hyperuricemia, 1 (3%) • Grade 3 neutrophil count decreased, 1 (3%) • Grade 3 thromboembolic event, 1 (3%) • Grade 5 stroke, 1 (3%) Grade 3 and higher AEs in control group: • Grade 3 fatigue, 1 (3%) • Grade 3 hyperlipasemia, 3 (10%) • Grade 3 thromboembolic event, 1 (3%) • Grade 3 hepatitis, 1 (3%) • Grade 3 hyperglycemia, 2 (7%) • Grade 4 platelet count decreased, 1 (3%) • Grade 5 cardiopulmonary event, 1 (3%)
Theelen et al., 2019[9] 3 centers in Netherlands NCT02492568 PEMBRO-RT	OS Median: 15.9 months SBRT; 7.6 months control; HR, 0.66 (95% CI, 0.37 to 1.18) **Male patients (HR, 0.42; 95%CI, 0.19 to 0.96; *P* = .04) and smokers (HR, 0.48; 95% CI, 0.25 to 0.93; *P* = .03) had improved survival with SBRT compared with pembrolizumab alone** Progression and PFS Median: 6.6 months SBRT; 1.9 months control; HR, 0.71 (95% CI, 0.42 to 1.18)	Disease control Objective response rate: 36% SBRT; 18% control *P* = .07 No difference by previous RT status	Grade 3 and higher fatigue: 3% SBRT; 0 control Grade 3 and higher dyspnea: 11% SBRT; 5% control Grade 3 and higher nausea: 3% SBRT; 5% control Grade 3 and higher pneumonia: 11% SBRT; 3% control

Citation Setting NCT or Other Trial ID or Study Name	Survival and Disease Control	Other Outcomes	Safety
			Grade 3 and higher weight loss: 6% SBRT; 3% control

Note. [a] Bold text indicates statistically significant findings.
Abbreviations. AE: adverse event; CI: confidence interval; NR: not reported; OR: odds ratio; RT: radiation therapy; SAE: serious adverse event.

Colorectal Cancer

No RCTs identified.

Uterine Cancer

No RCTs identified.

Melanoma

Table C9. Evidence Tables for Randomized Controlled Trials[a]

Citation Setting NCT or Other Trial ID or Study Name	Survival and Disease Control	Other Outcomes	Safety
Melanoma			
Kim et al., 2022[10] 2 centers, 1 academic, in US NCT03071406	OS Immunotherapy naïve: • Median: not reached in either group • HR, 2.12 (95% CI, 0.13 to 34.23) Previous immunotherapy: • Median: 9.7 months SBRT; 14.9 months control • HR, 2.15 (95% CI, 0.83 to 5.57) PFS	Remission and local control Response: 12 (52%) SBRT; 18 (72%) control; *P* = .26) No other outcomes reported	8 (16%) discontinued protocol treatment due to toxicity No deaths attributed to treatment No formal analysis between groups Any grade 3 toxicity: 13 (26%) overall; 6 (24%) in SBRT group and 7 (28%) in control group Any grade 4 toxicity: 5 (10%) overall; 2 (8%) in SBRT group and 3 (12%) in control group

Citation Setting NCT or Other Trial ID or Study Name	Survival and Disease Control	Other Outcomes	Safety
	Immunotherapy naïve: • Median: not reached in either group • HR, 1.77 (95% CI, 0.11 to 28.38) Previous immunotherapy: • Median: 2.7 months SBRT; 4.2 months control • HR, 1.60 (95% CI, 0.68 to 3.75)		Grade 3 fatigue: 1 (2%) overall; 0 in SBRT group and 1 (4%) in control group Grade 3 diarrhea: 2 (4%) overall; 1 (4%) in SBRT group and 1 (4%) in control group Grade 3 rash or dermatitis: 1 (2%) overall; 1 (4%) in SBRT group and 0 in control group Grade 3 elevated pancreatic enzymes: 2 (4%) overall; 2 (8%) in SBRT group and 0 in control group Grade 4 elevated pancreatic enzymes: 4 (8%) overall; 2 (8%) in SBRT group and 2 (8%) in control group Grade 3 arthralgia: 3 (6%) overall; 1 (4%) in SBRT group and 2 (8%) in control group Grade 3 elevated transaminases: 3 (6%) overall; 0 in SBRT group and 3 (12%) in control group Grade 3 hyponatremia: 1 (2%) overall; 0 in SBRT group and 1 (4%) in control group Grade 4 hyponatremia: 1 (2%) overall; 0 in SBRT group and 1 (4%) in control group Grade 3 adrenal insufficiency: 1 (2%) overall; 0 in SBRT group and 1 (4%) in control group Grade 3 dysgeusia: 1 (2%) overall; 1 (4%) in SBRT group and 0 in control group Grade 3 anemia: 1 (2%) overall; 1 (4%) in SBRT group and 0 in control group Grade 3 colitis: 3 (6%) overall; 2 (8%) in SBRT group and 1 (4%) in control group

Citation Setting NCT or Other Trial ID or Study Name	Survival and Disease Control	Other Outcomes	Safety
			Grade 4 acute kidney injury: 1 (2%) overall; 0 in SBRT group and 1 (4%) in control group Grade 3 hypocalcemia: 1 (2%) overall; 1 (4%) in SBRT group and 0 in control group Grade 3 systemic inflammatory syndrome: 1 (2%) overall; 1 (4%) in SBRT group and 0 in control group Grade 3 myocarditis: 1 (2%) overall; 0 in SBRT group and 1 (4%) in control group Grade 3 pancreatitis: 1 (2%) overall; 1 (4%) in SBRT group and 0 in control group Grade 3 syncope: 1 (2%) overall; 0 in SBRT group and 1 (4%) in control group

Note. [a] Bold text indicates statistically significant findings.
Abbreviations. CI: confidence interval; HR: hazard ratio; SBRT: stereotactic body radiation therapy.

Renal Cancer

No RCTs identified.

Pancreatic Cancer

No RCTs identified.

Head and Neck Cancer

Table C10. Evidence Tables for Randomized Controlled Trials[a]

Citation Setting NCT or Other Trial ID or Study Name	Survival and Disease Control	Other Outcomes	Safety
Head and Neck Cancer			
McBride et al., 2021[11] Single center in US NCT02684253	OS Median: 13.9 months SBRT; 14.2 months control; *P* = .75 At 12 months: 54.4% SBRT; 50.2% control Progression and PFS Median: 2.6 months SBRT; 1.9 months control; *P* = .79 At 12 months: 16.8% SBRT; 32.2% control	Remission and local control Objective response: 29.0% SBRT; 34.5% control; *P* = .86; OR, 0.80; 95% CI, 0.24 to 2.61 No difference by viral status Median duration of response: 9.4 months, SBRT; not reached, control; *P* = .26 No other outcomes reported	Grade 3 and higher toxicity: 9.7% SBRT; 13.3% control; *P* = .70

Note. [a] Bold text indicates statistically significant findings.
Abbreviations. NCT: US National Clinical Trial; OS: overall survival; PFS: progression-free survival; SBRT: stereotactic body radiation therapy

Ovarian Cancer

No RCTs identified.

Liver Cancer

No RCTs identified.

Cervical Cancer

No RCTs identified.

Esophageal Cancer

No RCTs identified.

Oligometastatic Cancer

Table C11. Evidence Tables for Randomized Controlled Trials[a]

Citation Setting NCT or Other Trial ID or Study Name	Survival and Disease Control	Other Outcomes	Safety
Ost et al., 2017[12,13] 6 centers, including academic centers, in Belgium NCT01558427 STOMP	OS NR Progression and PFS ADT-free survival: 21 months SBRT; 13 months surveillance; HR, 0.60 (95% CI, 0.31 to 1.11) **Biochemical recurrence-free survival: HR, 0.53 (95% CI, 0.30 to 0.94) favoring treatment** No difference by PSA doubling time or metastatic location (nodal vs non-nodal) In pooled analysis of ORIOLE and STOMP, at median follow-up of 53 months: • OS: median not reached in either group (HR, 0.53; 95% CI, 0.13 to 2.11) • PFS: 11.9 months treatment: 5.9 months surveillance; HR, 0.44 (95% CI, 0.29 to 0.66) • Castration-resistant prostate cancer-free survival: median not reached, treatment; 63 months surveillance; HR, 0.67 (95% CI, 0.34 to 1.31) • Radiographic PFS: 18 months treatment; 17 months surveillance; HR, 0.81 (95% CI, 0.50 to 1.29)	Quality of life Quality of life was similar between arms at baseline and remained comparable at 3-month and 1-year follow-up	6 patients developed grade 1 toxicity in treatment arm No grade 2 to 5 toxicity was observed
Palma et al., 2019[14-18]	At a median follow-up (IQR): 26 months (23 to 37), SBRT; 25 months (19 to 54), control OS	Lesion control **Absence of progression in lesions present at randomization: 75 of 100**	Deaths in SBRT group due to radiation pneumonitis (n = 1), pulmonary abscess (n = 1), and subdural hemorrhage after

Citation Setting NCT or Other Trial ID or Study Name	Survival and Disease Control	Other Outcomes	Safety
10 hospitals in Canada, Netherlands, Scotland, and Australia NCT01446744 SABR-COMET	All-cause mortality: 24 of 66 (36%), SBRT; 16 of 33 (48%), control; *P* value NR Median OS (95% CI): 41 months (26 to not reached), SBRT; 28 months (19 to 33), control Over 5 years: HR, 0.57 (95% CI, 0.30 to 1.10); *P* = .09 No difference in subgroup analysis by sex, age, dose or comorbidity status; having a lung primary was significantly associated with worse OS and having a prostate primary was significantly associated with better OS <u>PFS</u> Progression events: 39 of 66 (59%), SBRT; 28 of 33 (85%), control; *P* value NR Median PFS (95% CI): 12.0 months (6.9 to 30.4), SBRT; 6.0 months (3.4 to 7.1), control **Over 5 years, HR: 0.47 (95% CI, 0.30 to 0.76); *P* = .001** No difference in subgroup analysis by sex, age, dose or comorbidity status; having a lung primary was significantly associated with worse OS and having a prostate primary was significantly associated with better PFS At a median follow-up (IQR): 51 months, overall <u>OS</u> All-cause mortality: 35 of 66 (53%), SBRT; 24 of 33 (73%), control; *P* value NR	**(75%), SBRT; 28 of 57 (49%), control; *P* = .001** **Absolute increase: 26% (95% CI, 10 to 41)** **Longer-term absence of progression in lesions present at randomisation: 65 of 104 (63%), SBRT; 26 of 57 (46%), control; *P* = .04** **Absolute increase: 17% (95% CI, 1 to 33)** **Significantly higher lesional control by lesion location (adrenal, 100%; bone, 72%; lung, 51%; liver, 50%; *P* = .04)** No significant difference for time to new metastases (*P* = .57) over longer term No difference in subgroup analysis by sex, age, dose or comorbidity status; having a lung primary was significantly associated with worse lesion control and having a prostate or breast primary was significantly associated with better lesion control <u>QoL and symptom control</u> Mean FACT-G score at 6 months (SD): 82.6 (16.6), SBRT; 82.5 (16.4), control; *P* = .99 No significant difference in QoL at 5 years	surgery to repair a SBRT-related perforated gastric ulcer (n = 1) Any AE grade 2 or higher: 40 of 66 (61%), SBRT; 15 of 33 (46%), control; *P* = .15 **Any treatment-related AE grade 2 or higher: 19 of 66 (29%), SBRT; 3 of 33 (9%), control; *P* = .03** No significant difference between SBRT and control for treatment-related fatigue, dyspnea, or pain Any AE associated with death: 3 of 66 (5%), SBRT; 0, control; *P* = .55 No new AEs (grade 2 to 5) over longer term

Citation Setting NCT or Other Trial ID or Study Name	Survival and Disease Control	Other Outcomes	Safety
	Median OS (95% CI): 50 months (29 to 83), SBRT; 28 months (18 to 39), control **Over 6 years, HR: 0.47 (95% CI, 0.27 to 0.81); *P* = .006** PFS Progression events: 45 of 66 (68%), SBRT; 29 of 33 (88%), control; *P* value NR Median PFS (95% CI): 11.6 months (6.1 to 23.4), SBRT; 5.4 months (3.2 to 6.8), control **Over 6 years, HR: 0.48 (95% CI, 0.31 to 0.76); *P* = .001**	No significant differences in any of physical, social, functional, or emotional QoL subscales at any time point (all *P* > .19) Costs and cost-effectiveness NR	
Phillips et al., 2020[19,20] 3 academic centers in US NCT02680587 ORIOLE	OS NR Progression and PFS **Progression at 6 months (composite of a PSA rise of at least 2 ng/dL and 25% above nadir; concern for radiologic progression by CT, MRI, or bone scan; symptomatic progression; initiation of ADT for any reason; or death): 7 of 36 (19%) SBRT; 11 of 18 (61%) observation; *P* =.005** **Progression at 6 months (defined by PSA level): 4 of 36 (11%) SBRT; 9 of 18 (50%) observation; *P* =.005** **Median PFS: not reached, SBRT; 5.8 months, observation; HR, 0.30 (95% CI, 0.11 to 0.81)** Complete response at 6 months: 25 (28%), SBRT; 4 (8%), observation; *P* value NR	QoL and symptom control No differences in Brief Pain Inventory (Short Form) scores were observed between arms or within either arm across time Costs and cost-effectiveness NR	Mortality: NR No grade 3 or higher AEs were observed Grade 2 urinary incontinence at 90 days: 1 (3%) SBRT; 0, observation Grade 2 urinary incontinence at 180 days: 1 (3%) SBRT; 0, observation Grade 2 esophagitis at 90 days: 1 (3%) SBRT; 0, observation Grade 2 esophagitis at 180 days: 0, SBRT; 0, observation Grade 2 dizziness at 90 days: 1 (3%) SBRT; 0, observation

Citation Setting NCT or Other Trial ID or Study Name	Survival and Disease Control	Other Outcomes	Safety
	Partial response at 6 months: 39 (43%), SBRT; 19 (39%), observation; *P* value NR		Grade 2 dizziness at 180 days: 0, SBRT; 0, observation Grade 2 bladder infection at 90 days: 0, SBRT; 0, observation Grade 2 bladder infection at 180 days: 1 (3%) SBRT; 0, observation

Note. [a] *Bold text indicates statistically significant findings.*
Abbreviations. ADT: androgen deprivation therapy; AE: adverse event; CI: confidence interval; HR: hazard ratio; NCT: US National Clinical Trial; NR: not reported; OS: overall survival; PFS: progression-free survival; PSA: prostate-specific androgen; QoL: quality of life; SBRT: stereotactic body radiation therapy.

Other Cancers

Table C12. Evidence Tables for Randomized Controlled Trials[a]

Citation Setting NCT or Other Trial ID or Study Name	Survival and Disease Control	Other Outcomes	Safety
Other cancers			
Bone cancer			
Nguyen et al., 2019[21] 1 academic center in US NCT02163226	OS Median survival time: 6.7 months in both groups (95% CI, 4.6 to 10.9) **Quality-life adjusted survival analysis found OS was significantly higher in SBRT group vs. MFRT group; *P* value NR** Progression and PFS	QoL and symptom control No significant differences in QoL between groups Pain Not a prespecified outcome of interest Costs and cost-effectiveness	Grade 2 nausea: 20 of 81 (21.0%), SBRT; 10 of 79 (25.3%), control; *P* = .58 Grade 3 nausea: 1 of 81 (1.2%), SBRT; 4 of 79 (5.1%), control; *P* = .21 Grade 2 vomiting: 7 of 81 (8.6%), SBRT; 11 of 79 (13.9%), control; *P* = .33

Citation Setting NCT or Other Trial ID or Study Name	Survival and Disease Control	Other Outcomes	Safety
	Cumulative incidence of local failure: 0 at 6 months, 0 at 12 months, 0 at 24 months, SBRT: 4.2% at 6 months, 5.9% at 12 months, 9.7% at 24 months; *P* = .02	NR	Grade 3 vomiting: 0, SBRT; 2 of 79 (2.5%), control; *P* = .24 Grade 3 fatigue: 8 of 81 (9.9%), SBRT; 4 of 79 (5.1%), control; *P* = .37 Radiation dermatitis: 1 of 81 (1.2%), SBRT; 2 of 79 (2.5%), control; *P* = .62 Fracture: 1 of 81 (1.2%), SBRT; 0, control; *P* = .99

Note. [a] *Bold text indicates statistically significant findings.*
Abbreviations. CI: confidence interval; NCT: US National Clinical Trial; NR: not reported; OS: overall survival; PFS: progression-free survival; QoL: quality of life; SBRT: stereotactic body radiation therapy.

Study Characteristics of Included Nonrandomized Studies

Breast Cancer

No eligible studies identified.

Prostate Cancer

Table C13. Study Characteristics for Nonrandomized and Registry-based Studies

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
Andruska et al., 2022[22] National Cancer Database (2004 to 2015) NR	To compare SBRT and cRT in people with unfavorable intermediate-risk prostate cancer	Inclusion criteria (must meet all): meet NCCN criteria for unfavorable	Total N = 28,028, comprising 1,428 in SBRT group, 532 in moderately fractionated RT	• SBRT ○ 35 to 40 Gy in 5 or fewer fractions	• Moderately fractionated RT ○ 60 Gy or higher in 2.4 to 3.2Gy per fraction

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
	Retrospective, comparative database analysis (propensity-matched) Median follow-up of 60 months	intermediate-risk disease Exclusion criteria (excluded if any criteria met): nodal or metastatic disease; receipt of surgery, brachytherapy, chemotherapy, or immunotherapy; unknown ADT status or missing information on number of days after diagnosis when ADT was initiated; ADT initiation > 180 days from diagnosis; previous radiation to prostate or pelvis; missing information on cumulative radiation dose, number of fractions, or numbers of days after diagnosed when RT was initiated; RT initiation > 180	group, and 25,856 in cRT Sex: men only Race/ethnicity: 1,183 (83%) White, 189 (13%) Black, 56 (4%) other, 58 (4%) Spanish or Hispanic, SBRT; 438 (82%) White, 77 (15%) Black, 17 (3%) other, 37 (7%) Spanish or Hispanic, moderately fractionated RT; 20,547 (79%) White, 4,585 (18%) Black, 724 (3%) other, 2,489 (10%) Spanish or Hispanic, cRT Mean age (SD): 67 years (7.4) SBRT; 69 years (7.9) moderately fractionated RT; 70 years (7.4) cRT Insurance status: 12 (1%) uninsured, 493 (35%) private insurance, 854 (60%) Medicare, 43 (2%) Medicaid or		○ Biologically effective doses of 120 and higher • cRT ○ 72 to 86.4 Gy in 1.8 to 2.0 Gy per fraction

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
		days after diagnosis; moderate-to-severe medical comorbidities	other government insurance, 35 (2%) unknown, SBRT; 13 (2%) uninsured, 164 (31%) private insurance, 319 (60%) Medicare, 31 (6%) Medicaid or other government insurance, 5 (1%) unknown, moderately fractionated RT; 362 (1%) uninsured, 6,438 (25%) private insurance, 17,264 (67%) Medicare, 1,394 (5%) Medicaid or other government insurance, 398 (2%) unknown, cRT Charlson-Deyo Comorbidity Index score of 1: 181 (13%) SBRT; 55 (10%) moderately fractionated RT; 3,363 (13%) cRT (men with scores higher than 1 were excluded)		

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			Clinical T-stage: 1,153 (81%) ≤ cT2a, 234 (16%) T2b-T2c, 41 (3%) cT2, NOS, SBRT; 411 (77%) ≤ cT2a, 109 (20%) T2b-T2c, 12 (3%) cT2, NOS, moderately fractionated RT; 18,277 (71%) ≤ cT2a, 6,753 (26%) T2b-T2c, 876 (3%) cT2, NOS, cRT Use of ADT: 1,428 (100%) SBRT; 251 (47%) moderately fractionated RT; 12,872 (50%) cRT		
Bolzicco et al, 2013[23] 1 academic center in Italy NR	To assess toxicity and biochemical efficacy of SBRT in prostate cancer Prospective, noncomparative study Median follow-up of 36 months	Inclusion criteria (must meet all): biopsy-proven organ-confined prostate carcinoma without any sign of severe obstruction; ECOG grade 0 to 1 Exclusion criteria (excluded if any criteria met): NR	Total N = 100 Sex: men only Race/ethnicity: NR Age: NR T stage: 44 (44%) T1c, 29 (29%) T2a-b, 27 (27%) T2c Mean PSA at diagnosis: 7.72 ng/mL	• SBRT ○ 35 Gy in 5 fractions of 7 Gy over consecutive days	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			Mean pre-treatment PSA: 5.03 ng/mL Risk: 41 (41%) low, 42 (42%) intermediate, 17 (17%) high TURP before SBRT: 7 (7%) ADT before SBRT: 8 of 29 (27%) ADT with or after SBRT: 21 of 29 (73%)		
Davis et al., 2015[24] RSSearch registry, including 27 sites and academic centers in US, Australia, and Turkey (2006 to 2015) NCT01885299	To report on initial patient characteristics, treatment practices, toxicity, and early biochemical disease-free survival Retrospective, noncomparative registry analysis Median follow-up of 20 months	Inclusion criteria (must meet all): clinically localized low- and intermediate-risk prostate cancer Exclusion criteria (excluded if any criteria met): incomplete data	Total N = 437 Sex: men only Race/ethnicity: 373 (85%) Caucasian, 45 (10%) African American, 7 (2%) Asian or Pacific Asian, 5 (1%) other, 7 (2%) NR Median PSA (range): 5.8 ng/ml (0.3 to 43) Clinical T-stage: 341 (79%) T1a to T1c, 70 (16%) T2a, 18 (4%) T2b, 5 (1%) T2c, 3 (1%) T3	• SBRT ○ 19.5 to 29 Gy in 2 to 3 fractions ○ 35 Gy in 5 fractions ○ 36.25 Gy in 5 fractions ○ 37 Gy in 5 fractions ○ 38 Gy in 4 fractions	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			Risk: 189 (43%) low, 315 (49%) intermediate, 33 (8%) high		
Flushing Radiation 2006 to 2009[25,26] Single center in US NR	To present first 10-year analysis of efficacy and toxicity of SBRT in treatment of early low-risk prostate cancer Retrospective (assumed), noncomparative study Up to 10 years	Inclusion criteria (must meet all): low risk prostate cancer Exclusion criteria (excluded if any criteria met): NR	Total N = 230 at 10 years Sex: men only Race/ethnicity: NR Median age (range): 69.5 years (47 to 86) Gleason score of 6: 230 (100%) Median PSA: 5.6 ng/ml Clinical T-stage: 207 (90%) T1c, 23 (10%) T2a Total N = 515 at 7 years Sex: men only Race/ethnicity: NR Median age (range): 69.0 years (44 to 89) Median PSA (range): 5.4 ng/ml (1.0 to 42.9)	• SBRT ○ 35 to 36.25 Gy in 5 daily fractions	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			Risk: 324 (63%) low, 153 (30%) intermediate, 38 (7%) high Clinical T-stage: 2 (< 1%) T1a, 462 (90%) T1c, 51 (10%) T2a Hormone treatment: 72 (14%)		
Flushing Radiation Winthrop 2006 to 2010 [27-29] Single academic center in US NR	To evaluate SBRT for organ confined, low- and intermediate-risk prostate cancer Prospective, noncomparative study Median follow-up of 72 months	Inclusion criteria (must meet all): newly diagnosed low- and intermediate-risk prostate cancer Exclusion criteria (excluded if any criteria met): NR	Total N = 477 Sex: men only Race/ethnicity: NR Median age (range: 67 years (44 to 89) Median PSA at treatment (range): 5.3 ng/ml (0.1 to 19) Risk: 324 (68%) low, 153 (32%) intermediate Clinical T-stage: 2 (< 1%) T1a, 434 (91%) T1c, 41 (9%) T2a Hormone treatment: 51 (11%)	• SBRT ○ 35 or 36.25 Gy over 5 fractions, daily	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			Reported 10-year patient characteristics only		
Freeman et al., 2015[30] Registry for Prostate Cancer Radiosurgery (RPCR; 2010 to 2013) NR	To report on design, methodology, and early outcome results of a multi-institutional registry study of prostate cancer radiosurgery Prospective, noncomparative analysis of a patient registry Followed up to 3 years	Inclusion criteria (must meet all): NR Exclusion criteria (excluded if any criteria met): NR	Total N = 1,743 Sex: men only Race/ethnicity: 77% Caucasian, 11% African American Mean age (range): 68 years (43 to 100) Risk: 708 (41%) low, 730 (42%) intermediate, 168 (10%) high, 4 (< 1%) very high, 3 (< 1%) metastatic	• SBRT ○ 35 to 40 Gy in 4 to 5 fractions ○ Boost following 45 to 50 Gy of EBRT	• No comparator
Fuller et al, 2018[31,32] 18 centers, including academic and community centers, in US NCT00643617	To report 5-yr efficacy, toxicity, and QoL outcomes of a novel 4-d SBRT regimen Prospective, noncomparative study Median follow-up of 5 years	Inclusion criteria (must meet all): low- or intermediate-risk prostate cancer; ECOG performance status 0 to 1 Exclusion criteria (excluded if any criteria met): prostatectomy; RT of prostate or	Total N = 259 Sex: men only Race/ethnicity:232 (90%) White, 8 (3%) Black or African American, 13 (5%) Hispanic or Latino, 2(1%) Asian, 4 (2%) other Age at diagnosis: 1 (0%) 40 to 49 years, 36 (14%) 50 to 59 years, 46 (18%) 60 to 64 years, 69	• SBRT ○ 38 Gy in 4 daily fractions of 9.5 Gy per fraction ○ ADT not allowed	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
		pelvis; PSA > 20 ng/mL	(27%) 65 to 69 years, 67 (26%) 70 to 74 years, 35 (14%) 75 to 79 years, 5 (2%) 80 years and older Risk: 112 (43%) low, 114 (44%) favorable intermediate, 33 (13%) unfavorable intermediate Median PSA at baseline (range): 5.1 ng/mL (0.1 to 19.3) Clinical T stage: 183 (71%) T1c, 73 (28%) T2a, 3 (1%) T2b TURP at baseline: 9 (4%)		
Georgetown 2008 to 2011[33-36] Single academic center in US NR	To report early experience using SBRT for localized prostate cancer Retrospective, noncomparative study Median follow-up of 2.3 years	Inclusion criteria (must meet all): histologically confirmed adenocarcinoma of prostate Exclusion criteria (excluded if any criteria met): clinical stage T3; involved lymph	Total N = 100 Sex: men only Race/ethnicity: 56 (56%) White, 37 (37%) Black, 5 (5%) Hispanic, 2 (2%) Asian Age: 8 (8%) < 60 years, 45 (45%) 60 to 69, 43 (43%) 70	• SBRT ○ 35 or 36.25 Gy in 5 fractions ○ Every other day	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
		nodes; distant metastases on imaging; previous pelvic RT	to 79, 4 (4%) 80 and older Pretreatment PSA (ng/mL): 87 (87%) ≤ 10, 12 (12%) > 10 and ≤ 20, 1 (1%) > 20 Risk group: 37 (37%) low, 55 (55%) intermediate, 8 (8%) high Hormone treatment: 11 (11%) Total N = 208 Sex: men only Race/ethnicity: 114 (54.8%) White, 79 (38.0%) Black, 15 (7.2%) other Median age (range): 69 years (48 to 90) No comorbidities: 142 (68.3%) Employed: 99 (47.6%) Risk: 82 (39.4%) low, 109 (52.4%) intermediate, 17 (8.2%) high		

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			ADT: 30 (14.4%) Total N = 269 Sex: men only Race/ethnicity: 55.8% White, 37.2% Black, 7.1% other Median age (range) 69 years (44 to 90) No comorbidities: 66.9%) Risk: 36.8% low, 53.2% intermediate, 10.0% high Hormone therapy: 16.4% Total N = 216 Sex: men only Race/ethnicity: 122 (57%) White, 81 (37%) Black, 13 (6%) other Median age (range) 69 years (48 to 90) Employed: 99 (46%) No comorbidities: 146 (65%)		

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			Clinical T-stage: 160 (74%) T1c, 29 (13%) T2a, 20 (9%) T2b, 7 (3%) T2c Risk: 83 (38%) low, 111 (51%) intermediate, 22 (10%) high Median PSA (range): 5.8 ng/ml (0.2 to 32.5) Procedures for BPH: 19 (9%) ADT: 29 (13%)		
Glowacki et al, 2015[37] Single center in Poland NR	To evaluate toxicity and efficacy of hypofractionated SBRT Prospective, noncomparative study Median follow-up of 8.5 months	Inclusion criteria (must meet all): biopsy proven localized low-to intermediate-risk prostate cancer; WHO performance status 0 to 1 Exclusion criteria (excluded if any criteria met): bone and nodal metastases; previous pelvic irradiation; prostatectomy;	Total N = 132 Sex: men only Race/ethnicity: NR Mean age (range): 69 years (53 to 83) Clinical T-stage: 59 (45%) T1c, 16 (12%) T2a, 40 (30%) T2b, 17 (13%) T2c Pretreatment maximal PSA: 106 (80%) < 10 ng/ml, 24 (18%) 10 to 20 ng/ml	• SBRT ○ 36.25 Gy in 5 fractions	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
		transurethral electroresection	Risk: 62(47%) low, 70 (53%) intermediate ADT: 74 (56%) No comorbidities: 52 (39%)		
Glowacki et al, 2017[38] Single center in Poland NR	To compare acute toxicity of SBRT and cRT in prostate cancer Prospective, comparative study Median follow-up NR	Inclusion criteria (must meet all): prostate cancer Exclusion criteria (excluded if any criteria met): NR	Total N = 216, comprising 109 in SBRT group and 107 in cRT group Sex: men only Race/ethnicity: NR Mean age(range): 70 years (54 to 83) SBRT; 69 years (49 to 85) cRT Clinical T-stage: 45 (42%) T1c, 10 (9%) T2a, 36 (33%) T2b, 17 (16%) T2c, 0 T3, SBRT; 56 (52%) T1c, 29 (27%) T2a, 17 (16%) T2b, 3 (3%) T2c, 2 (2%) T3, cRT Risk: 50 (46%) low, 58 (53%) intermediate, 1 (1%) high, SBRT; 32 (30%) low, 73 (68%)	• SBRT ○ 36.25 Gy in 5 fractions in 2 weeks	• cRT ○ Total dose of 76 Gy in 2 Gy fractions

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			intermediate, 2 (2) high, cRT Pretreatment PSA: 90 (82%) < 10 ng/mL, 16 (15%) 10 to 20 ng/mL, 1 (1%) > 20 ng/mL, SBRT; 55 (51%) < 10 ng/mL, 51 (48%) 10 to 20 ng/mL, 1 (1%) > 20 ng/mL, cRT Adjuvant ADT: 63 (58%) SBRT; 86 (80%) cRT No comorbidities: 41 (38%) SBRT; 40 (37%) cRT		

Halpern et al., 2016[39]
 	
Surveillance, Epidemiology, and End Results Program (SEER)-Medicare (2004 to 2011)
 	
NR
	To report current trends of SBRT use within US among older men diagnosed with prostate cancer
	
	Retrospective, comparative analysis
	
	Followed-up for at least 1 year
		Inclusion criteria (must meet all): primary diagnosis of prostate cancer without evidence of metastases; no history of nonprostate malignancy; continuously enrolled in Medicare Parts A and B and not	Total N = 17,889 for 1 year and 15,678 for 2-year outcomes; 237 in SBRT group, 4,136 in BT group, 10,715 in IMRT group, 363 in proton beam therapy group, and 2,438 in combination group
			
			Sex: men only
				• SBRT
				  ○ Based on ICD-9 and CPT-4 codes
					• BT
					• IMRT
					• Proton beam
					• Combination
					  ○ All based on ICD-9 and CPT-4 codes

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
		enrolled in a health maintenance organization from 1 year before diagnosis through death or last available record in 2012 Exclusion criteria (excluded if any criteria met): diagnosed previous to 2004; exhibiting comorbidities associated with RT complications before index RT	Race/ethnicity: 207 (87.3%) White, 17 (7.2%) Black, 13 (5.5%) other, SBRT; 3,630 (87.8%) White, 284 (6.9%) Black, 222 (5.4%) other, BT; 8,861 (82.7%) White, 1,108 (10.3%) Black, 746 (7.0%) other, IMRT; 337 (92.8%) White, 11 (3.0%) Black, 15 (4.1%) other, proton beam; 2,041 (83.7%) White, 243 (10.0%) Black, 154 (6.3%) other, combination Age at diagnosis: 58 (24.5%) 65 to 69 years, 96 (40.5%) 70 to 74 years, 83 (35.0%) 75 and older, SBRT; 1,188 (28.7%) 65 to 69 years, 1,560 (37.7%) 70 to 74 years, 1,388 (33.6%) 75 and older, BT; 2,065 (19.3%) 65 to 69 years, 3,712 (34.6%) 70 to 74 years, 4,938 (46.1%) 75		

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			and older, IMRT; 120 (33.1%) 65 to 69 years, 121 (33.3%) 70 to 74 years, 122 (33.6%) 75 and older, proton beam; 641 (26.3%) 65 to 69 years, 948 (38.9%) 70 to 74 years, 849 (34.8%) 75 and older, combination Metropolitan location of residence: 225 (94.9%) SBRT; 3,317 (80.2%) BT; 8,752 (81.7%) IMRT; 326 (89.8%) proton beam; 2,112 (86.6%) combination Clinical T-stage T1: 162 (68.4%) SBRT; 2,639 (63.8%) BT; 6,132 (52.7%) IMRT; 223 (61.4%) proton beam; 1,420 (58.2%) combination Concurrent ADT: 30 (12.7%) SBRT; 781 (18.9%) BT; 5,174 (48.3%) IMRT; 60 (16.5%) proton		

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			beam; 1,152 (47.3%) combination		
Johansson et al., 2019 [40] Single center in Sweden NR	To report outcome of hypofractionated proton boost as an alternative to high dose-rate BT boost in patients with localized prostate cancer Retrospective, noncomparative study Up to 10 years, with a median follow-up of 108 months	Inclusion criteria (must meet all): prostate cancer Exclusion criteria (excluded if any criteria met): NR	Total N = 531 Sex: men only Race/ethnicity: NR Median age at diagnosis (range): 66 years (45 to 79) NCCN risk group: 94 (19%) low, 158 (31%) intermediate, 135 (27%) high, 117 (23%) very high Median PSA (range): 11 ng/mL (1 to 158) No planned ADT: 227 (45%)	• SBRT ○ Boost of 20 Gy in 4 daily fractions ○ Followed by photon therapy (50 Gy in 2 Gy fractions)	• No comparator
Katz et al., 2012[41] Single academic center in US and 10 hospitals in Spain NR	To compare QoL after SBRT and radical prostatectomy Retrospective, comparative study Followed up to 36 months	Inclusion criteria for SBRT (must meet all): treated at least 3 years previous to analysis Exclusion criteria for SBRT (excluded if any criteria met): hormonal therapy Inclusion criteria for surgery (must meet all): stage T1	Total N = 339, comprising 216 in SBRT group and 123 in surgery group Sex: men only Race/ethnicity: NR Median age (range): 69 years (44 to 89 years) SBRT; 65 years (45 to 75) surgery	• SBRT ○ 35 or 36.25 Gy in 5 daily fractions	• Surgery ○ Radical retropubic prostatectomy with nerve-sparing at surgeon's discretion

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
		or T2 prostate cancer; no previous TURP Exclusion criteria for surgery (excluded if any criteria met): neoadjuvant or adjuvant hormonal therapy	Median PSA (range): 5.37 ng/ml (0.74 to 20.50) SBRT; 7.40 ng/ml (3.80 to 22.70) Clinical T-stage: 191 (88%) T1, 25 (12%) T2, SBRT; 82 (67%) T1, 41 (33%) T2, surgery Risk: 156 (72%) low, 56 (26%) intermediate, 4 (2%) high, SBRT; 52 (42%) low, 67 (55%) intermediate, 4 (3%) high		
Koskela et al., 2017[42] Not clear (assumed a single center), based in Finland NR	To evaluate safety and short-term efficacy of robotic SBRT in a clinical patient cohort with localized prostate cancer Retrospective, noncomparative study Median follow-up of 23 months	Inclusion criteria (must meet all): referred to RT by urologists following patients' decisions to request active radical treatment and not preferring surgery Exclusion criteria (excluded if any criteria met): ADT as primary treatment; SBRT as a booster with	Total N = 218 Sex: men only Race/ethnicity: NR Median age (range: 70 years (47 to 86) Clinical T-stage: 116 (53%) T1a-c, 13 (6%) T2a-b, 18 (8%) T2c, 70 (32%) T3-4 Risk group: 48 (22%) low, 59 (27%) intermediate, 111 (51%) high	• SBRT ○ 35 or 36.25 Gy in 5 fractions of 7 or 7.25 Gy, respectively, delivered on every other day	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
		EBRT; SBRT as salvage therapy post BT; SBRT as palliative care; deviation in fractionation; pervious pelvic irradiation; missing data	Initial PSA: 109 (50%) ≤ 10 ng/ml, 75 (34%) 10 to 20 ng/ml 32 (15%) > 20 ng/ml ADT: 142 (65%)		
Lee et al., 2016[43] Single academic center in Korea NR	To compare PSA kinetics between SBRT and cRT in low- and intermediate-risk prostate cancer Prospective, comparative study Median follow-up of 53.6 months	Inclusion criteria (must meet all): new diagnosis of low or intermediate risk prostate cancer; at least 1 year of follow-up Exclusion criteria (excluded if any criteria met): ADT	Total N = 69, comprising 34 in SBRT group and 35 in cRT group Sex: men only Race/ethnicity: NR Median age (range): 68 years (56 to 75) SBRT; 71 years (61 to 78) cRT ECOG performance status: 23 (68%) 0, 11 (32%) 1, SBRT; 23 (66%) 0, 12 (34%) 1, cRT Clinical T-stage: 8 (23%) T1 to T2a, 26 (77%) T2b to T2c, SBRT; 6 (17%) T1 to T2a, 29 (83%) T2b to T2c, cRT	• SBRT ○ 36.25 Gy, delivered in 5 fractions	• cRT ○ 70.2 to 75.6 Gy in 39 to 42 fractions

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			Median PSA (range) pretreatment: 7.62 ng/ml (3.45 to 15.73) SBRT; 8.75 ng/ml (5.34 to 14.81) cRT Risk: 9 (27%) low, 25 (74%) intermediate, SBRT; 6 (17%) low, 29 (83%) intermediate, cRT		

Loblaw et al., 2017[44]
4 centers in Canada
NR
	To compare biochemical failure-free survival and overall survival for prostate cancer treated with SBRT
	Retrospective, comparative database analysis (propensity-matched)
	Median follow-up of 5.07 years for SBRT, 5.70 for low dose BT, and 6.97 for EBRT
		Inclusion criteria (must meet all): low risk localized prostate cancer
		Exclusion criteria (excluded if any criteria met): ADT
			Total N = 673, comprising 151 in SBRT group, 458 in BT group, and 64 in EBRT group (364 included in matched group)
			Sex: men only
			Race/ethnicity: NR
			Mean age (SD): 66.35 years (7.26) SBRT; 62.96 years (6.79) BT; 67.33 years (6.92) SBRT; 69.83 (6.39) years EBRT
			Mean PSA at baseline (SD): 5.71 ng/ml (2.18) SBRT;
				• SBRT
				  ○ 35 Gy in 5 fractions
					• Low dose BT
					  ○ I-125
					  ○ monotherapy in 144 to 145 Gy
					• EBRT
					  ○ 74 to 79.8 Gy in 37 to 42 fractions

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			5.39 ng/ml (2.10) BT; 5.56 ng/ml (2.17) SBRT; 6.35 (2.17) ng/ml EBRT Clinical T-stage T1c: 75 (94%) SBRT; 310 (68%) BT; 66 (93%) SBRT; 38 (59%) EBRT; all other patients were T2a		
Ma et al., 2022[45] 2 academic centers in US NCT03541850 SCIMITAR	To evaluate short-term physician-scored GU and GI toxicities and patient-reported outcomes after postprostatectomy SBRT Prospective, noncomparative study Up to 6 months (safety)	Inclusion criteria (must meet all): history of clinical localized prostate cancer treated with radical prostatectomy; at least 1 adverse or recurrent pathologic features at time of prostatectomy Exclusion criteria (excluded if any criteria met): NR	Total N = 100 Sex: men only Race/ethnicity: 9 (9%) Black, 85 (85%) White, 3 (3%) Asian, 2 (2%) other, 1 (1%) unknown Median age (range): 8.6 ng/mL (2.7 to 78.9) Median PSA at initial diagnosis (range): 69 years (50 to 82) Pathologic T stage: 44 (44%) T2, 33 (33%) T3a, 22 (22%) T3b, 1 (1%) T4 Adverse pathologic feature: 10 (10%)	• SBRT ○ Median prostate bed dose, 32 Gy (range, 30 to 34) ○ Median prostate bed boost dose, 40 Gy (range, 36 to 40)	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			bladder neck involvement, 39 (39%) positive margin, 17 (17%) tertiary grade 5 Median time from prostatectomy to SBRT (range): 22.8 months (3.8 to 184.1) Concurrent ADT: 41 (41%) Median duration of ADT (range): 6 months (1 to 8)		
Mantz, 2014[46] Single center (assumed) in US NR	To report results of a phase II trial of SBRT monotherapy for low-risk prostate cancer Retrospective (assumed), noncomparative study Followed up for a minimum of 5 years	Inclusion criteria (must meet all): clinical stageT1c to T2a; presenting serum PSA ≤ 10 ng/ml; Gleason score of 6 or less; Gleason score of 7 if primary histologic score of 3 and ≤ 25% of biopsy cores positive Exclusion criteria (excluded if any criteria met): prostate volume	Total N = 102 Sex: men only Race/ethnicity: NR Mean age: NR Mean PSA at presentation (range): 7.30 ng/ml (3.24 to 10.0)	• SBRT ○ 40Gy in 5 fractions, delivered every other day	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
		> 60 cc; previous hormonal therapy; IPSS > 18; history of TURP; history of colostomy; history of pelvic RT; history of chemotherapy			
Meier et al., 2018[47] 21 centers in US, including 1 academic center NCT00643994	To assess whether dose escalated SBRT can be safely administered across multiple institutions, with favorable 5-year disease-free survival rates compared with historical controls Prospective, noncomparative study Median follow-up of 61 months	Inclusion criteria (must meet all): previously untreated prostate adenocarcinoma; Zubrod performance status of 0 to 2; no invasive malignancy within 5 years; no ADT within 2 months of enrollment; estimated prostate volume ≤ 100 cm^3 Exclusion criteria (excluded if any criteria met): NR	Total N = 309 Sex: men only Race/ethnicity: 6 (2%) Asian, 18 (6%) African American, 5 (2%) Hispanic or Latino, 279 (90%) White Zubrod performance of 0: 292 (94%) Clinical T-stage: 3 (1%) T1b, 244 (79%) T1c, 53 (17%) T2a, 9 (3%) T2b Mean initial PSA (range): 5.5 ng/mL (0.04 to 17.90) Risk: 172 (55.7%) low, 83 (26.9%) favorable intermediate risk, 54	• SBRT ○ 40 Gy in 5 fractions of 8 Gy	• No comparator (historical controls only)

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			(17.5%) unfavorable intermediate		
Miszczyk et al., 2017[48,49] Single center in Poland NR	To evaluate tolerance and effectiveness of SBRT for low and intermediate risk prostate cancer Retrospective (assumed), noncomparative study Median follow-up of 15 months	Inclusion criteria (must meet all): low-to-intermediate-risk prostate cancer Exclusion criteria (excluded if any criteria met): NR	Total N = 400 Sex: men only Race/ethnicity: NR Median age (range): 69 years (53 to 83) No comorbidities: 117 (29%) ADT: 241 (60.3%) Median PSA (range): 2.3 ng/ml (0.008 to 20.4)	• SBRT ○ 7.25 Gy to a total of 36.25 Gy on every other day over a period of 9 days	• No comparator
Monaco et al., 2022[50] Single center in US NR	To review QoL metrics between patients who underwent definitive SBRT vs. AS for management of low- to intermediate-risk prostate cancer Retrospective, comparative analysis Followed-up for up to 48 months	Inclusion criteria (must meet all): completed at least 1 survey within 4 years post treatment; had very-low-to-intermediate-risk prostate cancer Exclusion criteria (excluded if any criteria met): AS then went on to definitive therapy; SBRT then salvage	Total N = 309, comprising 161 in SBRT group and 148 in AS group Sex: men only Race/ethnicity: 142 (88%) Caucasian, 16 (10%) Black or African American, 1 (< 1%) other, 2 (1%) NR, SBRT; 132 (89%) Caucasian, 7 (5%) Black or African American, 3 (2%) other, 6 (4%) NR, AS	• SBRT ○ 35 to 36.25 Gy fractions delivered in 5 consecutive treatments over 5 days	• AS ○ PSA testing every 3 months ○ Annual multiparametric MRI ○ Biopsy if PSA rise, unfavorable genomics, or disease progression on imaging ○ Treatment based on patient preference, Gleason score increases, or

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
		therapy; BPH surgery	Mean age (SD): 67.15 years (7.41) SBRT; 65.5 years (7.42) AS Risk: 33 (21%) very low, 18 (11%) low, 56 (35) favorable intermediate, 54 (34%) unfavorable intermediate, SBRT; 82 (55%) very low, 24 (16%) low, 37 (25) favorable intermediate, 5 (3%) unfavorable intermediate, AS Median PSA (IQR): 5.8 ng/mL (4.2 to 8.2) SBRT; 5.3 ng/mL (4.0 to 6.7)		increased tumor volume
Oliai et al., 2016[51-53] 1 community hospital and 1 academic center in US NR	To compare efficacy and toxicity outcomes of prostate cancer patients treated with SBRT or IMRT Retrospective, comparative, propensity-matched analysis	Inclusion criteria (must meet all): localized prostate cancer Exclusion criteria (excluded if any criteria met): NR	Total N = 263, comprising 142 in SBRT group and 121 in IMRT group Sex: men only Race/ethnicity: NR Mean age (SD): 66.9 years (8.0) SBRT; 71.6 years (6.7) IMRT	• SBRT ○ 36.25 Gy in 5 fractions for most patients	• IMRT ○ 75.6 Gy in 42 fractions for most patients

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
	Median follow-up of 34 months (SBRT) and 51 months (IMRT)		Mean pre-treatment PSA (SD): 8.1 ng/mL (7.7) SBRT; 11.0 ng/mL (18.8) IMRT Risk group: 28 (20%) very low, 33 (23%) low, 50 (35%) favorable intermediate, 13 (9%) unfavorable intermediate, 18 (13%) high, SBRT; 9 (7%) very low, 13 (11%) low, 39 (32%) favorable intermediate, 28 (23%) unfavorable intermediate, 32 (27%) high, IMRT Use of ADT: 40 (28%) SBRT; 87 (72%) IMRT Tumor stage T1b, T1c, T2a, T2b: 132 (93%) SBRT; 91 (76%) IMRT		
Pan et al., 2018[54] MarketScan Commercial Claims and Encounters database (2008 to 2015) NR	To compare toxicities and cost of proton radiation and SBRT with IMRT for prostate cancer among men younger	Inclusion criteria (must meet all): primary diagnosis of prostate cancer; continuous coverage from 6	Total N = 12,128, comprising 312 in SBRT group, 693 in proton therapy group, and 11,123 in IMRT group	• SBRT ○ Median treatment fractions, 5 (IQR, 5 to 5)	• Proton therapy ○ Median treatment fractions, 39 (IQR, 39 to 44) • IMRT

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
	than 65 years of age with private insurance Retrospective, comparative (propensity-matched) database analysis Median follow-up of 18 months for SBRT, 23 months for proton therapy, and 23 months for IMRT	months before through 6 months after starting treatment Exclusion criteria (excluded if any criteria met): BT or combined radiation modalities; pretreatment claims indicated metastatic disease, radical prostatectomy, or other malignancy	Sex: men only Race/ethnicity: NR Age: 72 (23%) 55 years and younger, 104 (33%) 56 to 60 years, 136 (44%) 61 to 64 years, SBRT; 198 (29%) 55 years and younger, 270 (39%) 56 to 60 years, 225 (32%) 61 to 64 years, proton therapy; 2,233 (20%) 55 years and younger, 4,033 (36%) 56 to 60 years, 4,857 (44%) 61 to 64 years, IMRT Residence: 22 (7%) rural,. 288 (92%) urban, 2 (1%) unknown, SBRT; 92 (13%) rural,. 578 (83%) urban, 23 (3%) unknown, proton therapy; 1,448 (13%) rural, 9,476 (85%) urban, 199 (2%) unknown, IMRT		○ Median treatment fractions, 42 (IQR, 38 to 44)

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			Comorbidity: 259 (83%) none, 40 (13%) 1, 13 (4%) 2 or more, SBRT; 604 (87%) none, 68 (10%) 1, 21 (3%) 2 or more, proton therapy; 8.685 (78%) none, 1,805 (16%) 1, 633 (6%) 2 or more, IMRT Concurrent ADT: 23 (7%) SBRT; 130 (19%) proton therapy, 3,330 (30%) IMRT		
Pasquier et al., 2019[55] 7 centers in France and Italy, including academic centers NR	To assess efficacy and safety of salvage SBRT in patients with biopsy-proven local prostate cancer recurrence RT Retrospective, noncomparative study Median follow-up of 29.2 months	Inclusion criteria (must meet all): histologically proven history of prostate cancer, initially irradiation with curative intent; biochemical recurrence according to Phoenix criteria occurring at least 2 years after external RT; histologically proven local recurrence; absence of pelvic	Total N = 100 Median age at diagnosis (range): 62 years (47 to 78) Median PSA (range) at initial diagnosis: 10.2 ng/mL (2.3 to 120) Risk: 21 of 92 (22%) low, 34 of 92 (36%) intermediate, 39 of 92 (41%) Initial RT: 80 (80%) external RT, 17	• SBRT ○ 36 Gy in 6 fractions administered every other day in most patients	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
		or distant metastasis; absence of residual toxicity of grade > 2 Exclusion criteria (excluded if any criteria met): prostatectomy	(17%) BT, 3 (3%) external RT and BT Median dose of initial RT (range): 74 Gy (66.6 to 80) Median fractions of initial RT (range): 37 (37 to 42)		

Patel et al., 2020[56]
 	
National Cancer Database (2004 to 2016)
 	
NR
	To compare SBRT plus ADT and EBRT plus ADT in higher-risk prostate cancer
	
	Retrospective, comparative database analysis
	
	Median follow-up of 74 months
		Inclusion criteria (must meet all): aged over 40; localized prostate cancer treated with external radiation and ADT with curative intent
		
		Exclusion criteria (excluded if any criteria met): had brachytherapy, surgery, chemotherapy, or immunotherapy; missing ADT or risk stratification data; received ADT > 180 days before or after start of RT
			Total N = 41,355, comprising 558 in SBRT group and 40,797 in EBRT group
			
			Sex: men only
			
			Race/ethnicity: 415 (76%) White, 114 (21%) Black, 19 (3%) other, SBRT; 32,076 (79%) White, 6,923 (17%) Black, 1,363 (3%) other, EBRT
			
			Insurance status: 12 (2%) not insured, 146 (27%) private, 387 (71%) government, SBRT; 744 (2%) not insured, 10,563 (26%) private,
				• SBRT
				  ○ At least 5 Gy in 5 fractions
					• cRT or moderate fractionation
					  ○ At least 3 Gy per fraction with a total dose of at least 60 Gy

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			28,931 (72%) government, EBRT Risk group: 130 (23%) unfavorable intermediate, 428 (77%) high, SBRT; 5,094 (12%) unfavorable intermediate, 35,703 (88%) high, SBRT Median age at diagnosis (range): 71 years (43 to 90), SBRT; 71 years (40 to 90), EBRT		
Paydar et al., 2016[57] Single academic center in US NR	To report acute bowel morbidity 1 week following prostate SBRT Prospective, noncomparative study Followed up to 3 months	Inclusion criteria (must meet all): localized prostate cancer Exclusion criteria (excluded if any criteria met):	Total N = 103 Sex: men only Race/ethnicity: 58 (56%) White, 29 (28%) Black, 16 (15%) other Median age (range): 69 years (48 to 85) Charlson Comorbidity Index: 63 (62%) 0, 31 (30%) 1, 9 (9%) 2 or higher	• SBRT ○ 35 or 36.25 Gy delivered in 5 fractions (7 to 7.25 Gy per fraction)	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			Median PSA (range) pretreatment: 7 ng/ml (2.2 to 50) Clinical T-stage: 65 (63%) T1c, 21 (20%) T2a, 13 (13%) T2b, 3 (3%) T2c, 1(1%) T3 Risk: 20 (19%) low, 67 (65%) intermediate, 16 (15%) high Hormone treatment: 17 (17%)		
Pryor et al., 2019[58] 5 centers in Australia, including academic centers ACTRN12615000223538 PROMETHEUS	To report feasibility, early toxicity, and PSA kinetics following gantry-based, SBRT boost Prospective, noncomparative study Median follow-up of 24 months	Inclusion criteria (must meet all): histological diagnosis of NCCN intermediate or high-risk prostate adenocarcinoma; ECOG performance status 0 to 1 Exclusion criteria (excluded if any criteria met): clinical T4 disease; nodal, or distant metastases; severe obstructive urinary; symptoms requiring	Total N = 135 Sex: men only Race/ethnicity: NR Median age (range): 70 years (53 to 81) Risk: 103 (76%) intermediate, 32 (24%) high No ADT: 62 (46%) SBRT dose: 42 (31%) 19 Gy, 93 (69%) 20 Gy Elective pelvic EBRT: 11 (8%)	• SBRT ○ 19 to 20Gy in 2 fractions delivered 1 week apart, followed by conventionally fractionated IMRT (46Gy in 23 fractions)	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
		catheterization or transurethral resection previous to RT, previous pelvic RT; inflammatory bowel disease; hip prosthesis; inability to undergo imaging or fiducial marker insertion			
Rana et al., 2015[59] Single center in US NR	To present institutional data on sexual function, voiding function, irritative symptoms, and treatment response following SBRT Retrospective, noncomparative study Median follow-up of 4.3 years	Inclusion criteria (must meet all): biopsy-proven newly diagnosed, nonmetastatic and untreated prostate cancer Exclusion criteria (excluded if any criteria met): NR	Total N = 101 Sex: men only Race/ethnicity: 55.6% White, 26.8% Black, 17.6% other Median age (range): 72 years (47 to 88) Risk: 36.3% low, 54.9% intermediate, 7.8% high ADT: 8.9%	• SBRT ○ 36.25 Gy (range 35 to 40 Gy) over 5 daily fractions	• No comparator
Ricco et al., 2017[60] National Cancer Database (2004 to 2013) NR	To compare SBRT and IMRT for organ-confined prostate cancer Retrospective, comparative database analysis	Inclusion criteria (must meet all): invasive adenocarcinoma of prostate; treated within 180 days of diagnosis	Total N = 5,430, comprising 2,715 in SBRT group and 2,715 in IMRT group Sex: men only	• SBRT ○ 35 to 50 Gy	• IMRT ○ 72 to 86.4 Gy

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
	(propensity-matched)	Exclusion criteria (excluded if any criteria met):previous prostate surgery; metastatic disease; node positive disease; > 1 previous cancer; stages 0 and 4 disease	Race/ethnicity: 316 (11.6%) Black, 41 (1.5%) other, 20 (0.7%) unknown, 2,338 (86.1%) White, SBRT; 281 (10.4%) Black, 38 (1.4%) other, 20 (0.7%) unknown, 2,376 (87.5%) White, IMRT Age: 152 (5.6%) < 55 years, 258 (9.5%) 55 to 59 years, 454 (16.7%) 60 to 64 years, 696 (25.6%) 65 to 69 years, 618 (22.8%) 70 to 74 years, 537 (19.8%) 75 to 90 years, SBRT; 123 (4.5%) < 55 years, 260 (9.6%) 55 to 59 years, 438 (16.1%) 60 to 64 years, 715 (23.6%) 65 to 69 years, 658 (24.2%) 70 to 74 years, 521 (19.2%) 75 to 90 years, IMRT Insurance status: 28 (1.0%) unknown, 26 (1.0%) Medicaid,		

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			1,636 (60.3%) Medicare, 26 (1.0%) not insured, 29 (1.1%) other government, 971 (35.7%) private, SBRT; 31 (1.1%) unknown, 24 (0.9%) Medicaid, 1,653 (60.9%) Medicare, 30 (1.1%) not insured, 23 (0.9%) other government, 954 (35.1%) private, IMRT Residence: 2,452 (90.3%) metropolitan, 27 (1.0%) rural, 236 (8.7%) urban, SBRT; 2,442 (89.9%) metropolitan, 21 (0.8%) rural, 252 (9.3%) urban, IMRT Charlson-Deyo comorbidity score of 0: 2,366 (87.2%) SBRT; 2,417 (89.0%) IMRT Clinical T-stage: 2,153 (79.3%) T1, 525 (19.3%) T2, 9 (0.3%) T3, SBRT;		

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			2,180 (80.3%) T1, 502 (18.5%) T2, 9 (0.3%) T3, IMRT ADT: 245 (9.0%) SBRT; 260 (9.6%) IMRT		
Tsang et al., 2021[61] Multicenter study in UK NR	To compare biochemical control rates and late toxicities in patients with low- and intermediate-risk prostate cancer treated with high dose-rate BT or SBRT Retrospective, comparative study Median follow-up of 60.1 months	Inclusion criteria (must meet all): low- and intermediate-risk prostate cancer Exclusion criteria (excluded if any criteria met): NR	Total N = 185, comprising 43 in SBRT group and 142 in BT group Sex: men only Race/ethnicity: NR Median age (range): 70.3 years (46.9 to 84.5) SBRT; 68.7 or 67.9 years (51.0 to 80.9), depending on BT dose Stage T1: 2 (5%) SBRT; 22 (15%) BT PSA ≤ 10 ng/mL: 30 (70%) SBRT; 82 (58%) BT Use of ADT: 8 (19%) SBRT; 62 (44%) BT Low risk: 2 (5%) SBRT; 6 (4%) BT	• SBRT ○ 36.25 Gy in 5 fractions ○ ADT for 6 months, commencing 1–3 months previous to RT, if T2c stage disease and either PSA > 10 or Gleason score of 7	• BT ○ 19 Gy in single dose or 26 Gy in 2 fractions ○ ADT for 6 months, commencing 1–3 months previous to RT, if T2c stage disease and either PSA > 10 or Gleason score of 7
Werneburg et al., 2018[62]	To investigate patient-reported	Inclusion criteria (must meet all):	Total N = 279, comprising 82 in	• SBRT	• Cryotherapy • AS

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
Single academic center in US NR	urinary function, bowel habits, and sexual function in patients following SBRT or cryotherapy Retrospective, comparative analysis Followed-up for 4 years	primary prostate cancer treatment from February 2011 to March 2017; completed at least 1 survey Exclusion criteria (excluded if any criteria met): SBRT boost; salvage cryotherapy	SBRT group, 129 in cryotherapy group, and 68 in AS group Sex: men only Race/ethnicity: 73 (89%) White, 8 (10%) Black, 0 Hispanic, 1 (1%) Asian, 0 other, SBRT; 99 (81%) White, 15 (12%) Black, 5 (4%) Hispanic, 1 (1%) Asian, 2 (2%) other, cryotherapy; 63 (96%) White, 3 (5%) Black, 0 Hispanic, 0 Asian, 0 other, AS Median age: 66 years, SBRT; 69 years, cryotherapy; 66 years, AS Median PSA at treatment or initiation of AS: 6.7 ng/mL SBRT; 6.1 ng/mL cryotherapy; 5.0 ng/mL AS	○ 5 consecutive treatments of 35 to 36.25 Gy fractions ○ Delivered in a period of 5 days	

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			Median Gleason score: 7 SBRT; 7 cryotherapy; 6 AS		
Yu et al., 2014[63] Chronic Conditions Warehouse (2008 to 2011) NR	To compare treatment cost and toxicity outcomes among patients receiving IMRT or SBRT for primary treatment of prostate cancer by using a comprehensive, population-based analysis of a national sample of Medicare beneficiaries with prostate cancer Retrospective, comparative database analysis, with matching Followed up to 24 months	Inclusion criteria (must meet all): patients with early-stage prostate cancer; aged 66 to 94 years Exclusion criteria (excluded if any criteria met): did not have Medicare Parts A and B fee-for-service coverage in 9 months before treatment date	Total N = 55,176, comprising 1,335 in SBRT group and 53,841 in IMRT group Sex: men only Race/ethnicity: 1,177 (88%) White, 11 (9%) Black, 44 (3%) other, SBRT; 45,658 (85%) White, 5,803 (11%) Black, 2,380 (4%) other, IMRT Age at diagnosis: 397 (30%) 67 to 69 years, 464 (35%) 70 to 74 years, 340 (25%) 75 to 79 years, 112 (8%) 80 to 84 years, 22 (2%) 85 to 94 years, SBRT; 12,447 (23%) 67 to 69 years, 19,021 (35%) 70 to 74 years, 15,148 (28%) 75 to 79 years, 5,954 (11%) 80 to 84 years, 22	• SBRT ○ Based on claim codes	• IMRT ○ Based on claim codes

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			(2%) 85 to 94 1,271, IMRT Residence: > 1,149 (> 86%) metro, 175 (13%) nonmetro, < 11 (< 1%) not known, SBRT; 42,337 (79%) metro, 11,430 (21%) nonmetro, 74 (< 1%) not known, IMRT No comorbidities: 801 (60%) SBRT, 30,171 (56%) IMRT ADT: 148 (11%) SBRT; 23,789 (44%) IMRT		

Abbreviations. ADT: androgen deprivation therapy; AE: adverse event; AS: active surveillance; BPH: benign prostatic hyperplasia; BT: brachytherapy; cRT: conventional radiation therapy; EBRT: external beam radiation therapy; ECOG: Eastern Cooperative Oncology Group; GI: gastrointestinal; GU: genitourinary; Gy: Gray; IMRT: intensity-modulated radiation therapy; IQR: interquartile range; MRI: magnetic resonance imaging; NCCN: National Comprehensive Cancer Network; NCT: US National Clinical Trial; NR: not reported; PSA: prostate-specific antigen; QoL: quality of life; RT: radiation therapy; SBRT: stereotactic body radiation therapy: TURP: transurethral resection of prostate; WHO: World Health Organization.

Lung Cancer

Table C14. Study Characteristics for Nonrandomized and Registry-based Studies

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
Berkovic et al., 2020[64] Single academic center in Belgium NR	To report on local control, lung and distant progression free survival and overall survival of patients with oligorecurrent lung metastases Retrospective, noncomparative study Median follow-up of 22 months	Inclusion criteria (must meet all): up to 5 oligorecurrent lung metastases Exclusion criteria (excluded if any criteria met): heavily compromised pulmonary function tests with grade IV COPD; co-existing ILD and IPF; pleural effusion; metastases with diameter > 6 cm; life expectancy < 6 months	Total N = 104 Sex: 49 (47%) female Race/ethnicity: NR Median age (range): 66 years (29 to 88) Primary sites: 49 (47%) lung, 35 (34%) GI, 20 (19%) other Primary histology: 67(64%) adenocarcinoma, 37 (36%) other Previous chemotherapy for primary tumor: 25 (24%) Performance status: 24 (23%) 0, 71 (68%) 1, 9 (9%) 2 Previous treatments per patient: 45 (34%) surgery, 47 (36%), 42 (32%) RT, 57 (43%) other	• SBRT ○ Delivered 3 times a week on every other day in 3 or 5 fractions to 60 Gy	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
Davis et al., 2015[65] RSSearch registry, including 18 sites and academic centers in US and Germany (2004 to 2014) NCT01885299	To evaluate treatment patterns and outcomes of SBRT for centrally located primary non-NSCLC or lung metastases Retrospective registry analysis Median follow-up of 17 months	Inclusion criteria (must meet all): centrally located T1- T2, N0, M0 NSCLC or lung metastasis Exclusion criteria (excluded if any criteria met): recurrent lung lesion; previous RT in SBRT-treated area	Total N = 111 Sex: 19 (40%) primary, 33 (52%) metastatic Race/ethnicity: NR Median age (range): 74 years (41 to 93) primary, 65 years (35 to 84) metastatic Previous treatment: 36 (77%) none, 8 (17%) chemotherapy, 3 (6%) surgery, 0 immunotherapy, 0 RFA, 2 (4%) other, primary: 17 (30%) none, 39 (68%) chemotherapy, 15 (26%) surgery, 5 (9%) immunotherapy, 2 (4%) RFA, 3 (5%) other, metastatic Clinical T-stage: 27 (56%) T1N0M0, 21 (44%) T2N0M0, primary only	• SBRT ○ Median 48 Gy (range, 20 to 60) in a median of 4 fractions (range, 1 to 5) for primary NSCLC ○ Median 37.5 Gy (range, 16 to 60) in a median of 3 fractions (range, 1 to 5) for metastatic disease	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			Tumor histology: 3 (6%) adenocarcinoma, 22 (46%) squamous cell, 23 (48%) NSCLC not specified, primary only		
Duijm et al., 2018[66] 2 centers in Netherlands (1 academic) NR	To correlate esophagus toxicity and dose-volume histogram parameters Retrospective, noncomparative study Median follow-up of 16 months	Inclusion criteria (must meet all): primary or metastatic central lung tumors Exclusion criteria (excluded if any criteria met): NR	Total N = 231 Sex: 82 (35%) female Race/ethnicity: NR Median (IQR): 74 years (67 to 80) Disease: 187 (81%) primary NSCLC, 44 (19%) lung metastasis Charlson Comorbidity Score: 119 (52%) 0 to 2, 93 (40%) 3 to 5, 19 (8%) 6 to 9	• SBRT ○ Tumors close to esophagus treated with 6 to 7 fractions of 7 to 8 Gy ○ Other central tumors received 5 fractions of 9 to 12 Gy, except 2 tumors which received 3 fractions of 20 Gy	• No comparator
Filippi et al., 2016[67] Single academic center in Italy NR	To explore effect of surgery or SBRT on survival in people with lung oligometastases	Inclusion criteria (must meet all): histological diagnosis of primary colorectal adenocarcinoma previously treated	Total N = 170, comprising 28 in SBRT group and 124 in surgery group Sex: 14 (50%) SBRT; 55 (39%) surgery	• SBRT ○ 26 Gy in a single fraction (n = 31), ○ 45 Gy in 3 fractions (n = 8)	• Surgery ○ Thoracoscopic resection (3%) ○ Wedge resection (67%) ○ Anatomical resection (26%)

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
	Retrospective, comparative study Median follow-up of 27 months in SBRT group and 46 months in surgery group	with radical surgery; 5 or fewer lung metastases; maximum tumor diameter ≤ 50mm; adequate pulmonary function; ECOG performance status 0 to 1; controlled primary tumor; controlled extra-lung metastases Exclusion criteria (excluded if any criteria met): NR	Race/ethnicity: NR Median age at treatment (IQR): 72 years (66 to 77) SBRT; 66 years (59 to 72) surgery No comorbidities: 12 (43%) SBRT; 71 (50%) surgery Previous metastases: 11 (39%) SBRT; 46 (32%) surgery More than 1 metastases: 11 (39%) SBRT; 64 (45%) surgery Synchronous lung metastases: 2 (7%) SBRT; 21 (15%) surgery	○ 55 Gy in 10 fractions (n = 2)8 ○ 60 Gy in eight fractions (n = 2)	○ Combined resection (3%)
Fleming et al., 2017[68] Single center in US NR	To describe palliative effect of cRT for lung metastases and compare local control with that of SBRT Retrospective, comparative study	Inclusion criteria (must meet all): thoracic RT for secondary lung malignancies Exclusion criteria (excluded if any criteria met): younger than 18	Total N = 182, comprising 88 in SBRT group and 94 in cRT group Sex: 48 (55%) female SBRT; 42 (44.7%) cRT Race/ethnicity: NR	• SBRT ○ Commonly 30 Gy in 10 fractions ○ Median of 45 Gy (range, 20 to 60 Gy) in a median 5	• cRT ○ Maximum of 50 Gy in conventional fractionation (maximum of 40 Gy per fraction) ○ Median dose of 30 Gy (range, 20 to 50 Gy) in a median 10 (range, 5 to 25) fractions

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
	Median follow-up of 16 months	years; re-irradiation to a site of local failure; treated for disease limited to mediastinum, ribs, or chest wall without involvement of lung parenchyma	Median age at RT start (range): 63 years (32 to 89) SBRT; 63 years (23 to 86) cRT Tumor histology: 16 of 91 (18%) radioresistant SBRT; 25 of 99 (25%) radioresistant, cRT	(range, 1 to 5) fractions	
Guckenberger et al., 2009[69] Single academic center in Germany NR	To evaluate outcome after image-guided SBRT for early-stage NSCLC and pulmonary metastases Retrospective, noncomparative study Median follow-up of 14 months	Inclusion criteria (must meet all): treated with SBRT Exclusion criteria (excluded if any criteria met): NR	Total N = 124 Sex: 46 (37%) female Race/ethnicity: NR Median age (range): 70 years (52 to 85) early NSCLC, 64 years (22 to 84) lung metastases Histology of primary lung tumor: 11 (27%) unknown, 19 (47%) squamous, 11 (27%) adenocarcinoma	• SBRT ○ 6 to 26 Gy in 1 to 8 fractions	• No comparator
Helou et al, 2017[70] Not clear NR	To assess association between colorectal cancer histology, dose, and local failure after	Inclusion criteria (must meet all): pulmonary metastases; adult patients with any	Total N = 120 Sex: 62 (52%) female	• SBRT ○ 48 to 52 Gy in 4 fractions for peripheral pulmonary	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
	SBRT for pulmonary metastases Prospective, noncomparative study Median follow-up of 22 months	solid primary tumor; met indications for SBRT Exclusion criteria (excluded if any criteria met): NR	Race/ethnicity: NR Mean age at treatment (SD): 67 years (11) ECOG 0 to 1 at treatment: 175 (95%) Indication for SBRT: 25 (14%) single metastasis, 99 (54%) oligometastasis, 38 (21%) oligoprogression, 22 (12%) dominant tumor 2 or more pulmonary lesions: 97 (53%) Primary cancer site by lesion: 101 (55%) colorectal, 26 (14%) lung, 21 (11%) renal cell, 18 (9%) breast, 18 (9%) other	○ metastases; increased to 56 to 60 Gy in 4 fractions ○ 50 Gy in 5 fractions for central tumors	
Jacobs et al., 2020[71] National Cancer Database (2004 to 2015)	To analyze practice patterns and perform comparative effectiveness of definitive radiotherapy	Inclusion criteria (must meet all): adults with stage IIB lung cancer Exclusion criteria (excluded if any	Total N = 4,401, comprising 989 in SBRT group, 484 in HFRT group, and 2,928 in cRT	• SBRT ○ Most common dose was 50 Gy in 5 fractions	• HFRT ○ Most common dose was 60 Gy in 20 fractions • cRT

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
NR	techniques for inoperable stage IIB NSCLC Retrospective database analysis Median follow-up of 19 months	criteria met): surgery to primary tumor; unknown surgery status; no or unknown receipt of RT, intraoperative RT or BT; RT to a nonthoracic site; excessively long RT duration (≥ 100 days)	Sex: 523 (53%) female, SBRT; 209 (43%) female, HFRT; 1,226 (42%) female, cRT Race/ethnicity: NR Median age at diagnosis (range): 74 years (68 to 80) SBRT; 77 years (69 to 82) HFRT; 71 years (64 to 78) cRT Charlson-Deyo comorbidity score 0 to 1: 809 (82%) SBRT; 401 (83%) HFRT; 2,530 (86%) cRT Histology: 425 (43%) adenocarcinoma, 408 (41%) squamous cell carcinoma, 156 (16%) other, SBRT; 150 (31%) adenocarcinoma, 256 (53%) squamous cell carcinoma, 78 (16%) other, HFRT; 843		○ Most common dose was 66 Gy in 33 fractions

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			(29%) adenocarcinoma, 1,559 (53%) squamous cell carcinoma, 526 (18%) other, cRT Tumor size: 652 (69%) 0.1 to 3 cm, 235 (25%) 3.1 to 5 cm, 63 (7%) 5.1 to 7 cm, SBRT; 131 (30%) 0.1 to 3 cm, 172 (40%) 3.1 to 5 cm, 128 (30%) 5.1 to 7 cm, HFRT; 459 (18%) 0.1 to 3 cm, 1,049 (42%) 3.1 to 5 cm, 996 (40%) 5.1 to 7 cm, cRT Systemic therapy use: 88 (9%) SBRT; 121 (25%) HFRT; 2,220 (77%) cRT		

Kanzaki et al., 2020[72]
 	
Single academic center in Japan
 	
NR
	To report short-term outcomes of PM or SBRT for pulmonary metastases
	
	Retrospective, comparative study
		Inclusion criteria for surgery (must meet all): pulmonary nodule deemed completely resectable; absence of apparent mediastinal lymph node metastasis on	Total N = 80, comprising 21 in SBRT group and 59 in PM group
			
			Sex: 7 (33%) SBRT; 24 (41%) PM
			
			Race/ethnicity: NR
				• SBRT
				  ○ Total dose of 52 Gy in 4 fractions
					• PM
					  ○ Type of resection selected according to size and location of tumor, overall general condition, and respiratory function of patient

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
	Median follow-up of 28 months	a preoperative radiological examination; metastatic disease limited to lungs or extrapulmonary distant metastasis was controlled or controllable if present; locoregional control of primary tumor; good overall general condition and sufficient respiratory function Inclusion criteria for surgery (must meet all): largest diameter of pulmonary nodule(s) > 5 cm; no more than 3 pulmonary nodules; extrapulmonary distant metastasis or controlled if present; apparent findings of	Mean age (SD): 67 years (11) SBRT; 61 years (15) PM Primary tumor: 6 (29%) colorectal, 2 (10%) gynecologic, 8 (38%) head and neck squamous, 0 renal cell, 0 salivary gland, 2 (10%) breast, 2 (10%) esophageal, 1 (5%) other, SBRT; 27 (46%) colorectal, 8 (14%) gynecologic, 3 (5%) head and neck squamous, 7 (12%) renal cell, 3 (5%) salivary gland, 1 (2%) breast, 3 (5%) esophageal, 7 (12%) other, PM Treatment for primary tumor: 11 (52%) surgery, 10 (48%) chemotherapy or RT, SBRT; 58 (98%) surgery, 1 (2%) chemotherapy or RT, PM Mean disease-free interval (range): 27 months (0 to 111)		

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
		interstitial lung diseases. Exclusion criteria (excluded if any criteria met): rapidly-progressing disease	SBRT; 28 months (0 to 128) PM Number of lesions: 15 (72%)1, 3 (14%) 2, 3 (14%) 4, 0 4, SBRT; 45 (76%)1, 10 (17%) 2, 3 (5%) 4, 1 (2%) 4, PM Previous chemotherapy for metastatic disease: 7 (33%) SBRT; 16 (27%) PM		
Lagerwaard et al., 2012[73] Single academic center in Netherlands NR	To evaluate outcomes in a cohort of patients with potentially operable stage I NSCLC treated with SBRT at a single center Prospective, noncomparative study Median follow-up of 31 months	Inclusion criteria (must meet all): stage IA-IB NSCLC; potentially operable Exclusion criteria (excluded if any criteria met): double lung tumors; second primary tumor after previous high-dose (chemo) RT; concurrent second malignancy; COPD of grade 3 to 4; WHO performance score	Total N = 177 Sex: 76 (43%) female Race/ethnicity: NR Median age (range): 76 years (50 to 91) Stage: 106 (60%) IA, 71 (40%) IB Never smoked: 9 (5%) No comorbidities: 18 (10%) Histology: 20 (33%) adenocarcinoma, 16 (27%) squamous	• SBRT ○ Patients with peripheral T1 tumors without broad contact with chest wall treated with 3 fractions of 20 Gy each; ○ Patients with T1 tumors that had broad contact with chest wall and T2 tumors treated with 5 fractions of 12 Gy each.	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
		of ≥ 3; serious cardiovascular comorbidity precluding surgery; other major comorbidities precluding surgery	cell, 24 (38%) undifferentiated	○ Patients with centrally tumors were treated with 8 fractions of 7.5 Gy each	
Lee et al. 2018[74] 1 academic center in South Korea NR	To compare outcomes of SBRT and metastasectomy in patients with pulmonary metastases Retrospective, comparative study Median follow-up of 14 months	Inclusion criteria (must meet all): presence of up to 3 pulmonary metastases arising from any nonhematological malignancy; ECOG performance status 0–2; surgery or RT performed with ablative intent; no previous history of thoracic RT Exclusion criteria (excluded if any criteria met): NR	Total N = 51, comprising 21 in SBRT group and 30 in surgery group Sex: 9 (43%) female, SBRT; 14 (47%) female, surgery Race/ethnicity: NR Median age (range): 69 years (35 to 85) SBRT; 63 years (28 to 78) surgery Never smoked: 18 (86%) SBRT; 19 (63%) surgery ECOG performance score: 6 (29%) 0, 11 (52%) 1, 4 (19%) 2, SBRT; 9 (30%) 0, 19 (63%) 1, 2 (7%) 2, surgery	• SBRT ○ 60 Gy in 3 fractions for peripheral lesions ○ 48 Gy in 4 fractions for central lesions	• Surgery ○ Wedge resection (93%) ○ Lobectomy (4%)

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			No comorbidities: 10 (48%) SBRT; 8 (27%) surgery Primary cancer: 6 (27%) colorectal, 5 (24%) hepatobiliary, 2 (9%) NSCLC, 1 (5%) breast, 2 (9%) renal cell, 2 (9%) esophagus1 (5%) stomach, 2 (9%) other, SBRT; 12 (40%) colorectal, 2 (7%) hepatobiliary, 4 (13%) NSCLC, 3 (10%) breast, 2 (7%) renal cell, 1 (3%) esophagus1 (3%) stomach, 5 (17%) other, surgery Time interval (range): 27 months (5 to 204) SBRT; 30 months (1 to 135) surgery Location: 4 (19%) central, 15 (71%) peripheral, 2 (9%) both, SBRT; 5 (17%) central, 24 (80%)		

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			peripheral, 1 (3%) both, surgery No synchronous other metastases: 9 (43%) SBRT; 24 (80%) surgery Previous chemotherapy: 1 (5%) SBRT; 9 (30%) surgery		
Lee et al., 2021[75] Single academic center in Korea NR	To compare treatment efficacy and safety of re-irradiation SBRT and initial SBRT for primary, recurrent lung cancer or metastatic lung tumor Retrospective, noncomparative study Median follow-up of 28 months	Inclusion criteria (must meet all): primary, recurrent lung cancer or metastatic lung tumor Exclusion criteria (excluded if any criteria met): NR	Total N = 336, comprising 20 in repeat SBRT group and 316 in initial SBRT group Sex: NR for unmatched cohort Race/ethnicity: NR for unmatched cohort Aged > 75 years: 15 (75%) repeat SBRT; 222 (70%) initial SBRT Underlying pulmonary disease: 8 (40%) repeat SBRT; 81 (26%) initial SBRT	• Re-irradiation with SBRT ○ Median prescribed dose 54 Gy (range 48 to 60 Gy), and all but 1 patient had 4 fractionations • Initial SBRT ○ Median prescribed dose of 60 Gy (range 45 to 60 Gy) ○ Median fractionation number of 4 (range 4 to 8)	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			Tumor size < 2 cm: 11 (55%) repeat SBRT; 133 (42%) initial SBRT		
Littau et al., 2022[76] National Cancer Database (2004 to 2016) NR	To compare effectiveness of SBRT vs. surgery on overall survival using a national database Retrospective, comparative database analysis (propensity-matched) Followed up to 5 years	Inclusion criteria (must meet all): clinical stage I (cT1N0) NSCLC; Charlson-Deyo comorbidity index of 0; offered surgery but declined and opted for SBRT; lung cancer as first and only cancer diagnosis; clinical T stage of T1 and tumor size < 3 cm Exclusion criteria (excluded if any criteria met): contraindication to surgery; pneumonectomy	Total N = 25,963, comprising 5,465 in SBRT group and 20,498 in surgery group Sex: 3,169 (58%) female, SBRT; 12,460 (61%) female, surgery Race/ethnicity: 4,831 (88%) White, 487 (9%) Black, 108 (2%) other, 39 (< 1%) unknown, SBRT; 17,781 (87%) White, 1,653 (8%) Black, 909 (4%) other, 155 (< 1%) unknown, surgery Age: 37 (< 1%) < 50 years, 1,609 (29%) 50 to 70 years, 3,819 (70%) over 70 years, SBRT; 1,318 (6%) < 50 years, 11,235 (55%) 50 to 70 years, 7,945	• SBRT ○ Based on codes (no details reported)	• Surgery ○ Lobar resection (wedge resection or segmentectomy) or lobectomy

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			(39%) older than 70 years, surgery Insurance status: 720 (13%) private, 4,544 (83%) government, 48 (1%) uninsured, 153 (3%) unknown, SBRT; 7,039 (34%) private, 12,724 (62%) government, 394 (2%) uninsured, 341 (2%) unknown, surgery Histology: 2,676 (49%) adenocarcinoma, 1,686 (31%) squamous cell carcinoma, 1,103 (20%) other, SBRT: 15,171 (74%) adenocarcinoma, 3,727 (18%) squamous cell carcinoma, 1,600 (8%) other, surgery Tumor size: 162 (3%) < 1cm, 3,018 (55%) 1 to 2 cm, 2,285 (42%) 2 to 3 cm, SBRT; 1,336		

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			(7%) < 1cm, 12,705 (62%) 1 to 2 cm, 6,457 (31%) 2 to 3 cm, surgery		

Lo et al., 2020[77]
National Cancer Database (2004 to 2015)
NR
	To compare SBRT and surgery using a large, contemporary national database in T1-2N0 LCNEC
	Retrospective (propensity-matched) database analysis
	Median follow-up of 39 months
		Inclusion criteria (must meet all): newly diagnosed, histologically confirmed T1-2N0M0 LCNEC
		Exclusion criteria (excluded if any criteria met): no treatment; nonablative RT; postoperative RT; < 1 month of follow-up
			Total N = 3,209, comprising 238 in SBRT group and 2,971 in surgery group
			Sex: 1,535 (48%) female
			Race/ethnicity: 2,832 (88%) Caucasian, 303 (9%) African American, 74 (3%) other
			Age: 1,497(47) older than 68 years
			Chemotherapy: 773 (24%)
			No comorbidities: 1,480 (46%)
			Grade: 18 (1%) well differentiated, 129 (5%) moderately differentiated, 2,533 (94%) poorly differentiated
				• SBRT
				  ○ Dose of 48 to 60 Gy in 3 to 5 fractions
					• Surgery
					  ○ Pneumonectomy, bi/lobectomy, or sublobar resection (e.g., wedge resection or segmentectomy)

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			Insurance: 67 (2%) none, 986 (31%) private, 2,124 (67%) government Clinical T-stage: 1,893 (59%) T1, 1,316 (41%) T2		

Nelson et al., 2019[78]
Single academic center in US
NR
	To determine rate of local recurrence after treatment of pulmonary metastases of a colorectal origin with wedge resection or SBRT
	Retrospective, comparative study (propensity-matched)
	Median follow-up of 4.4 years
		Inclusion criteria (must meet all): pulmonary metastases of a colorectal origin
		Exclusion criteria (excluded if any criteria met): R1 or R2 resection, absence of follow-up imaging, or recurrent treatment
			Total N = 381, comprising 37 in SBRT group, 327 in surgery group, and 17 patients who received both SBRT and surgery, depending on nodule
			Sex: 14 (38%) female, SBRT; 139 (34%) female, surgery, 6 (35%) female, both
			Race/ethnicity: NR
			Mean age at first treatment (SD): 62 years (10) SBRT; 57 years (12) surgery; 55 years (12) both
			Primary tumor location: 21 (57%) colon, 16 (43%)
				• SBRT
				  ○ Ranged from 50 Gy to 70 Gy in 3 to 10 fractions
					• Surgery
					  ○ Wedge resection
					• Both surgery and SBRT

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			rectum, SBRT; 182 (56%) colon, 145 (44%) rectum, surgery; 10 (59%) colon, 7 (41%) rectum, both Primary tumor grade: 0 well differentiated, 33 (89%) moderately differentiated, 4 (11%) poorly differentiated, SBRT; 5 (2%) well differentiated, 285 (87%) moderately differentiated, 37 (11%) poorly differentiated, surgery; 1 (6%) well differentiated, 16 (94%) moderately differentiated, 0 poorly differentiated, both		
Osti et al., 2018[79] 1 academic center in Italy NR	To evaluate local and long-term adverse effects in a series of patients with lung metastases who received 30 Gy in single dose with	Inclusion criteria (must meet all): ECOG performance status 0 to 2; oligorecurrent/ oligometastatic	Total N = 129 Sex: 52 (41%) female Race/ethnicity: NR	• SBRT ○ 30 Gy in 1 dose	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
	stereotactic technique Retrospective, noncomparative study Median follow-up of 38 months	state (5 or fewer synchronous or metachronous metastases at time of treatment); controlled primary/ extrathoracic disease; no other active sites of distant metastasis; not suitable for surgery Exclusion criteria (excluded if any criteria met): NR	Mean age (range): 69 years (24 to 89) Primary tumor: 51 (39%) NSCLC, 41 (32%) colorectal, 8 (6%) breast, 5 (4%) renal cell, 5 (4%) uterus, 19 (15%) other Number of lung lesions: 99 (77%) 1, 27 (221%) 2, 7 (5%) 3 to 5 Timing of SBRT: 98 (76%) synchronous, 27 (1%) primary recurrence, 4 (2%) secondary recurrence		

Rosen et al., 2016[80]
National Cancer Database (2008 to 2012)
NR
	To compare long-term survival for lobectomy and SBRT in healthy patients with clinical stage I disease
	Retrospective (propensity-matched) database analysis
		Inclusion criteria (must meet all): aged older than 20 years; invasive clinical stage I NSCLC; treated by lobectomy or with SBRT; no chemotherapy or RT previous to surgery or SBRT;	Total N = 15,433, comprising 1,781 in SBRT group and 13,652 in surgery group
			Sex: 1,014 (57%) female SBRT; 7.541 (55%) female, surgery
			Race/ethnicity: 1,616 (91%) White,
				• SBRT
				  ○ BED of between 100 and 200 Gy in 3 to 5 treatment fractions
					• Surgery
					  ○ Lobectomy

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
	Median follow-up of 29 months in SBRT and 32 months in surgery group (matched)	Charlson-Deyo score of 0 Exclusion criteria (excluded if any criteria met): surgery contraindicated	165 (9%) Nonwhite, 24 (1%) Spanish or Hispanic, SBRT; 11,938 (87%) White, 1,714 (13%) Nonwhite, 361 (3%) Spanish or Hispanic, surgery Primary payer: 52 (3%) Medicaid, 1,440 (79%) Medicare, 16 (1%) none, 61 (3%) other government, 228 (13%) private, SBRT; 588 (4%) Medicaid, 7,642 (56%) Medicare, 320 (2%) none, 142 (1%) other government, 4,768 (35%) private, surgery Clinical T-stage: 1,371 (77%) T1, 410 (23%) T2, SBRT: 9,543 (70%) T1, 4,109 (30%) T2, surgery		
Scotti et al., 2019[81] 2 academic centers in Italy	To report results of a retrospective analysis conducted on a large, well-	Inclusion criteria (must meet all):	Total N = 187, comprising 93 in	• SBRT ○ Dose schedules were prescribed to reach a BED	• Surgery ○ Lobectomy

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
NR	controlled cohort of patients with stage I to II NSCLC who underwent lobectomy or SBRT Retrospective, comparative study Median follow-up of 23 months	stage T1a-T2bN0MO NSCLC Exclusion criteria (excluded if any criteria met): < 1 month of follow-up	SBRT group and 94 in surgery group Sex: 54 (29%) overall Race/ethnicity: NR Mean age: 77 years, SBRT; 68 years, surgery Histology: 42 (59%) adenocarcinoma, 27 (38%) squamous cell, 2 (3%) other, SBRT; 60 (73%) adenocarcinoma, 24 (25%) squamous cell, 1 (1%) other, surgery Clinical T-stage: 36 (39%) T1a, 30 (32%) T1b, 24 (26%) T2a, 3 (3%) T2b, SBRT; 37 (39%) T1a, 33 (35%) T1b, 20 (21%) T2a, 4 (4%) T2b, surgery Performance status: 18 (19%) 0, 46 (49%) 1, 29 (31%) 2, SBRT; 62 (66%) 0,	of at least 100 Gy (with an alpha/beta ratio of 10), and fractionation was chosen depending on lesion site and dimensions	

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			29 (31%) 1, 3 (3%) 2, surgery		
Sharma et al., 2018[82,83] Single center in Netherlands NR	To evaluate overall survival and identify associated factors for inoperable pulmonary oligometastases treated with SBRT Retrospective, noncomparative study Median follow-up of 26 months	Inclusion criteria (must meet all): metastases limited to 2 organs; total of 5 metastases at time of treatment; assessed as being inoperable Exclusion criteria (excluded if any criteria met): polymetastatic progression; previous thoracic RT	Total N = 206 Sex: 85 (41%) female Race/ethnicity: NR Median age (range): 68 years (28 to 87) No comorbidities: 73 (35%) Primary tumor location: 118 (57%) colorectal, 36 (17%) NSCLC, 11 (5%) melanoma, 10 (5%) sarcoma, 7 (3%) breast, 24 (12%) other Distribution of metastasis: 120 (57%) lung only Number of metastases in lung: 90 (44%) 1, 116 (56%) 2 or more Pre-SBRT chemotherapy: 99 (48%)	• SBRT ○ Peripheral tumors treated with 51 Gy to 6 0Gy in 3 fractions or a single fraction of 30 Gy. ○ Central tumors received 45 to 60 Gy in 5 to 8 fractions	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
Takeda et al., 2010[84] Single center in Japan NR	To investigate factors associated with grade 3 or higher radiation pneumonitis in patients with lung tumors treated with SBRT Retrospective, noncomparative study Median follow-up of 12 months	Inclusion criteria (must meet all): minimum follow-up of 6 months or had grade 1 or higher RP and followed up for more than 5 months Exclusion criteria (excluded if any criteria met): NR	Total N = 128, with 133 tumors Sex: 40 (30%) female Median age (range): 77 years (43 to 92) Disease: 111 (83%) primary lung cancer (of which 6 [5%] were NSCLC), 22 (17%) lung metastases Inoperable: 99 (74%)	• SBRT ○ 40 to 60 Gy in 5 to 10 fractions	• No comparator
Wegner et al., 2020[85] National Cancer Database (2004 to 2015) NR	To compare SBRT and cRT in T1-2N0 LCNEC Retrospective (propensity-matched) database analysis Median follow-up of 30 months	Inclusion criteria (must meet all): histologically-confirmed T1-2N0M0 LCNEC Exclusion criteria (excluded if any criteria met): < 1 month of follow-up	Total N = 754, comprising 238 in SBRT group and 516 in cRT group Sex: 365 (48%) female Race/ethnicity: 664 (88%) White, 77 (10%) African American, 13 (2%) other Age: 355 (47) older than 73 years Chemotherapy: 242 (32%)	• SBRT ○ Median dose was 50 Gy (48 to 60 Gy) in 4 fractions (3 to 5 fractions)	• cRT ○ Median dose was 65 Gy (60 to 68 Gy) in 33 fractions (27 to 35 fractions)

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			No comorbidities: 467 (62%) Grade: 3 (1%) well differentiated, 8 (1%) moderately differentiated, 371 (49%) poorly differentiated Insurance: 9 (1%) none, 115 (15%) private, 620 (82%) government Clinical T-stage: 416 (55%) T1, 388 (45%) T2		
Yamamoto et al. 2020[86] 68 institutions in Japan NR	To identify factors affecting local control and to determine survival benefit of local control after SBRT for pulmonary oligometastases Retrospective, noncomparative study Median follow-up of 24 months	Inclusion criteria (must meet all): number of metastasis limited to 1 to 5; controlled primary lesion and other extrathoracic lesions Exclusion criteria (excluded if any criteria met): local recurrence of a primary thoracic tumor	Total N = 1,378 Sex: 553 (36%) female Race/ethnicity: NR Median age (range): 72 years (17 to 93) ECOG performance status: 841 (54%) 0, 529 (34%) 1, 90 (6%) 2, 19 (1%) 2 Primary lesion sites: 451 (29%) lung, 391 (25%) colorectal, 126 (8%) head and	• SBRT ○ Most typical dose was 48 Gy in 4-fraction	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			neck, 132 (9%) esophageal, 447 (29%) other Primary lesion pathology: 861 (56%) adenocarcinoma, 396 (26%) squamous cell, 47 (3%) sarcoma, 168 (11%) other Primary lesion control: 1,222 (79%) surgery, 130 (8%) chemotherapy, 70 (5%) RT, 40 (3%) other Median disease-free interval (range): 17.5 months (0 to 424) Oligometastatic state: 1,157 (75%) oligo-recurrences, 133 (9%) sync-oligometastases, 133 (9%) unclassified Chemotherapy: 591 (38%) before SBRT, 34 (2%) with SBRT,		

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			242 (16%) after SBRT Number of metastases: 1,036 (67%) 1		

Abbreviations. BED: biologically-equivalent dose; BT: brachytherapy; COPD: chronic obstructive pulmonary disease; cRT: conventional radiotherapy; ECOG: Eastern Cooperative Oncology Group; GI: gastrointestinal; Gy: Gray; HFRT: hypofractionated radiotherapy; ILD: interstitial lung disease; IPF: idiopathic pulmonary fibrosis NR: not reported; LCNEC: large cell neuroendocrine carcinoma of lung; NSCLC: non-small cell lung cancer; PM: pulmonary metastasectomy; RFA: radiofrequency ablation; RT: radiotherapy; SBRT: stereotactic body radiation therapy.

Colorectal Cancer

No eligible studies identified.

Uterine Cancer

No eligible studies identified.

Melanoma

No eligible studies identified.

Renal Cancer

Table C15. Study Characteristics for Nonrandomized and Registry-based Studies

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
Siva et al., 2022[87] International Radiosurgery Consortium of the Kidney (IROCK)	To assess the local efficacy of SBRT for primary renal cell carcinoma	Inclusion criteria (must meet all): minimum potential follow-up of 2 years; non-	Total N = 190 Sex: 51 (27%) female Race/ethnicity: NR	• SBRT ○ Median total dose of 30 (IQR, 25 to 42) in median	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
NR	Minumum follow-up of 2 years	metastatic RCC; aged 18 and older; no contraindication to primary RCC SBRT Exclusion criteria (excluded if any criteria met): previous abdominal radiotherapy; upper tract urothelial carcinoma	Median age (IQR): 73.6 years (66.2 to 82.0) Good performance status: 163 of 186 (88%) Medically inoperable: 96 of 128 (75%) Median time from diagnosis to SBRT (IQR): 4.1 months (1.4 to 18.5)	of 3 fractions (IQR, 1 to 4)	
Uhlig et al., 2020[88] National Cancer Database (2004 to 2015) NR	To assess use of SBRT for stage I RCC and compare outcomes with TA and PN Retrospective, comparative database analysis (propensity-matched) Median follow-up of 58 months	Inclusion criteria (must meet all): histopathologically proven RCC; treated with SBRT, cryoablation, RFA, MWS or PN; stage I RCC Exclusion criteria (excluded if any criteria met): RCC stage II and above; radiation to metastatic RCC sites; age < 18 years; unknown primary cancer	Total N = 91,965, comprising 174 in SBRT group, 3,432 in RFA group, 5,446 in CA group, and 82,913 in PN group Sex: 60 (35%) female, SBRT; 1,245 (36%) female, RFA; 2,009 (37%) female, CA; 32,200 (39%) female, PN Race/ethnicity: 149 (85%) White, 21 (12%) African	• SBRT ○ Median dose of 40 Gy (IQR, 32 to 48) in median of 3 fractions (IQR, 2 to 4)	• RFA • CA • PN

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
		side; unknown cancer histology; unknown survival status or follow-up time	American, 4 (2%) other, SBRT; 2,963 (86%) White, 361 (11%) African American, 108 (3%) other, RFA; 4.665 (85%) White, 637 (12%) African American, 154 (3%) other, CA; 69,672 (84%) White, 21 (12%) 9,484 (11%) African American, 3,757 (5%) other, PN Median age (IQR): 73 years (64 to 82) SBRT; 69 years (61 to 77) RFA; 68 years (60 to 76) CA; 59 years (50 to 68) PN No comorbidities: 136 (78%) SBRT; 2,372 (69%) RFA; 3,639 (67%) CA; 58,840 (71%) PN RCC as first neoplasm: 94 (54%) SBRT; 2,151 (62%) RFA; 3,385 (62%)		

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			CA; 61,176 (74%) PN Tumor grade: 22 (13%) I, 42 (24%) II, 3 (2%) III, 0 IV, 107 (61%) unknown, SBRT; 511 (15%) I, 884 (26%) II, 137 (4%) III, 12 (< 1%) IV, 1,888 (55%) unknown, RFA; 974 (18%) I, 1,510 (28%) II, 204 (4%) III, 14 (< 1%) IV, 2,744 (50%) unknown, CA; 12,518 (15%) I, 40,968 (49%) II, 13,748 (17%) III, 1,039 (1%) IV, 14,640 (18%) unknown, PN No systematic therapy: 166 (95%) SBRT; 3,411 (99%) RFA; 5,431 (98%) CA; 82,732 (100%) PN		

Abbreviations. CA: cryoablation; Gy: Gray; IQR: interquartile range; MWA: microwave ablation; PN: partial nephrectomy; RCC: renal cell carcinoma; RFA: radiofrequency ablation; SBRT: stereotactic body radiation therapy; TA: thermal ablation.

Pancreatic Cancer

Table C16. Study Characteristics for Nonrandomized and Registry-based Studies

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
de Geus et al., 2017[89] National Cancer Database (2004 to 2012) NR	To evaluate survival impact of SBRT on patients with unresected pancreatic cancer Retrospective, comparative database analysis (propensity matched) Followed up to 20 months	Inclusion criteria (must meet all): diagnosis of pancreatic adenocarcinoma Exclusion criteria (excluded if any criteria met): metastatic disease at diagnosis; surgery of primary site; no treatment at reporting center; other malignancies; did not receive CT; RT included electrons or neutrons; proton therapy; radioisotopes; started treatment more than 90 days after diagnosis; died or last contacted within 3 months of diagnosis; missing data	Total N = 14,331, comprising 322 in SBRT group, 5,464 in CT group, 6,418 in cRT group, and 2,127 in IMRT group Sex: 155 (48%) female, SBRT; 2,854 (52%) female, CT; 3,169 (49%) female cRT; 1,049 (49%) female IMRT Race/ethnicity: 269 (83%) White SBRT; 4,262 (78%) White CT; 5,153 (80%) White, cRT; 1,714 (81%) White, IMRT Aged younger than 65 years: 118 (37%) SBRT; 2,264 (41%) CT; 3,029 (47%) cRT; 1,019 (48%) IMRT No comorbidities: 239 (74%) SBRT; 3,837 (70%) CT;	• SBRT ◦ Median dose of 30.0 Gy (IQR, 24.0 to 35.0) ◦ Median of 3 fractions (IQR, 3 to 5)	• CT • cRT ◦ Median dose of 45.0 Gy (IQR, 45.0 to 50.4) ◦ Median of 28 fractions (IQR, 25 to 29) • IMRT ◦ Median dose of 50.4 Gy (IQR, 45.0 to 50.4) ◦ Median of 28 fractions (IQR, 25 to 30)

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			4,646 (72%) cRT; 1,529 (72%) IMRT Private insurance: 127 (39%) SBRT; 1,991 (36%) CT; 2,651 (41%) cRT; 835 (39%) IMRT Facility: 237 (74%) academic, SBRT; 3,010 (55%) academic, CT; 3,009 (47%) academic. cRT; 1,034 (49%) IMRT Tumor location: 224 (70%) pancreas head, SBRT; 3,552 (65%) pancreas head, CT; 4,421 (67%) pancreas head, cRT; 1,468 (69%) IMRT Clinical stage: 28 (9%) stage I, 129 (40%) stage II, 165 (51%) stage III, SBRT; 652 (12%) stage I, 2,108 (39%) stage II, 2,704 (49%) stage III, CT; 640 (10%) stage I, 2,279		

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			(35%) stage II, 3,499 (55%) stage III, cRT; 228 (11%) stage II, 787 (37%) stage II, 1,112 (52%) stage III, IMRT		
Moningi et al., 2022[90] Surveillance, Epidemiology, and End Results (SEER) and Texas Cancer Registry, linked with Medicare; MarketScan Commercial Claims and Encounter database NR	To assess RT use and complications for unresectable pancreatic cancer in US, cRT and SBRT to inform real-world expected outcomes and practice Retrospective, comparative database analysis Follow-up of at least 9 months	Older cohort (aged > 65) Inclusion criteria (must meet all): pathologically confirmed primary cancer diagnosis of localized or regional pancreatic adenocarcinoma; continuous Medicare non-HMO Part A & B coverage from 12 months previous to diagnosis to 12 months after diagnosis; survived at least 3 months after diagnosis Exclusion criteria (excluded if any criteria met): pancreaticoduodenectomy within 10 months of diagnosis date; failed to complete at least 1 cycle of CT Younger cohort (aged 18 to 64) Inclusion criteria (must meet all): nonmetastatic	Total N = 5,624 comprising 2,552 older patients (105 SBRT, 1,187 CT, 1,230 cRT) and 3,102 younger patients (101 SBRT, 1,519 CT, 1,482 cRT) Sex: 58 (55%) SBRT, 677 (57%) CT, 683 (55%) cRT, female older cohort; 47 (47%) SBRT, 682 (45%) CT, 669 (45%) cRT, female younger cohort Race/ethnicity: NR Aged older than 80: 34 (32%) SBRT, 328 (28%) CT, 253 (21%) cRT, older cohort Aged 18 to 49: 18 (18%) SBRT, 199	• SBRT	• CT • cRT

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
		pancreatic cancer; CT codes; continuous insurance coverage 3 months previous to 3 months post-CT initiation Exclusion criteria (excluded if any criteria met): received pancreaticoduodenectomy within 1 year previous to and 1 year after CT initiation; code for death within 3 months in inpatient claims file; not have at least 9 months of follow-up	(13%) CT, 237 (16%) cRT, younger cohort No comorbidities: 50 (48%) SBRT, 507 (43%) CT, 472 (38%) cRT, older cohort; 79 (78%) SBRT, 1,007 (71%) CT, 1,030 (69%) cRT, younger cohort Performance status of 0: 90 (86%) SBRT, 1,064 (90%) CT, 1,119 (91%) cRT, older cohort; 98 (97%) SBRT, 1,443 (95%) CT, 1,404 (95%) cRT, younger cohort		

Zhong et al., 2017[91]
 	
National Cancer Database (2004 to 20123
 	
NR
	To investigate and compare clinical outcomes with cRT and SBRT for patients with locally advanced, nonmetastatic pancreatic ductal adenocarcinoma
	
	Retrospective, comparative
		Inclusion criteria (must meet all): first and only cancer diagnosis of pancreatic adenocarcinoma (tumor stage 2 to 4 and nodal stage 0 to I); received RT designated for abdomen or pancreas
		
		Exclusion criteria (excluded if any criteria met): tumors in tail of
			Total N = 8,450, comprising 631 in SBRT group and 7,819 in cRT group
			
			Sex: 320 (51%) female, SBRT; 3,887 (50%) female cRT
			
			Race/ethnicity: NR
			
			Median age at diagnosis: 69 years SBRT; 66 years cRT
				• SBRT
				  ○ Median of 8.0 Gy (10th percentile of 5.0 and 90th percentile of 20.0) in median 5 fractions (10th percentile of 2 and 90th percentile of 5)
					• cRT
					  ○ Median of 1.8 Gy (10th percentile of 1.8 and 90th percentile of 1.9) in median 28 fractions (10th percentile of 21 and 90th percentile of 31)

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
	database analysis (propensity matched) Median follow-up of 26 months	pancreas; diagnosis of metastatic disease; receipt of RT after surgery; brachytherapy	Clinical T-stage: 97 (15%) 2, 258 (41%) 3, 276 (44%) 4, SBRT; 1,238(16%) 2, 2,753 (35%) 3, 3,828 (49%) 4, cRT Clinical N-stage: 427 (68%) 0, SBRT; 4,929 (63%) cRT No comorbidities: 466 (74%) SBRT; 5,459 (70%) cRT CT: 515 (87%) SBRT; 7,381 (96%) cRT No surgery: 562 (89%) SBRT; 7,098 (91%) cRT		

Abbreviations. cRT: conventional RT; CT: chemotherapy; Gy: Gray; IMRT: intensity-modulated radiotherapy; IQR: interquartile range; NCT: US National Clinical Trial; NR: not reported; SBRT: stereotactic body radiation therapy.

Head and Neck Cancer

Table C17. Study Characteristics for Nonrandomized and Registry-based Studies

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
Al-Mamgani et al., 2013[92] Single center in Netherlands NR	To compare outcome, toxicity and QoL of 2 boost modalities for T1-2 oropharyngeal carcinoma Retrospective, comparative study Median follow-up of 56 month in SBRT group and 57 months in BT group	Inclusion criteria (must meet all): T1-2N0-3 oropharyngeal carcinoma treated with curative intention Exclusion criteria (excluded if any criteria met): NR	Total N = 250, comprising 102 in SBRT group and 148 in BT group Sex: 34 (33%) female, SBRT; 47 (32%) female, BT Race/ethnicity: NR Median age (range): 56 years (40 to 83) SBRT; 57 years (38 to 78) BT Tumor stage: 34 (33%) T1, 68 (67%) T2, SBRT; 55 (37%) T1, 93 (63%) T2, BT Tumor subsite: 61 (60%) tonsillar fossa and soft palate, 31 (30%) base of tongue, 10 (10%) other, SBRT; 95 (64%) tonsillar fossa and soft palate, 41 (28%) base of tongue, 12 (8%) other, BT	• SBRT boost after RT ○ 3 fractions, 5.5 Gy per fraction within 1 week to primary tumor	• BT boost after RT

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			Unilateral neck irradiation: 44 (43%) SBRT; 68 (46%) BT Chemotherapy: 7 (7%) SBRT; 9 (6%) BT		
Ozyigit et al., 2011[93] Single academic center in Turkey NR	To compare SBRT and 3D-conformal RT in terms of survival, local control, and treatment associated late toxicity in salvage treatment of locally recurrent nasopharyngeal carcinoma Retrospective, comparative study Median follow-up of 24 months	Inclusion criteria (must meet all); locally recurrent nasopharyngeal cancer; receiving re-irradiation Exclusion criteria (excluded if any criteria met): 2D-conventional radiotherapy; third course of irradiation with robotic SBRT	Total N = 51, comprising 24 in SBRT group and 27 in conformal RT group Sex: 9 (37%) female, SBRT; 6 (22%) female, conformal RT Race/ethnicity: NR Aged 46 years and older: 14 (58%) SBRT; 13 (48%) conformal RT T stage: 7 (29%) T1, 4 (17%) T2, 7 (29%) T3, 6 (26%) T4 SBRT; 8 (20%) T1, 5 (18%) T2, 7 (26%) T3, 7 (26%) T4 conformal RT	• SBRT ○ 30 Gy delivered over 5 consecutive days	• Conformal RT

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			CT at first diagnosis: 16 (67%) SBRT; 16 (59%) conformal RT No chemotherapy at recurrence: 14 (58%) SBRT; 12 (44%) conformal RT		
Vargo et al., 2018[94] 8 academic centers in US NR	To compare SBRT and IMRT in patients with recurrent or second primary squamous cell carcinoma of head and neck Retrospective, comparative study Median follow-up of 24 months in SBRT group and 28 months in IMRT group	Inclusion criteria (must meet all); undergoing re-irradiation within a field previously irradiated to ≥ 40 Gy and then re-irradiated with either IMRT to ≥ 40 Gy or SBRT delivered in 1 to 5 fractions of ≥ 5 Gy per fraction Exclusion criteria (excluded if any criteria met): nonsquamous histology; concurrent metastatic disease; unrecorded radiation dose	Total N = 414, comprising 197 in SBRT group and 217 in IMRT group Sex: 54 (27%) female, SBRT; 68 (31%) female, IMRT Race/ethnicity: NR Median age (range): 64 years (39 to 90) SBRT; 64 years (21 to 93) IMRT Previous surgery to primary: 106 (54%) SBRT; 94 (44%) IMRT Previous neck dissection: 89 (45%) SBRT; 73 (34%) IMRT Previous systemic therapy: 126 (64%)	• SBRT ○ Median 40 Gy (range, 16 to 50) in median of 5 fractions (range, 1 to 8)	• IMRT ○ Median 60 Gy (range, 40 to 72) in median of 33 fractions (range, 12 to 60)

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			SBRT; 99 (46%) IMRT Second tumor site: 35 (18%) oral cavity, 53 (27%) oropharynx, 28 (14%) larynx or hypopharynx, 3 (1%) sinonasal, 41 (21%) neck only, 10 (5%) skin or salivary, 27 (14%) nasopharynx or base of skull, SBRT; 23 (11%) oral cavity, 80 (37%) oropharynx, 36 (16%) larynx or hypopharynx, 7 (3%) sinonasal, 33 (15%) neck only, 1 (1%) skin or salivary, 37 (17%) nasopharynx or base of skull, IMRT Second systematic treatment: 108 (55%) SBRT; 183 (84%) IMRT		
Yamazaki et al., 2017[95,96]	To examine outcomes of re-irradiation for recurrent head and	Inclusion criteria (must meet all);	Total N = 176, comprising 117 in SBRT group, 33 in IMRT group and 26	• SBRT ○ Median 32 Gy (range, 25 to 39) in median of	• IMRT ○ Median 60 Gy (range, 30 to 69) in median of

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
3 centers, including an academic center, in Japan NR	neck cancers using different modalities Retrospective, comparative study Median follow-up of 8 months	recurrent head and neck cancer Exclusion criteria (excluded if any criteria met): NR	in charged particle RT group Sex: 30 (26%) SBRT; 6 (18%) IMRT; 11 (42%) charged particle RT Race/ethnicity: NR Median age (range): 64 years (35 to 88) SBRT; 64 years (33 to 82) IMRT; 55 years (19 to 82) charged particle RT Primary site: 43 (37%) nasopharynx, 34 (29%) orohypopharynx, 16 (14%) oral, 1 (< 1%) salivary gland, 23 (20%) nasal and paranasal sinus, 0 other, SBRT; 4 (12%) nasopharynx, 6 (18%) orohypopharynx, 6 (18%) oral, 0 salivary gland, 4 (12%) nasal and paranasal sinus, 13 (39%) other, IMRT; 4 (15%) nasopharynx, 0	5 fractions (range, 3 to 8)	20 fractions (range, 5 to 30) • Charged particle RT ○ Median 57.6 Gy (range, 43.2 to 70.2) in median of 16 fractions (range, 12 to 30)

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			orohypopharynx, 2 (8%) oral, 3 (12%) salivary gland, 15 (58%) nasal and paranasal sinus, 2 (8%) other, charged particle RT Previous surgery: 62 (53%) SBRT; 7 (21%) IMRT; 17 (65%) charged particle RT		

Abbreviations. BT: brachytherapy; Gy: Gray; IMRT: intensity-modulated radiation therapy; NR: not reported; RT: radiation therapy; SBRT: stereotactic body radiation therapy.

Ovarian Cancer

No eligible studies identified.

Liver Cancer

Table C18. Study Characteristics for Nonrandomized and Registry-based Studies

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
Liver cancer					
Andratschke et al., 2018[97] 17 centers in Germany and Switzerland	To analyze patterns of care of SBRT for liver oligometastases and to derive factors influencing treated metastases control	Inclusion criteria (must meet all): patients with liver oligometastases from any histology-proven primary	Total N = 474 Sex: 206 (43%) female Race/ethnicity: NR	• SBRT ◦ Median 18.5 Gy (range, 3 to 37.5 Gy) in median 1	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
NR	and overall survival in a large patient cohort Retrospective, noncomparative study Median follow-up of 15 months	solid tumor; medically inoperable; nonresectable metastases not qualifying for alternative focal treatment; refused invasive therapies Exclusion criteria (excluded if any criteria met):	Median age (range): 64 years (15 to 93) Histology: 228 (48%) colorectal, 63 (13%) breast, 29 (6%) lung, 24 (5%) pancreas, 130 (27%) other Previous chemotherapy: 325 (66%) More than 1 liver metastasis: 102 (21%) Status of extrahepatic disease: 119 (25%) oligorecurrence, 235 (50%) synchronous	fraction (range, 1 to 13)	
Berber et al., 2013[98] 4 academic centers in US NR	To evaluate results of SBRT for secondary liver tumors from a combined multicenter database Retrospective (assumed), noncomparative study	Inclusion criteria (must meet all): biopsy-proven metastatic liver malignancy; nonresectable disease; life expectancy of at least 3 months	Total N = 153 Sex: 91 (59%) female Race/ethnicity: NR Mean age (SD): 59 years (8) Lesions per patient (range): 1 to 6	• SBRT ○ 27 to 46.5 Gy in around 3 to 10 fractions	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
	Median follow-up of 25 months	Exclusion criteria (excluded if any criteria met): NR			
Bettinger et al., 2019[99] 15 centers, including academic centers across Germany, UK, Italy, Switzerland, Japan and South Korea NR	To analyze toxicity profiles and survival in patients with HCC who are not eligible for other treatments Retrospective, comparative analysis (propensity-matched) Median follow-up NR	Inclusion criteria (must meet all): adults with confirmed HCC; eligible for sorafenib or treated with SBRT (after TACE failure, alternative to sorafenib, progression with sorafenib) Exclusion criteria (excluded if any criteria met): NR	Total N = 1,023, comprising 122 in SBRT group and 901 in sorafenib group Sex: 21 (17%) SBRT; 172 (19%) sorafenib Race/ethnicity: NR Mean age (SD): 67 years (9) SBRT; 67 years (12) sorafenib ECOG score: 75 (61%) 0, 46 (38%) 1, 1 (< 1%) 2 SBRT; 595 (66%) 0, 186 (21%) 1, 120 (13%) 2, sorafenib Child-Pugh score A: 79 (65%) SBRT; 544 (60%) sorafenib Previous treatment: 21 (17%) surgery, 6 (5%) RFA, 51 (42%) TACE, SBRT; 163 (18%) surgery, 184 (20%0 RFA, 485	• SBRT ○ Median total dose of 44 Gy (range, 21 to 66) in 3 to 12 fractions	• Sorafenib ○ 800 mg per day

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			(54%) TACE sorafenib BCLC stage: 6 (5%) A, 69 (57%) B, 47 (39%) C, SBRT; 41 (5%) A, 242 (27%) B, 618 (69%) C, sorafenib Extrahepatic metastases: 16 (13%) SBRT; 322 (36%) sorafenib		
Bujold et al., 2013[100-102] Single academic center in Canada NCT00914355 and NCT00152906	To describe outcomes of 2 prospective trials of SBRT for HCC Prospective, noncomparative study Median follow-up of 31 months	Inclusion criteria (must meet all): diagnosis of HCC; unsuitable for surgery, TACE, RFA, or alcohol ablation; life expectancy more than 12 weeks; at least 700 mL of uninvolved liver; ECOG performance score ≤ 2; Child-Turcotte-Pugh A class; adequate liver function; no clinical ascites encephalopathy, active hepatitis, or	Total N = 102 Sex: 22 (22%) female Median age (range): 69 years (40 to 90) Race/ethnicity: 54 (53%) White, 45 (44%) Asian, 3 (3%) other Underlying liver disease: 39 (38%) HBV, 39 (38%) HCV, 25 (25%) alcohol, 14 (14%) other, 7 (7%) none	• SBRT ○ Median dose of 36 Gy in 6 fractions	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
		gastric, duodenal, or variceal bleed within 2 months of registration Exclusion criteria (excluded if any criteria met): NR	Child-Turcotte-Pugh score: 73 (72%) 5, 29 (28%) 6 ECOG performance score 0 to 1: 85 (84%) Previous treatment: 53 (52%) BCLC stage: 35 (34%) A or B, 67 (66%) C Clinical TNM stage: 13 (13%) I, 14 (14%) II, 67 (66%) III, 8 (8%) IV Extrahepatic disease: 12 (12%) Multiple lesions: 62 (61%)		
Hara et al., 2019[103] Two centers (1 academic) in Japan NR	To compare outcomes and toxicities of SBRT compared with RFA for patients with HCC Retrospective, comparative study (propensity-matched)	Inclusion criteria (must meet all): diagnosis of HCC with pathological confirmation or typical HCC findings on CT or MRI; inoperable because of unfeasibility, difficulty, or	Total N = 374, with 143 in SBRT group and 231 in RFA group Sex: 47 (33%) female, SBRT; 66 (29%) female RFA Race/ethnicity: NR	• SBRT ◦ Total dose of 40 GY and 35 Gy in 5 fractions ◦ Also, minority treated with 36 to 45 Gy in 12 to 15 fractions	• RFA ◦ Performed percutaneously under ultrasound guidance ◦ 1 to 3 insertions performed to achieve complete ablation, requiring a 5 mm ablative safety margin for each tumor

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
	Median follow-up of 30 months in SBRT group and 34 months in RFA group	patient refusal; tumor number ≤ 3; maximum tumor diameter ≤ 3 cm; no extrahepatic metastasis; curative intent Exclusion criteria (excluded if any criteria met): refractory ascites	Median age (range): 73 years (48 to 93) SBRT; 73 years (31 to 90) RFA Etiology: 13 (9%) HBV, 101 (71%) HCV, 29 (20%) not HBV or HCV, SBRT; 29 (13%) HBV, 156 (67%) HCV, 47 (20%) not HBV or HCV, RFA BCLC stage: 56 (39%) 0, 56 (39%) A, 0 B, 31 (22%) C, SBRT; 137 (59%) 0, 90 (39%) A, 0 B, 4 (2%) C, RFA Child-Pugh class A: 137 (96%) SBRT; 214 (93%) RFA Previous treatment: 89 (62%) SBRT; 132 (57%) RFA More than 1 lesion: 16 (11%) SBRT; 38 (17%) RFA ECOG performance score: 112 (78%) 0, 22 (15%) 1, 9 (6%) 2		

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			SBRT; 228 (99%) 0, 3 (1%) 1, 0 2		
Honda et al., 2013[104] Single academic center in Japan NR	To compare tumor control and safety of SBRT combined with TACE for small, solitary, and hypervascular HCC with TACE alone Retrospective, comparative study Median follow-up of 12 months for SBRT and 30 months for TACE	Inclusion criteria (must meet all): solitary hypervascular HCC nodule, up to 30 mm in diameter, without portal venous thrombosis or extrahepatic metastases; Child-Turcotte-Pugh (CTP) score ≤ 7 Exclusion criteria (excluded if any criteria met): NR	Total N = 68, comprising 30 in TACE-SBRT group and 38 in TACE group Sex: 11 (37%) female, TACE-SBRT; 23 (61%) female, TACE Race/ethnicity: NR Median age (range): 70 years (49 to 90) TACE-SBRT; 73 years (48 to 92) TACE HBV: 4 (13%) TACE-SBRT; 4 (11%) TACE HCV: 24 (80%) TACE-SBRT; 31 (82%) TACE Not HCV or HBV: 1 (3%) TACE-SBRT; 2 (5%) TACE HCV and HBV: 1 (3%) TACE-SBRT; 1 (3%) TACE	• TACE-SBRT ○ Total dose of 48 or 60 Gy delivered in 4 or 8 fractions in 4 to 10 days	• TACE ○ All treatment naïve

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			Child-Pugh score 5 to 6: 24 (80%) TACE-SBRT;31 (82%) TACE		
Jacob et al., 2015[105] Single academic center in US NR	To measure survival in HCC patients treated with adjuvant SBRT following TACE Retrospective, comparative study Median follow-up not reported	Inclusion criteria (must meet all): diagnosed with HCC; treated with TACE or TACE-SBRT; nonresectable HCC tumors of ≥ 3 cm Exclusion criteria (excluded if any criteria met): NR	Total N = 161, comprising 37 in TACE-SBRT group and 124 in TACE group Sex: 27% female, TACE-SBRT; 24% female, TACE Race/ethnicity: 22% Black, 76% White, 3% other, TACE-SBRT; 17% Black, 76% White, 7% other, TACE Mean age (SD): 64 years (13) TACE-SBRT; 62 years (9) TACE Etiology: 19% alcohol, 8% HBV, 51% HCV, 19% NASH, 5% haemochromatosis, TACE-SBRT; 24% alcohol, 7% HBV, 45 HCV, 20% NASH, 2%	• TACE-SBRT ○ 36 to 60 Gy in 3 fractions	• TACE

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			haemochromatosis, TACE Mean Child-Pugh score (SD): 6.3 (1.2) TACE-SBRT; 6.7 (1.5) TACE BCLC stage: 17% B1, 56% B2, 8% B3, 19% BA TACE-SBRT; 22% B1, 36% B2, 14% B3, 28% B4, TACE		
Jeong et al., 2021[106,107] Single center in South Korea NR	To compare clinical outcomes of RFA and SBRT in small (≤ 3 cm) HCC Retrospective, comparative study (also retrospective noncomparative cohort from same institution reporting on harms) Median follow-up of 50 months	Inclusion criteria (must meet all): 3 or fewer HCC lesions (longest diameter ≤ 3 cm and sum of longest diameters ≤ 6 cm); no evidence of macroscopic vascular invasion; no evidence of extrahepatic metastasis; Child–Pugh hepatic function A or B; ECOG performance status of 0 or 1; not suitable for surgery because of liver	Total N = 266, comprising 87 in SBRT group and 179 in RFA group Sex: 16 (18%) female, SBRT; 46 (26%) female, RFA Race/ethnicity: NR Median age (range): 63 years (41 to 90) SBRT; 60 years (40 to 87) RFA ECOG performance status: 82 (94%) 0, 5 (6%) 1, SBRT; 176 (98%) 0, 3 (2%) 1, RFA	• SBRT ○ Median total dose was 45 Gy (range 30 to 60) ○ Median dose of 15 Gy (range, 10 to 15) per fraction given over 3 to 4 consecutive days	• RFA ○ Performed percutaneously under ultrasonographic guidance ○ Radiofrequency current was emitted for 10 to 15 min using a 200W generator set

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
		cirrhosis or insufficient remnant liver volume for hepatic resection; a sufficient distance between HCC and gastrointestinal tracts to perform RFA or SBRT Exclusion criteria (excluded if any criteria met): uncontrolled ascites or hepatic encephalopathy; sequential or combined multimodal treatments for same HCC lesion; history of liver transplantation before or after HCC treatment by RFA or SBRT; history of other malignancy	Child-Pugh class: 80 (92%) A, 7 (8%) B, SBRT; 156 (87%) A, 23 (13%) B, RFA HBV: 66 (76%) SBRT; 132 (74%) RFA HCV: 11 (13%) SBRT; 29 (16%) RFA Non-B, non-C: 10 (11%) SBRT; 18 (10%) RFA BCLC stage at diagnosis: 25 (29%) 0, 46 (53%) A, 15 (17%) B, SBRT; 68 (38%) 0, 86 (48%) A, 25 (14%) B, RFA No previous treatment: 4 (5%) SBRT; 86 (48%) RFA Total N = 290 Sex: 60 (21%) female Median age (range): 61 years (36 to 90)		

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			ECOG performance status: 213 (73%) 0, 68 (23%) 1, 9 (3%) 2 Child-Pugh class A: 250 (86%) Etiology: 214 (74%) HBV, 37 (13%) HCV, 39 (13%) not HBV or HCV More than 1 tumor: 29 (10%) No previous treatment: 8 (3%)		
Ji et al., 2022[108] Single academic center in Hong Kong NR	To compare clinical outcome between SBRT and RFA for patients with unresectable HCC Retrospective, comparative study Median follow-up of 26 months	Inclusion criteria (must meet all): diagnosis of HCC; unresectable because of poor liver function; tumor size ≤ 5cm and/or number of tumors ≤ 3; absence of portal vein invasion; absence of extrahepatic metastasis; liver function status of Child-Pugh grade A or B	Total N = 60, comprising 22 in SBRT group and 38 in RFA group Sex: 7 (32%) female, SBRT; 7 (18%) female, RFA; Race/ethnicity: NR Median age (range): 67 years (35 to 87) SBRT; 61 years (43 to 77) RFA HBV: 14 (64%) SBRT; 26 (68%) RFA HCV: 0 SBRT; 0 RFA	• SBRT ○ 5.5 to 10 Gy per day for 5 doses in 1 week, to a total of 27.5 to 50 Gy	• RFA ○ RFA through percutaneous approach under ultrasound or CT guidance ○ Each cycle lasted for 8 to 12 minutes

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
		Exclusion criteria (excluded if any criteria met): tumor invasion to major intrahepatic vasculature; extrahepatic tumor metastasis; liver function status of Child-Pugh grade C	Cirrhosis: 12 (55%) SBRT; 19 (50%) RFA Comorbidity: 15 (68%) SBRT; 31 (82%) RFA Child-Pugh rating A: 21 (95%) SBRT; 35 (92%) RFA		
Jun et al, 2018[109] 4 centers in South Korea, including 3 academic centers NR	To investigate effect of SBRT and TACE combination vs. TACE alone on tumor response and patient survival Retrospective, comparative study Median follow-up NR	Inclusion criteria (must meet all): tumor size ≤ 5 cm of long diameter; ≤ 3 lesions present; ineligible for resection or local ablative therapies; Child-Pugh class A or B Exclusion criteria (excluded if any criteria met): previous treatment of resection or RFA or TACE; extrahepatic metastasis; presence of vascular invasion or portal vein tumor thrombosis	Total N = 199, comprising 85 in SBRT-TACE group and 114 in TACE group Sex: 20 (23%) female, SBRT-TACE; 26 (23%) female TACE Race/ethnicity: NR Mean age (SD): 63 years (10) SBRT-TACE; 63 years (10) TACE More than 1 tumor: 30 (35%) SBRT-TACE; 59 (52%) TACE Child-Pugh class A: 71 (83%) SBRT-	• SBRT ◦ Total dose of 40 to 60 Gy (median, 55 Gy) administered in 3 to 5 fractions over consecutive days or twice a week ◦ In combination with TACE	• TACE alone

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			TACE; 96 (84%) TACE BCLC stage: 22 (26%) 0, 55 (65%) A. 8 (9%) B, SBRT-TACE; 32 (28%) 0, 51 (65%) A. 24 (21%) B, TACE Etiology: 22 (26%) alcohol, 47 (55%) HBV, 11 (13%) HCV, 5 (6%) other, SBRT-TACE; 27 (24%) alcohol, 65 (57%) HBV, 13 (11%) HCV, 9 (8%) other, TACE		
Kibe et al., 2022[110] Single center in Japan NR	To clarify feasibility of marker-less SBRT for HCC by reviewing clinical outcomes of marker-less SBRT for locally untreated HCC tumors Retrospective, noncomparative study Median follow-up of 39 months	Inclusion criteria (must meet all): no previous RT to liver; no previous histories of other cancers; treated with RT by 5 or fewer fractions; treated with RT with more than 7 Gy per fraction; no previous local treatment to target tumor of SBRT	Total N = 180 Sex: 54 (30%) female Race/ethnicity: NR Median age (range): 74 years (46 to 93) Type of chronic hepatitis: 10 (6%) none, 17 (9%) HBV, 117 (75%) HCV, 20 (11%) alcoholic, 8 (4%) NASH, 8 (4%) others	• SBRT ◦ 35 Gy in 5 fractions or 40 Gy in 5 fractions	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
		Exclusion criteria (excluded if any criteria met): NR General criteria for treatment with SBRT: HCC patients who are unsuitable for resection and RFA or decline these treatments; Child–Pugh Classification A or B; maximum tumor diameter ≤ 5 cm; number of tumors ≤ 3; normal liver V20 (volume receiving >20 Gy) not exceeding 20%	Child Pugh score: 132 (73%) 5, 33 (18%) 6, 11 (6%) 7, 3 (2%) 8, 1 (< 1%) 9 BCLC stage at treatment: 61 (34%) 0, 60 (33%) A, 7 (4%) B, 49 (27%) C, 3 (2%) D		
Kim et al., 2020[111] 7 centers in Korea, Taiwan, China, and Hong Kong NR	To compare effectiveness of SBRT and RFA in patients with unresectable HCC Retrospective, comparative (propensity-matched) study Median follow-up of 28 months	Inclusion criteria (must meet all): histologically or radiologically confirmed HCC; RFA or SBRT with curative intent regardless of previous liver-directed treatment; age ≥ 15 years; maximum tumor diameter ≤ 6 cm	Total N = 2,064, comprising 496 in SBRT group and 1,568 in RFA group Sex: 118 (24%) female, SBRT; 456 (29%) female, RFA Race/ethnicity: NR Median age (IQR): 65 years (57 to 75)	• SBRT ◦ Median dose of 72.0 Gy (IQR 65.6 to 88.0) in 2.0 Gy fractions	• RFA ◦ Performed percutaneously under ultrasound guidance ◦ Complete ablation with a 0.5 to 1.0 cm margin

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
		for a single tumor or sum of diameters being ≤ 6 cm for up to 3 lesions Exclusion criteria (excluded if any criteria met): history of RFA or SBRT to target area; liver transplantation; missing follow-up data, percutaneous ethanol injection combined with RFA; tumors with vascular invasion	SBRT; 65 years (57 to 73) RFA ECOG performance score: 251 (51%) 0, 210 (42%) 1, 35 (7%) 2 to 3, SBRT; 681 (43%) 0, 847 (54%) 1, 40 (3%) 2 to 3, RFA Etiology: 293 (59%) HBV, 136 (27%) HCV, 67 (13%) not HBV or HCV, SBRT; 968 (62%) HBV, 426 (27%) 62, 174 (11%) not HBV or HCV, RFA Child-Pugh class A: 422 (85%) SBRT; 1,401 (89%) RFA BCLC stage: 80 (15%) 0, 92 (19%) A, 105 (21%) B, 219 (44%) C, SBRT; 559 (36%) 0, 758 (48%) A, 127 (8%) B, 124 (8%) C, RFA More than 1 tumor treated: 21 (4%) SBRT; 132 (8%) RFA		

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			Previous liver treatment: 401 (81%) SBRT; 766 (49%) RFA		
Kimura et al., 2018[112] 2 centers in Japan (1 academic center) NR	To compare efficacy and safety of SBRT with or without TACE in patients with small HCC who were ineligible for resection or ablation therapies Retrospective, comparative study Median follow-up of 16 month in SBRT group and 29 months in combination group	Inclusion criteria (must meet all): older than 20 years; ECOG performance status of 0 to 2; Child-Turcotte-Pugh Class A or B; < 3 HCC nodules, each up to 50 mm in diameter without portal venous thrombosis or extrahepatic metastases; inoperability because of poor general condition or surgery refusal; unsuitability for RFA Exclusion criteria (excluded if any criteria met): NR	Total N = 150, comprising 28 in SBRT group and 122 in combination group Sex: 11 (39%) female, SBRT; 40 (33%) female, combination Race/ethnicity: NR ECOG performance of 0: 21 (75%) SBRT; 107 (88%) combination BCLC stage: 17 (61%) 0, 11 (39%) A, SBRT; 63 (52%) A, 59 (48%) B, combination Initial case: 13 (46%) SBRT; 23 (16%) combination	• SBRT ○ 48 Gy in 4 fractions at isocenter and 40 Gy in 4 or 5 fractions at dose covering 95% of planning target volume	• SBRT and TACE
Lock et al., 2022[113]	To compare outcomes of patients who received	Inclusion criteria (must meet all): liver cancer	Total N = 397	• SBRT ○ Median dose of 42 Gy	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
Single academic center in Canada NR	moderately hypofractionated and hypofractionated RT treatments for liver tumors Prospective, noncomparative study Followed up to 2 years	diagnosis; Zubrod performance status of 0 to 2l Child-Pugh score of ≤ B7 within 14 days of study enrollment Exclusion criteria (excluded if any criteria met): NR	Sex: 249 (63%) female Race/ethnicity: NR Mean age (SD): 65 years (13) Primary diagnosis: 123 (31%) HCC, 106 (27%) colorectal, 47 (12%) cholangiocarcinoma, 27 (7%) breast, 20 (5%) lung, 74 (19%) other Ascites: 54 (14%) Hepatitis: 65 (16%) Cirrhosis: 85 (21%) Previous treatment: 210 (53%) chemotherapy, 67 (17%) resection, 41 (10%) abdominal RT; 27 (7%) RFA		
Loi et al., 2021[114] Single center in Italy NR	To evaluate SBRT in HCC patients and to identify predictors of outcome and toxicity Retrospective, noncomparative study	Inclusion criteria (must meet all): HCC; treated with SBRT Exclusion criteria (excluded if any criteria met): NR	Total N = 128 Sex: NR Race/ethnicity: NR Aged older than 75: 66 (52%)	• SBRT ○ 3 to 30 fractions	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
	Median follow-up of 19 months		Child-Pugh score: 92 (72%) A, 36 (28%) B BCLC stage: 40 (31%) A, 72 (56%) B, 16 (13%) C HCV: 69 (54%) HBV: 15 (11%) Alcohol abuse: 30 (23%) NASH: 28 (22%) Previous local treatment: 94 (73%)		
Mahadevan et al., 2018[115] RSSearch registry, including 25 sites and academic centers in US, Germany, and Australia (2005 to 2017) NCT01885299	To investigate factors associated with clinical outcomes for liver metastases treated with SBRT from a multicenter, international patient registry Retrospective, noncomparative registry analysis Median follow-up of 14 months	Inclusion criteria (must meet all): patients with liver metastasis Exclusion criteria (excluded if any criteria met): incomplete data	Total N = 427 Sex: 218 (51%) Race/ethnicity: NR Median age (range): 67 years (31 to 91) Primary tumor: 189 (44%) colorectal, 52 (12%) lung, 42 (10%) breast, 33 (8%) gastrointestinal, 26 (6%) gynecological, 20 (5%) pancreas, 65 (15%) other	• SBRT ○ Median dose of 45 Gy (range, 12 to 60) in a median of 3 fractions (range, 1 to 5)	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			Previous treatment: 314 (73%) chemotherapy, 73 (17%) surgery, 9 (2%) RFA, 8 (2%) RT, 3 (< 1%) TACE, 1 (< 1%) cryotherapy, 72 (17%) none		
Méndez Romero et al., 2021[116] 13 centers, including academic centers, in Netherlands and Belgium NR	To validate outcomes in a large multi-institution patient cohort treated in accordance with a common protocol for SBRT Mixed (some data entered retrospectively), noncomparative study Median follow-up of 2.3 years	Inclusion criteria (must meet all): liver metastases; SBRT delivered according to 1 of 4 specified fractionation schemes, at least 1 follow-up Exclusion criteria (excluded if any criteria met): NR	Total N = 515 Sex: 196 (38%) female Race/ethnicity: NR Median age (range): 71 years (27 to 91) ECOG score: 256 (50%) 0, 215 (42%) 1, 30 (6%) 2, 1 (< 1%) 2 Median number of metastases treated per patient (range): 1 (1 to 6) Synchronous metastases: 150 (34%) No previous treatment: 227 (51%)	• SBRT ◦ 18 to 20 Gy in 3 fractions ◦ 11 to 12 Gy in 5 fractions ◦ 7.5 Gy in 8 fractions ◦ 5 Gy in 12 fractions	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			Previous treatment: 108 (24%) chemotherapy, 31 (7%) RFA/microwave ablation, 29 (7%) surgery, 2 (< 1%) SBRT, 2 (< 1%) unknown Primary site: 359 (80%) colorectal, 40 (9%) lung, 18 (4%0 breast, 2 (< 1%) stomach, 2 (< 1%) ovary, 2 (< 1%) melanoma, 24 (5%) other		
Munoz-Schuffenegger et al., 2021[117] Single center in Canada NR	To assess long-term outcomes of SBRT in patients with HCC and macrovascular invasion Retrospective, noncomparative study Median follow-up of 11 months	Inclusion criteria (must meet all): radiologically diagnosed HCC; unsuitable for or with progression following surgery, TACE, or RFA Exclusion criteria (excluded if any criteria met): NR	Total N = 128 Sex: 17 (13%) female Race/ethnicity: NR Median age (range): 61 years (39 to 90) Underlying liver disease: 30 (23%) HBV, 58 (45%) HCV, 17 (13%) alcohol-related, 8 (6%) others	• SBRT ○ Median dose of 33 Gy (range, 27 to 54) in a median of 5 fractions (range, 5 to 6)	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			Child-Pugh score: 86 (67%) A5, 25 (19%) A6, 13 (10%) B7, 4 (3%) B8 ECOG of 1 or higher: 61 (48%)		
Nabavizadeh et al., 2021[118] Single academic center in US NR	To compare outcomes for inoperable HCC between TACE with percutaneous TA and TACE with SBRT using propensity score–weighted cohorts Retrospective, propensity-matched analysis Median follow-up of 48 months	Inclusion criteria (must meet all): inoperable lesions Exclusion criteria (excluded if any criteria met): none	Total N = 190, comprising 90 in TACE-SBRT group and 100 in TACA-TA group Sex: 16 (18%) female, TACE-SBRT; 32 (32%) female, TACE-TA Race/ethnicity: NR Median age (IQR): 60 years (56 to 65) TACE-SBRT; 61 years (58 to 64) TACE-TA Liver transplant: 14 (16%) TACE-SBRT; 15 (15%) TACE-TA More than 2 TACE sessions before treatment: 22 (24%) TACE-SBRT; 2 (2%) TACE-TA	• TACE-SBRT ○ 5 fractions	• TACE-TA ○ Performed using CT and ultrasound guidance

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			Underlying disease: 3 (3%) HBV, 61 (68%) HCV, 21 (23%) alcoholic cirrhosis, 8 (9%) NASH cirrhosis, 3 (3%) other, TACE-SBRT; 6 (6%) HBV, 86 (86%) HCV, 46 (46%) alcoholic cirrhosis, 7 (7%) NASH cirrhosis, 2 (2%) other, TACE-TA Child-Pugh score: 46 (51%) A, 20 (22%) B7, 17 (19%) B8 or B9, 7 (8%) C, TACE-SBRT; 57 (57%) A, 16 (16%) B7, 27 (27%) B8 or B9, 0 C, TACE-TA BCLC stage: 66 (73%) A, 13 (14%) B, 4 (4%) C, 7 (8%) D, TACE-SBRT; 96 (96%) A, 4 (4%) B, 0 C, 0 D, TACE-TA		
Nieuwenhuizen et al., 2021[119]	To compare safety, efficacy and long-term oncological outcomes of TA and	Inclusion criteria (must meet all): history of solely TA or SBRT for	Total N = 199, comprising 55 in	• SBRT ○ 60 Gy in 3, 5, 8 or 12 fractions	• TA ○ RFA or microwave ablation

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
AmCORE (2007 to 2020) NR	SBRT in people with unresectable colorectal liver metastases Prospective registry, comparative analysis Median follow-up of 29 months	previously untreated colorectal liver metastases within a single session Exclusion criteria (excluded if any criteria met): simultaneous bowel surgery	SBRT group and 144 in TA group Sex: 25 (45%) female, SBRT; 37 (26%) female, TA Race/ethnicity: NR Median age (IQR):71 years (13) SBRT; 67 years (17) TA Low Charlson comorbidity score (0 to 5): 20 (36%) SBRT; 70 (49%) TA Primary site: 19 (35%) rectum, 24 (44%) left-sided colon, 12 (22%) right-sided colon, SBRT; 45 (31%) rectum, 69 (48%) left-sided colon, 30 (21%) right-sided colon, TA Primary T-status: 6 (13%) T1 to 2 SBRT; 21 (16%) T1 to 2, TA History of chemotherapy: 35		

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			(73%) SBRT; 74 (59%) TA History of partial hepatectomy: 42 (76%0 SBRT; 95 (66%) TA		
Oladeru et al., 2016[120] Surveillance, Epidemiology, and End Results Program (SEER)-Medicare (2004 to 2011) NR	To compare outcomes of overall and disease specific survival using SIRT vs. SBRT to treat HCC Retrospective database analysis Median follow-up NR	Inclusion criteria (must meet all): histologically diagnosed HCC Exclusion criteria (excluded if any criteria met): unknown stage or grade; > 1 primary tumor; metastatic disease; no radiation administered; unknown RT modality; hepatectomy; preoperative RT	Total N = 189, comprising 112 in SBRT group and 77 in SIRT group Sex: 24 (21%) female, SBRT; 13 (17%) female SIRT Race/ethnicity: 10 (9%) Asian, 20 (18%) African American, 6 (6%) other, 76 (68%) Caucasian, SBRT; 4 (5%) Asian, 15 (19%) African American, 2 (3%) other, 56 (73%) Caucasian, SIRT Mean age at diagnosis: 64 years (12) SBRT; 63 years (10) SIRT Grade: 38 (34%) well differentiated, 46 (41%) moderately	• SBRT ○ No details	• SIRT

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			differentiated, 28 (25%) poorly or un-differentiated, SBRT; 31 (40%) well differentiated, 36 (47%) moderately differentiated, 10 (13%) poorly or un-differentiated, SIRT Stage: 37 (33%) I, 19 (17%) II, 56 (50%) IIIA-IIIN, SBRT; 21 (27%) I, 18 (23%) II, 38 (49%) IIIA-IIIN, SIRT RT after surgery: 28 (25%) SBRT; 12 (13%) SIRT		
Parikh et al., 2018[121] Surveillance, Epidemiology, and End Results Program (SEER)-Medicare (2004 to 2011) NR	To assess differences in outcomes and resource requirements between local ablation and SBRT using US Surveillance, Epidemiology, and End Results (SEER)-Medicare linked database	Inclusion criteria (must meet all): stage I or II HCC; treated with RFA or SBRT as first treatment within 6 months of diagnosis Exclusion criteria (excluded if any criteria met): another treatment within 30 days of	Total N = 440, comprising 32 in SBRT group and 408 in RFA group Sex: 12 (38%) female, SBRT; 154 (42%) female, RFA Race/ethnicity: 24 (75%) White, NR for Black and other, SBRT; 236 (58%) White, 32 (8%)	• SBRT ○ No details	• RFA

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
	Retrospective database analysis (propensity-matched) Median follow-up of 16 months in SBRT group and 25 months in RFA group	RFA or SBRT; missing stage data; another malignant primary tumor diagnosed previous to HCC diagnosis; HCC diagnosed upon death; dates of birth that differed between CMS and SEER by more than a year; autopsy or death certificate-only records	Black, 140 (34%) other, RFA Tumor stage: NR, SBRT; 296 (73%) I, 112 (27%) II, RFA Median Charlson Comorbidity Index (IQR): 1 (1 to 2) SBRT; 1 (0 to 1) RFA Median treatment count post initial SBRT or RFA (IQR): 1 (1 to 1) SBRT; 1 (1 to 2) RFA Treatment post initial SBRT or RFA: NR, SBRT; 21 (5%) liver transplant, 111 (27%0 TACE, NR SBRT, RFA		
Rajyaguru et al., 2018[122] National Cancer Database (2004 to 2013) NR	To compare effectiveness of RFA vs. SBRT in nonsurgically managed patients with stage I or II HCC Retrospective, comparative database analysis	Inclusion criteria (must meet all): clinical stage I (T1N0M0) or stage II (T2N0M0) HCC Exclusion criteria (excluded if any criteria met): lobectomy, extended	Total N = 3,980, comprising 296 in SBRT group and 3,684 in RFA group Sex: 89 (30%) female, SBRT; 1,039 (28%) female, RFA Race/ethnicity: 35 (12%) White, 16 (5%) Black, 245	• SBRT ○ Dose range from < 30 Gy in 1 to 2 fractions to 50 or more Gy (number of fractions NR)	• RFA

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
	Median follow-up of 25 months	lobectomy, resection, hepatectomy, or liver transplantation at any time; other ablative therapy; chemotherapy or chemotherapy status unknown	(83%) other or unknown, SBRT; 2,740 (74%) White, 462 (13%) Black, 482 (13%) other or unknown, RFA Age: 12 (4%) 49 years and younger, 77 (26%) 50 to 59 years, 84 (28%) 60 to 70 years, 123 (42%) 71 and older, SBRT; 262 (7%) 49 years and younger, 1,236 (34%) 50 to 59 years, 1,225 (33%) 60 to 70 years, 961 (26%) 71 and older, RFA Insurance status: 69 (23%) private, 32 (11%) Medicaid, 182 (61%) Medicare, 5 (2%) other government, 7 (2%) not insured, 1 (< 1%) unknown, SBRT; 1,154 (31%) private, 486 (13%) Medicaid, 1,771 (48%) Medicare, 86 (2%) other government,		

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			131 (4%) not insured, 55 (1%) unknown, RFA No comorbidities: 190 (64%) SBRT; 1,594 (43%) RFA Clinical T-stage: 202 (68%) I, 94 (32%) II, SBRT; 2,718 (74%) I, 966 (26%) II, RFA Grade: 52 (18%) well differentiated, 29 (10%) moderately differentiated, 12 (4%) poorly or un-differentiated, SBRT; 676 (18%) well differentiated, 550 (15%) moderately differentiated, 135 (4%) poorly or un-differentiated, RFA		
Sapisochin et al., 2017[123] Single center in Canada NR	To ascertain safety and efficacy of SBRT on an intention-to-treat basis compared with TACE and RFA as a bridge to liver transplantation in a	Inclusion criteria (must meet all): treated either with SBRT, TACE or RFA as bridging therapies	Total N = 594, comprising 36 in SBRT group, 99 in TACE group, and 244 in RFA group Sex: 5 (14%) female, SBRT; 11 (11%0	• SBRT ○ Median prescribed dose was 36 Gy in 6 fractions (IQR, 30 to 40 in 6 fractions)	• TACE • RFA

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
	large cohort of patients with HCC Retrospective (assumed), comparative study Median follow-up of 47 months	Exclusion criteria (excluded if any criteria met): NR	female, TACE, 35 (15%) female, RFA Race/ethnicity: NR Median age (range): 60 years (56 to 65) SBRT; 58 years (53 to 64) TACE; 58 years (54 to 62) RFA HCV: 17 (47%) SBRT; 45 (45%) TACE; 127 (60%) RFA HBV: 6 (17%) SBRT; 32 (32%) TACE; 51 (21%) RFA Tumor differentiation: 3 (10%) well differentiated, 25 (83%) moderately differentiated, 2 (7%) poorly differentiated, SBRT; 6 (7%) well differentiated, 64 (81%) moderately differentiated, 5 (6%) poorly differentiated, TACE; 50 (25%) well differentiated, 105		

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			(52%) moderately differentiated, 14 (7%) poorly differentiated, RFA Macrovascular invasion: 2 (7%) SBRT; 9 (11%) TACE, 10 (5%) RFA		

Sebastian et al., 2019[124]
 	
National Cancer Database (2004 to 2014)
 	
NR
	To compare overall survival of patients treated with SBRT, CRT, and TARE
	
	Retrospective, comparative database analysis
	
	Median follow-up of 17 months
		Inclusion criteria (must meet all): histologically or cytologically confirmed intrahepatic adenocarcinoma of biliary tract; no more than 85 years old; Charlson comorbidity score of 0 to 2
		
		Exclusion criteria (excluded if any criteria met): surgery; metastatic or lymph node positive disease; missing T-stage or tumor size data
			Total N = 141, comprising 27 in SBRT group, 60 in TARE group and 54 in cRT group
			
			Sex: 9 (33%) female, SBRT; 33 (55%) female, TARE; 29 (54%) cRT
			
			Race/ethnicity: 25 (93%) White, 1 (4%) Black, 1 (4%) other, SBRT; 51 (85%) White, 2 (3%) Black, 7 (12%) other, TARE; 46 (85%) White, 2 (4%) Black, 6 (11%) other, cRT
			
			Median age (IQR): 71 years (61 to 80) SBRT; 65 years (57
				• SBRT
				  ○ 30 Gy or higher delivered in 5 or fewer fractions
				  ○ Median dose and number of fractions was 45 Gy (IQR, 40 to 50 Gy) and 5 fractions (IQR, 3 to 5)
					• TARE
					• cRT
					  ○ median dose and number of fractions was 50.4 Gy (IQR, 45 to 54 Gy) and 28 fractions (IQR 25 to 30)

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			to 75) TARE; 67 years (61 to 74) cRT Charlson Comorbidity score of 1 or 2: 10 (37%) SBRT; 19 (32%) TARE; 15 (28%) cRT Vascular invasion: 7 (26%) SBRT; 21 (35%) TARE; 22 (41%) cRT Chemotherapy: 11 (41%) SBRT; 32 (53%) TARE; 54 (100%) cRT		
Stintzing et al., 2019[125] Single center in Germany NR	To present long-term survival data in patients with oligo-metastatic disease limited to liver Prospective, noncomparative study Median follow-up of 30 months	Inclusion criteria (must meet all): received SBRT with curative intent for liver lesions Exclusion criteria (excluded if any criteria met): NR	Total N = 126 Sex: 54 (43%) female Race/ethnicity: NR Median age (range): 65 years (33 to 87) Tumor entities: 71 (56%) colorectal, 13 (10%) gastrointestinal, 14 (11%) breast, 15 (12%) urogenital, 5 (4%) bronchial, 1	• SBRT ○ 20 to 45 Gy in 1 to 3 fractions	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			(< 1%) liver, 8 (6%) other Systematic pretreatment: 103 (82%) Local pretreatment: 95 (75%)		
Voglhuber et al., 2021[126] Single academic center in Germany NR	To evaluate high-precision SBRT for liver metastases Retrospective, noncomparative study Median follow-up of 11 months	Inclusion criteria (must meet all): received SBRT for treatment of singular and multiple liver metastases Exclusion criteria (excluded if any criteria met): any other type of RT	Total N = 115 Sex: 56 (49%) female Race/ethnicity: NR Median age (range): 66 years (35 to 86) Primary site: 16 (14%0 rectum, 38 (33%) colon, 12 (10%) esophagus or stomach, 20 (17%) breast, 5 (4%) lung, 4 (3%) pancreas, 4 (4%) ovary, 16 (14%) others Controlled primary: 102 (90%) Synchronous metastases: 58 (50%)	• SBRT ○ Median cumulative dose of 35 Gy (range, 12 to 60 Gy) with a median single dose of 7 Gy (range, 2.5 to 20 Gy) in 5 (range, 2 to 16)	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			Systemic therapy within 4 weeks of RT: 38 (33%)		
Wahl et al., 2016[127] Single academic center in US NR	To compare outcomes between SBRT and RFA for HCC Retrospective, comparative study Median follow-up of 13 months for SBRT and 20 months for RFA	Inclusion criteria (must meet all): inoperable, nonmetastatic HCC Exclusion criteria (excluded if any criteria met): NR	Total N = 224, comprising 63 in SBRT group and 161 in RFA group Sex: 9 (14%) female, SBRT; 44 (27%) female, RFA Race/ethnicity: 36 (57%) White, 2 (3%) African American, 1 (2%) Asian, 24 (38%) other or unknown, SBRT; 132 (82%) White, 14 (9%) African American, 7 (4%) Asian, 8 (5%) other or unknown, RFA Median age (range): 62 years (35 to 85) SBRT; 60 years (31 to 81) RFA Median number of lesions (range): 1 (1 to 4) SBRT; 1 (1 to 6) RFA	• SBRT ○ 3 or 5 fractions delivered 2 to 3 times per week with median doses of 30 or 50 Gy, with a range of 27 to 60 Gy	• RFA ○ Majority percutaneous (97%)

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			HBV: 3 (4%) SBRT; 24 (10%) RFA HCV: 44 (53%) SBRT; 149 (60%) RFA# Alcoholic cirrhosis: 10 (12%) SBRT; 21 (8%) RFA NAFLD: 1 (1%) SBRT; 13 (5%) RFA Mean Child-Pugh score: 6.2 SBRT; 6.9 RFA Median number of previous treatments (range): 2 (0 to 7) SBRT; 0 (0 to 7) RFA Clinical T-stage: 38 (46%) T1, 40 (48%) T2, 0 T3a, 5 (6%) T3b, SBRT; 123 (50%) T1, 121 (49%) T2, 3 (1%) T3a, 0 T3b, RFA		
Wang et al., 2021[128] Single academic center in Japan NR	To evaluate safety and efficacy of administration of RFA and SBRT in short term to	Inclusion criteria (must meet all): BCLC stage 0–B1; curative rather than palliative treatment; primary	Total N = 98, comprising 26 in SBRT group and 72 in RFA group	• SBRT ○ Total dose of 35 Gy delivered in 5 fractions over 5 to 7 days	• RFA

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
	patients with BCLC stages 0–B1 HCC Retrospective, comparative study (propensity-matched) Median follow-up of 36 months	treatment RFA; subsequent treatment (multifocal HCC lesions in same patients or local/intrahepatic recurrence after initial RFA) RFA or SBRT; time interval between primary treatment and subsequent treatment no more than 3 months Exclusion criteria (excluded if any criteria met): NR	Sex: 7 (27%) female, SBRT; 14 (19%) female, RFA Race/ethnicity: NR Mean age (SD): 68 years (12) SBRT; 71 years (9) RFA Child-Pugh score: 25 (96%) A, 1 (4%) B, SBRT; 64 (89%) A, 8 (11%) B, RFA History of HCC: 8 (31%) SBRT; 46 (64%) RFA BCLC stage: 6 (23%) 0, 17 (65%) A, 3 (11%) B1, SBRT; 15 (21%) 0, 52 (68%) A, 5 (7%) B1, RFA Etiology: 19 (73%) HCV, 1 (4%) HBV, 6 (23%) not HCV or HBC, SBRT; 55 (76%) HCV, 5 (7%) HBV, 12 (17%) not HCV or HBC, RFA		
Wong et al., 2019[129]	To compare outcomes of TACE + SBRT vs. TACE alone for	Inclusion criteria (must meet all): ≥ 700 mL of uninvolved liver;	Total N = 251, comprising 49 in	• SBRT ○ Total dose ranged from 5 to 8.5 Gy for 6	• TACE

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
2 centers (1 academic) in Hong Kong NR	nonresectable, nontransplantable and nonablatable HCC patients Retrospective, comparative study (propensity-matched) Median follow-up of 13 months	ECOG ≤ 2; Child's score up to B7; adequate organ function; no ascites or encephalopathy Exclusion criteria (excluded if any criteria met): > 5 tumor nodules	TACE + SBRT and 202 in TACE group Sex: 7 (14%) female, TACE + SBRT; 42 (21%) TACE Race/ethnicity: NR Median age (range): 61 years (28 to 87) TACE + SBRT; 69 years (20 to 94) TACE HBV: 39 (80%) TACE + SBRT; 131 (65%) TACE ECOG 0 to 2: 49 (100%) TACE + SBRT; 192 (95%) TACE Child-Pugh score A: 46 (94%) TACE + SBRT; 164 (81%) TACE Metastatic disease: 0 TACE + SBRT; 0 TACE More than 1 tumor: 22 (45%) TACE + SBRT; 114 (56%) TACE	fractions to 4 Gy for 6 to 10 fractions	

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)

Wong et al., 2021[130]
Single academic center in Hong Kong
NCT03950102
	To evaluate efficacy and safety of SBRT as bridging therapy, compared with TACE and HIFU
	Prospective, comparative study using retrospective comparison groups
	Minimum follow-up of 12 months
		Inclusion criteria (must meet all): HCC; on transplant waitlist; Child score ≤ 8; adequate hematological function; ECOG performance status ≤ 2
		Exclusion criteria (excluded if any criteria met): age < 18 years old; extrahepatic metastasis; radiological vascular invasion; previous RT to liver; positive pregnancy test
		Patients were selected for TACE if: absence of main portal vein thrombosis; no significant ascites or recurrent hepatic encephalopathy; Child A; adequate coagulation profile; estimated
			Total N = 150, comprising 40 in SBRT group, 59 in TACE group, and 51 in HIFU group
			Sex: 14 (35%0 female, SBRT; 9 (15%) female, TACE; 10 (20%) female, HIFU
			Race/ethnicity: NR
			Median age (range): 60 years (36 to 69) SBRT; 58 years (42 to 69) TACE; 59 years (38 to 68) HIFU
			HBV: 34 (85%) SBRT; 45 (76%) TACE; 41 (80%) HIFU
			HCV: 3 (7%) SBRT; 8 (14%) TACE; 9 (18%) HIFU
			Child-Pugh score A: 21 (53%) SBRT; 36 (61%) TACE; 17 (33%0 HIFU
				• SBRT
				  ○ Median dose of 50 Gy in 5 fractions
					• TACE
					  ○ Median number per patient was 3 (range, 1 to 9)
					• RFA

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
		glomerular filtration rate ≥ 45 mL/min; ECOG ≤ 2 Patients with ascites, pleural effusion, borderline liver function, and thrombocytopenia were offered HIFU			

Abbreviations. BCLC: Barcelona clinic liver cancer staging system; cRT: conventional radiation therapy; CT: computed tomography; ECOG: Eastern Cooperative Oncology Group; Gy: Gray; HBV: hepatitis B virus; HCV: hepatitis C virus; HCC: hepatocellular carcinoma; HIFU: high-intensity focused ultrasound; IQR: interquartile range: MRI: magnetic resonance imaging; NAFLD: nonalcoholic fatty liver disease; NASH: nonalcoholic steatohepatitis; NR: not reported; RFA: radiofrequency ablation; RT: radiation therapy; SBRT: stereotactic body radiation therapy; SD: standard deviation; SIRT: selective internal radiotherapy; TA: thermal ablation; TACE: transarterial chemoembolization; TARE: transarterial radioembolization.

Cervical Cancer

No eligible studies identified.

Esophageal Cancer

No eligible identified.

Oligometastatic Cancer

Table C19. Study Characteristics for Nonrandomized and Registry-based Studies

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
Bouman-Wammes et al., 2017[131]	To investigate impact of SBRT in	Inclusion criteria (must meet all): histologically	Total N = 63, comprising 43 in SBRT group and 20	• SBRT ○ 3 Gy in 10 fractions (67%)	• No SBRT

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
Single center in Netherlands NR	delaying start of ADT Retrospective, comparative study Median follow-up of 2.6 years	proven diagnosis of prostate cancer; initially treated with curative intent; biochemical PSA relapse; metabolically active oligometastatic disease; received SBRT to all lesions as initial oligometastatic treatment Exclusion criteria (excluded if any criteria met): ADT or chemotherapy initiated for metastatic disease before SBRT; 1 or more other types of carcinoma apart from prostate cancer	in control group (no SBRT) Sex: men only Race/ethnicity: NR Mean age (range): 68 years (53 to 81) SBRT; 70 years (54 to 85) control Median PSA at diagnosis (range): 12.4 ng/ml (4.2 to 94.9) SBRT; 8.5 ng/ml (2.7 to 27.4) control Primary treatment: 24 (56%) prostatectomy, 5 (12%) prostatectomy and RT, 8 (19%) RT, 6 (14%) brachytherapy, SBRT; 7 (35%) prostatectomy, 2 (10%) prostatectomy and RT, 7 (35%) RT, 4 (20%) brachytherapy, control	○ 3 Gy in 15 fractions (9%) ○ 5 Gy in 7 fractions (23%)	

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			Number of metastases: 35 (81%) 1, 6 (14%) 2, 1 (2%) 3, 1 (2%) 4, SBRT; 9 (45%) 1, 8 (40%) 2, 3 (15%) 3, 0 4, control Type of metastases: 33 (77%) lymph node, 9 (21%) bone, 1 (2%) both, SBRT; 13 (65%) lymph node, 7 (35%) bone, 0 both, control		
Bowden et al., 2020[132] Single center in Australia ACTRN12618000566235 TRANSFORM	To determine proportion of patients not requiring treatment escalation following SBRT Prospective, noncomparative study Median follow-up of 35 months	Inclusion criteria (must meet all): men with a prostate cancer; previous definitive local treatment; 5 or fewer synchronous metastases; ECOG performance status of 0 or 1 Exclusion criteria (excluded if any criteria met): previous palliative RT; presented with active local disease in prostate bed	Total N = 199 Sex: men only Race/ethnicity: NR Mean age (SD): 67 years (7) Primary therapy: 185 (93%) radical prostatectomy, 9 (5%) RT, 3 1%) brachytherapy, 2 (1%) not stated Previous androgen deprivation therapy: 33 (17%) Number of oligometastatic	• SBRT ○ 50 Gy in 10 daily fractions	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			lesions: 81 (41%) 1, 50 (25%) 2, 33 (17%) 3, 24 (12%) 4, 10 (5%) 5 Site of oligometastatic lesions: 45 (23%) bone, 126 (63%) lymph node, 24 (12%0 bone and node, 4 (2%) other		
Chalkidou et al., 2021[133] 17 centers in England NR	To present results of a national study of patients with extracranial oligometastases undergoing SBRT Prospective, noncomparative study Median follow-up of 13 months	Inclusion criteria (must meet all): aged 18 years or older with a radically treated and controlled, histologically or cytologically confirmed primary carcinoma (excluding hematological malignancies), as well as men with prostate-specific antigen lower than 50 ng/mL and clinical evidence of prostate cancer; 3 or fewer sites of metachronous extracranial	Total N = 1,422 Sex: 475 (33%) Race/ethnicity: NR Age: 31 (2%) 19 to 29 years, 20 (1%) 30 to 39 years, 52 (4%) 40 to 49 years, 174 (12%) 50 to 59 years, 436 (31%) 60 to 69 years, 501 (35%) 70 to 79 years, 208 (15%) 80 years and older WHO performance status: 1,000 (71%) 0, 342 (24%) 1, 64 (5%) 2 Primary site: 406 (29%) prostate, 397 (28%) colorectal,	• SBRT ○ Median BED 105 Gy (IQR, 72 to 130) in 3 to 8 fractions	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
		metastases (with exception of synchronous colorectal liver metastases) and a maximum of 2 sites of spinal metastatic disease, amenable to treatment with SBRT but unsuitable for surgery; maximum size of 6 cm for any single metastasis (5 cm for lung or liver metastases); life expectancy of more than 6 months; WHO performance status of 2 or lower Exclusion criteria (excluded if any criteria met): occult brain metastases; spinal compression; previous RT to site of metastases	143 (10%) renal, 78 (5%) breast, 64 (5%) lung, 58 (4%) melanoma, 276 (19%) other Site of treated metastases: 411 (29%) lung, 132 (9%) spine, 169 (12%) bone, 41 (3%) adrenal, 135 (10%) liver, 439 (31%0 lymph nodes, 77 (5%) other Number of metastases: 1,074 (76%) 1, 279 (20%) 2, 68 (5%) 3 Previous systemic therapy: 850 (60%) Post systemic therapy: 349 (25%)		

De Bleser et al., 2019[134]
 	
15 centers, including academic centers, across Europe
	To explore differences in toxicity and efficacy profiles of SBRT and ENRT for	Inclusion criteria (must meet all): prostate cancer; 5 or fewer oligorecurrent	Total N = 506, comprising 309 in SBRT group and 197 in ENRT group	• SBRT
				  ○ High dose of RT (minimum 5Gy per fraction) directed to
					• ENRT
					  ○ RT to suspicious and elective nodes with a

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
NR	oligorecurrent nodal prostate cancer in a large patient cohort Retrospective, comparative study Median follow-up of 36 months	lymph nodes: following local therapy with curative intent Exclusion criteria (excluded if any criteria met): synchronous prostate relapse; bone or visceral metastasis at recurrence; testosterone level of < 50 ng/dl at time of metastatic recurrence; presenting with oligometastasis	Sex: men only Race/ethnicity: NR Median age at diagnosis (IQR): 63 years (58 to 68) SBRT; 63 years (59 to 68) ENRT Median prostate-specific antigen (IQR): 9.3 ng/ml (6.7 to 14.0) SBRT; 9.2 ng/ml (6.7 to 16.0) Primary treatment: 87 (28%) radical prostatectomy, 66 (21%) RT, 156 (50%) both, SBRT; 67 (34%) radical prostatectomy, 29 (15%) RT, 101 (51%) both, ENRT Androgen deprivation therapy for primary cancer: 120 (39%) SBRT; 63 (32%) ENRT Metastatic site: 222 (72%) pelvic, 69 (22%) extrapelvic, 18 (6%) both, SBRT;	suspicious node(s) in maximum 10 fractions	minimum dose of 45 Gy in 25 fractions

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			143 (73%) pelvic, 29 (15%) extrapelvic, 25 (13%) both, ENRT Number of positive nodes: 243 (79%) 1, 50 (16%) 2, 13 (4%) 3, 2 (1%) 4, 1 (< 1%) 5, SBRT; 90 (50%) 1, 55 (28%) 2, 23 (12%) 3, 13 (7%) 4, 8 (4%) ENRT Adjuvant androgen deprivation therapy at recurrence: 71 (23%) SBRT; 119 (60%) ENRT		
Franzese et al., 2021[135] Multiple centers in Italy NR	To investigate SBRT's possible benefit in terms of disease control, delay of next-line systemic therapy and safety of concomitant treatments Retrospective, noncomparative study Median follow-up of 19 months	Inclusion criteria (must meet all): oligostatic disease treated with SBRT; primary renal cell carcinoma Exclusion criteria (excluded if any criteria met): palliative treatment; brain disease; treated for 6 or more extracranial metastases	Total N = 207 Sex: 48 (23%) female Race/ethnicity: NR Median age (range): 67 years (30 to 86) Performance status: 177 (72%) 0, 63 (26%) 1, 5 (2%) 2 Bone metastases: 85 (35%) Total number of metastases: 70	• SBRT ○ Median dose of 36 Gy (range, 10 to 75) in median of 5 fractions (range, 1 to 10)	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			(29%) 1, 52 (22%) 2, 36 (15%) 3, 17 (7%) 4, 19 (18%) 5, 51 (21%) > 5 Treated lesions: 142 (58%) 1, 61 (25%) 2, 29 (12%) 3, 9 (40%) 4, 4 (2%) 5 Site of metastases: 24 (6%) liver, 79 (21%) lymph node 8 (2%) renal bed; 5 (1%) muscles, 116 (30%) bone, 23 (6%) pancreas, 1 (< 1%) pleura, 116 (30%) lung, 13 (2%) adrenal Previous systemic therapy: 137 (56%) Systemic therapy during SBRT: 78 (32%)		
Hurmuz et al., 2020[136] Multiple centers in Turkey TROD-09-002	To assess outcomes of treatment in synchronous or metachronous oligometastatic prostate cancer patients with ≤ 5	Inclusion criteria (must meet all): synchronous or metachronous bone or lymph node metastasis limited to ≤ 5 sites; minimum of 3	Total N = 176, comprising 129 in SBRT group and 47 in cRT group Sex: men only Race/ethnicity: NR	• SBRT ○ Median total dose of 27 Gy (range, 15 to 40) in median of 3 (range, 1 to 5) fractions	• cRT

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
	bone or lymph node metastases Retrospective, comparative study Median follow-up of 23 months	months follow-up after MDT Exclusion criteria (excluded if any criteria met): ECOG performance status of 2 or higher; treated previously with RT to same oligometastatic site	Median age (range): 65 years (24 to 84) overall Median prostate-specific antigen (range): 18.0 ng/ml (4.28 to 40.5.0) Clinical T-stage: 4 (2%) T2b, 61 (35%) T2c, 53 (30%) T3a, 48 (27%) T3b, 10 (6%) T4 Risk: 64 (36%) intermediate, 112 (64%) high Adjuvant hormone therapy: 140 (79%) Metastasis: 117 (67) oligoprogression, 59 (33) new oligometastasis Metastasis site: 75 (43%) bone, 61 (35%) lymph node, 40 (23%) bone and lymph node Primary treatment: 28 (16%) surgery, 96 (55%) RT, 38 (22%) surgery and RT, 14 (8%) androgen		

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			deprivation treatment, with or without chemotherapy		
Macchia et al., 2020[137] Multiple centers, including academic centers, in Italy MITO RT1	To define activity and safety of SBRT in a very large, real-world data set of patients with metastatic, persistent, and recurrent ovarian cancer Retrospective, noncomparative study Median follow-up of 22 months	Inclusion criteria (must meet all): > 18 years; oligo-recurrent, persistent, progressive disease with histological documentation of ovarian cancer at primary diagnosis; up to 5 synchronous lesions; any site of disease; salvage surgery or other local therapies not feasible, relative contraindication to further systemic therapy Exclusion criteria (excluded if any criteria met): uncertain diagnosis of ovarian carcinoma; > 5 synchronous lesions	Total N =261 Sex: women only Race/ethnicity: NR Median age (range): 60 years (28 to 85) ECOG performance status: 190 (73%) 0, 29 (11%) 1, 38 (15%) 2, 4 (1%) 3 No comorbidities: 154 (59%) Surgery before SBRT: 256 (100%) Previous in-site RT: 9 (3%) Site of lesions (by lesion): 248 (55%) abdomen, 85 (19%) pelvis, 6 (15%) thorax, 37 (8%) brain, 13 (5%) neck Patients bearing: 146 (56%) 1 lesion, 70 (27%) 2 lesions, 28 (11%) 3 lesions, 9	• SBRT ○ Median total dose 25 Gy (range, 5 to 75) in median of 4 fractions (range, 1 to 13)	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			(3%) 4 lesions, 6 (2%) 5 lesions, 2 (< 1%) 56 to 7 lesions		
Milano et al., 2008[138,139] Single academic center in US NR	To determine patient and tumor variables that predict a better outcome after SBRT treatment Prospective, noncomparative study Followed-up for up to 10 years	Inclusion criteria (must meet all): age ≥ 18 years; Karnofsky performance status ≥ 70; 1 to 5 extracranial metastases Exclusion criteria (excluded if any criteria met): NR	Total N = 121 Sex: NR Race/ethnicity: NR Median age (range): 60 years (34 to 88) Primary site: 39 (32%) breast, 31 (2%) colorectal, 23 (19%) head or neck, lung, esophagus, 28 (23%) other Oligometastatic sites: 50 (41%) lung, 24 (20%) thoracic lymph nodes, 54 (45%) liver, 6 (5%) liver or abdomen, 5 (4%) brain, 15 (12%) bone More than 1 initial involved organ: 29 (24%) Previously had more than 5 metastatic lesions: 21 (17%)	• SBRT ◦ Median of 38 Gy (range, 0.3 to 422) ◦ Most treated with 10 fractions of 5 Gy	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			Previous curative therapy: 36 (30%) Number of lesions: 37 (31%) 1, 32 (26%) 2, 28 (23%) 3, 12 (10%) 4, 12 (10%) 5		
Nicosia et al., 2020[140] Multiple centers, including academic centers, in Italy and Germany NR	To evaluate oncological outcome and pattern of recurrence in patients treated with SBRT to lymph node metastases Retrospective, noncomparative study Median follow-up of 16 months	Inclusion criteria (must meet all): histological diagnosis of adenocarcinoma of prostate; ECOG performance status of ≤ 2; controlled primary tumor; ≤ 5 lymph node metastases at time of treatment; serum testosterone level ≤ 50ng/ml during androgen deprivation therapy; no other active sites of distant metastases; minimum of 6 months follow-up after SBRT Exclusion criteria (excluded if any criteria met): use of new androgen	Total N = 109 Sex: men only Race/ethnicity: NR Mean age (range): 71 years (51 to 84) ECOG performance status: 75 (69%) 0, 30 (27%) 1, 4 (3%) 2 Initial treatment: 66 (61%) surgery with or without androgen depravation therapy; 17 (15%) surgery and RT with or without androgen depravation therapy, 12 (11%) RT with or without androgen depravation therapy, 14 (13%) high-focused ultrasound	• SBRT ○ Median does of 36 Gy (range, 25 to 48) in median of 7 fractions (range, 5 to 12)	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
		receptor-targeted agents; chemotherapy before or during SBRT; castration-resistant at time of detection of metastases	Initial stage: 1 (1%) T1, 22 (20%) T2, 56 (51%) T3, 1 (1%) T4 Initial prostate-specific antigen: 10.59 ng/ml (3.2 to 117) Oligometastatic status: 56 (53%) oligorecurrent, 53 (49%) oligoprogressive Number of treated lesions: 76 (70%) 1, 23 (21%) 2, 8 (7%) 3, 1 (< 1%) 4, 1 (< 1%) 5 Androgen deprivation therapy: 50 (46%)		
Olsen et al., 2022[141] 6 centers in Canada NCT02933242 SABR-5	To document toxic effects of treatment with SBRT in a large cohort from a population-based, provincial cancer program Retrospective (assumed), noncomparative study	Inclusion criteria (must meet all): adult patients with a histologically confirmed cancer; ECOG score of 0 to 2; life expectancy of > 6 months; metastatic disease on imaging; primary tumor treated radically or	Total N = 381 Sex: 122 (32%) female Race/ethnicity: NR Mean age (range): 68 years (30 to 97) Primary cancer site: 123 (32%) prostate, 63 (17%) colorectal, 42 (11%) breast, 33	• SBRT ○ 48 or 54 Gy in 4 or 3 fractions daily or every other day, peripheral lung ○ 60 Gy in 8 fractions daily, lung ○ 35 or 24 Gy in 5 or 2 fractions	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
	Median follow-up of 25 months	controlled by previous palliative RT or systemic therapy; maximum of 5 metastases (either 5 in total for oligometastatic disease or 5 not controlled in oligoprogressive setting) Exclusion criteria (excluded if any criteria met): brain metastases only with no other site of disease	(9%) lung, 34 (9%) kidney, 86 (23%) other Site of metastases treated with SBRT: 188 (34%) lung, 136 (25%) nonspine bone, 85 (16%) spine, 78(14%) lymph node, 29 (5%) liver, 15 (3%) adrenal, 17 (3%) other Number of metastases treated: 263 (59%) 1, 82 (22%) 2, 26 (7%) 3, 10 (3%) 4 to 5 Type of disease: 318 (82%) oligometastatic, 63 (17%) oligoprogressive	daily or every other day, bone ○ 54 Gy in 3 fractions every other day, liver ○ 40 or 60 Gy in 5 or 8 fractions daily, adrenal ○ 40 Gy in 5 fractions daily, lymph node or soft tissue ○ SRS protocol, brain	
Ost et al., 2016[142] Multicenter study (sites not clear) NR	To pool individual patient data from different institutions treating oligometastatic prostate cancer recurrence with SBRT	Inclusion criteria (must meet all): histologically proven diagnosis of prostate cancer; biochemical relapse following radical local prostate treatment;	Total N = 119 Sex: men only Race/ethnicity: NR Median age (IQR): 61 years (56 to 65) Primary therapy: 21 (18%) radical	• SBRT ○ At least 5 Gy per fraction to a BED of at least 80 Gy using an alpha:beta ratio of 3	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
	Retrospective, noncomparative study Median follow-up of 36 months	detection of up to 3 N1 or M1alpha/beta/c lesions Exclusion criteria (excluded if any criteria met): serum testosterone levels < 50 ng/ml at time of detection of metastases; had received ADT for > 12 months at time of SBRT; biochemical relapse while on active treatment with ADT; received previous treatment with a cytotoxic agent for prostate cancer	prostatectomy, 37 (31%) radical prostatectomy with RT, 31 (26%) radical prostatectomy with RT and ADT, 22 (19%) radical prostatectomy with ADT, 8 (7%) RT alone Median PSA (IQR) at diagnosis: 10.7 ng/ml (6.8 to 19.0) Risk: 5 (4%) low, 30 (25%) intermediate, 51 (43% high, 30 (25%) very high, 3 (3%) unknown Number of lesions: 86 (72%) 1, 22 (19%) 2, 11 (9%) 3 Site of metastases: 72 (60%) lymph nodes, 43 (36%) bone, 1 (1%) liver, 1 (1%) lung, 2 (2%) more than 1 site ADT: 60 (50%)		
Poon et al., 2020[143]	To evaluate overall outcomes, and	Inclusion criteria (must meet all): 18	Total N = 1,033	• SBRT	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
6 high-volume academic centers in US, Canada, Australia, and Italy NR	survival factors from a pooled data set of 1033 patients with extracranial oligometastasis Retrospective, noncomparative study Median follow-up of 24 months	years or older; pathologically confirmed cancer diagnosis; radical curative-intent treatment delivered to primary tumor, and development of oligometastases (defined as 5 or fewer extracranial metastases Exclusion criteria (excluded if any criteria met): downstaged to an oligometastatic state; brain metastases; primary hematologic, central nervous system or germ cell tumor	Sex: 432 (42%) Race/ethnicity: NR Median age (range): 68 years (18 to 94) Primary site: 84 (8%) breast, 235 (23%) colorectal, 63 (6%) kidney, 260 (25%) lung, 132 (13%) prostate, 37 (4%) melanoma, 36 (3%) sarcoma, 47 (5%) head and neck, 11 (1%) thyroid, 28 (3%) pancreas, 18 (2%) hepatic or biliary, 19 (2%) gynecologic, 18 (2%) other gastrointestinal, 17 (2%) other genitourinary, 23 (2%) other Metastatic presentation: 279 (27%) synchronous Number of metastases: 596 (58%) 1, 245 (24%) 2, 105 (10%) 3, 55 (5%) 4, 32 (3%) 5	○ Varied over time and by institution	

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			Previous therapy for metastases: 228 (22%) Previous systemic therapy for metastases: 368 (36%) Previous systemic therapy for primary: 555 (54%)		
Sogono et al., 2021[144] Single center in Australia NR	To report outcomes after single-fraction SRT in patients with oligometastatic disease Retrospective, noncomparative study Median follow-up of 3.1 years	Inclusion criteria (must meet all): solid-organ malignancies with metastatic disease; aged ≥ 18 years; treated with single-fraction SBRT to 1 to 5 sites of disease Exclusion criteria (excluded if any criteria met): NR	Total N = 371 Sex: 126 (34%) female Race/ethnicity: NR Median age (range): 67 years (23 to 95) Primary site: 28 (8%) bone or soft tissue, 42 (11%) breast, 51 (14%) gastrointestinal, 52 (14%) genitourinary (not prostate), 107 (29%) prostate, 63 (17%) lung, 21 (6%) skin, 7 (2%) other Synchronous metastases: 91 (25%)	• SBRT ○ Median dose of 20 Gy (range, 16 to 28) in a single fraction	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			Radical treatment of primary: 356 (96%) Surgery to primary: 284 (77%) RT to primary: 196 (53%) Previous therapy for metastases: 105 (28%) ECOG performance status: 248 (68%) 0, 100 (28%) 1, 14 (4%) 2, 1 (< 1%) 3 Number of treated metastases: 273 (74%) 1, 70 (19%) 2, 19 (5%) 3, 7 (2%) 4, 2 (1%) 5 Number of known metastases: 179 (48%) 1, 82 (22%) 2, 53 (14%) 3, 30 (8%) 4, 20 (5%) 5, 4 (1%) 6, 1 (< 1%) 7, 1 (< 1%) 8		
Sutera et al., 2019[145] Single academic center in US NCT01345552	To evaluate safety and feasibility of SBRT for patients with oligometastatic cancer	Inclusion criteria (must meet all): aged 18 years or older; biopsy-proven oligometastatic or	Total N = 147 Sex: 75 (51%) female Race/ethnicity: 99 (67%) Caucasian, 4	• SBRT ○ Median dose of 48 Gy (IQR, 41 to 54) in median of 4 fractions (IQR, 3 to 5)	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
	Prospective, noncomparative study Median follow-up of 41.3 months	recurrent cancer (defined as 5 or fewer total sites of metastases in 3 or fewer organs) Zubrod performance status of 0 to 1; adequate laboratory parameters Exclusion criteria (excluded if any criteria met): lymphoma; leukemia; multiple myeloma; CNS primaries; another primary cancer diagnosed or treated within past 3 years (other than cutaneous skin cancer); diffuse metastatic spread confined to 1 organ; metastatic disease sites not treatable by SBRT; pregnancy; severe active medical comorbidities; synchronous oligometastases	(3%) African American, 1 (< 1%) Asian, 43 (29%) unknown Median age (IQR): 66 years (60 to 75) Primary site: 32 (22%) lung, 31 (21%) colorectal, 16 (11%) head and neck, 13 (9%) breast, 11 (7%) prostate, 8 (5%) kidney, 7 (5%) esophagus, 5 (3%) uterus, 5 (3%) ovaries, 5 (3%) bladder, 14 (9%) other Initial surgery: 108 (73%) Initial chemotherapy: 94 (64%) Initial RT: 74 (50%) Previous surgery for distant metastases or recurrence: 38 (26%) Previous chemotherapy for distant metastases		

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
			or recurrence: 51 (35%) Previous RT for distant metastases or recurrence: 22 (15%) Previous immunotherapy for distant metastases or recurrence: 1 (< 1%) Number of treated lesions: 104 (71%) 1, 28 (19%) 2, 10 7(%) 3, 1 (< 1%) 4, 4 (3%) 5 Lesion location: 11 (52%) lung, 36 (17%) lymph node, 32 (15%) bone, 15 (7%) liver, 8 (4%) adrenal, 5 (2%) hilar mass, 3 (1%) pelvis, 2 (< 1%) head and neck, 2 (< 1%) brain, 1 (< 1%) muscle		
Triggiani et al., 2017[146] 9 centers, including academic centers, in Italy NR	To evaluate impact of metastases-directed SBRT in oligometastatic prostate cancer	Inclusion criteria (must meet all): histologically proven diagnosis of PC; oligorecurrent PC, defined as	Total N = 100 Sex: men only Race/ecocity: NR	• SBRT ○ Median of 116 Gy (range, 80 to 217); fractions NR	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
	Retrospective, noncomparative study Median follow-up of 20 months	presence of 1 to 3 lesions (bone or nodes) oligo-castration resistant prostate cancer; treated with SBRT with a dose of at least 5Gy per fraction t a BED of at least 80 Gy using an alpha/beta of 3 Gy Exclusion criteria (excluded if any criteria met): adjuvant or neo-adjuvant ADT for more than 1 year; treated with SBRT after second-line treatment	Median age (range): 67 years (49 to 81) Median PSA at diagnosis: 9.8 ng/ml Risk group: 5 (5%) low, 21 (21%) intermediate, 43 (43%) high, 31 (31%) very high Treatment at diagnosis: 24 (24%) radical prostatectomy, 16 (16%) RT, 2 (2%) brachytherapy, 35 (35%) radical prostatectomy and adjuvant RT, 23 (23%) radical prostatectomy and salvage RT Site of lesion: 117 (84%) lymph node, 22 (16%) bone Prophylactic pelvic RT with SBRT: 7(7%) ADT with SBRT: 24 (24%)		

Abbreviations. ADT: androgen deprivation therapy; BED: biologically effective dose; CNS: central nervous system; cRT: conventional RT; ECOG: Eastern Cooperative Oncology Group; ENRT: elective nodal radiation therapy; Gy: Gray; IQR: interquartile range; NR: not reported; PSA: prostate-specific antigen; RT: radiation therapy; SBRT: stereotactic body radiation therapy; SD: standard deviation; SRS: stereotactic radiosurgery; WHO: World Health Organization.

Other Cancers

Table C20. Study Characteristics for Nonrandomized and Registry-based Studies

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
Adrenal cancer					
Franzese et al., 2021[147] 3 centers, including academic centers, in Italy NR	To report results of a multi-institutional experience aiming to investigate clinical outcomes of SBRT for treatment of adrenal metastases in oligometastatic or oligoprogressive setting Retrospective, noncomparative study Median follow-up of 14 months	Inclusion criteria (must meet all): oligostatic disease treated with SBRT; adrenal gland carcinoma; primary tumor controlled Exclusion criteria (excluded if any criteria met): NR	Total N = 142 Sex: 43 (30%) female Race/ethnicity: NR Median age (range): 70 years (27 to 87) ECOG performance status: 57 (40%) 0, 68 (48%) 1, 17 (12%) 2 Primary tumor: 83 (58%) lung, 13 (9%) kidney, 13 (9%) colorectal, 10 (7%) melanoma, 8 (6%) liver, 15 (11%) other Metastases in other organs: 100 (70%) Monolateral: 135 (95%) Systematic therapy before RT: 104 (73%) Systematic therapy during RT: 27 (19%)	• SBRT ○ Median dose of 40 Gy (range, 10 to 60) in median 4 fractions (1 to 10)	• No comparator
Large tumors					
Grozman et al., 2021[148]	To report Karolinska experience of SBRT	Inclusion criteria (must meet all): large tumor(s) defined as gross tumor volume of at	Total N = 164 Sex: 81 (49%) female	• SBRT ○ 40 Gy in 5 fractions	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
Single academic center in Sweden NR	Retrospective, noncomparative study Median follow-up of 17 months	least 70 cc; SBRT with curative intent Exclusion criteria (excluded if any criteria met): NR	Race/ethnicity: NR Median age (range): 70 years (24 to 92) Tumor location: 46 (26%) peripheral lung, 40 (23%) central lung, 27 (16%) liver, 62 (35%) abdomen	○ 40 Gy in 4 fractions	
Mixed cancers					
McCammon et al., 2009[149] Single academic center in US NR	To determine whether an SBRT dose-response relationship for local control is observed and explore influence of other variables on local control after SBRT Retrospective, noncomparative study Median follow-up of 8 months	Inclusion criteria (must meet all): treated with 3-fraction SBRT to thoracic sites or liver Exclusion criteria (excluded if any criteria met): if treated after Sept 2005 (to ensure adequate follow-up)	Total N = 141 Sex: 65 (46%) female Race/ethnicity: NR Median age (range): 62 years (26 to 88) Treatment site: 165 (67%) lungs, 81 (33%) liver Type: 65 (26%) primary or recurrent; 181 (74%) metastatic	• SBRT ○ Most common dose of 60 Gy in 3 fractions (range, < 30 to 60)	• No comparator
Yoon et al., 2021[150] Single academic center in US NR	To report clinical outcomes of stereotactic MRI-guided adaptive radiotherapy (SMART) for primary and metastatic tumors in abdomen and pelvis Retrospective, noncomparative study	Inclusion criteria (must meet all): medically inoperable tumors or oligometastatic disease, defined as involving less than or equal to 5 disease sites; clinically and technically eligible for SBRT Exclusion criteria (excluded if any criteria met): contraindications toward	Total N = 106 Sex: 56 (53%) female Race/ethnicity: NR Mean age (SD): 65 years (13) Diagnosis: 25 (25%) pancreas, 16 (15%) cholangiocarcinoma; 11 (10%) hepatocellular, 9	• SBRT ○ Median total dose of 40 (range, 24 to 60) in median 5 fractions (range, 3 to 5).	• No comparator

Citation Setting NCT or Other Trial ID	Study Aim Study Design and Duration	Inclusion and Exclusion Criteria	Patient Characteristics	Description of Intervention	Description of Comparator(s)
	Median follow-up of 20 months	MRT; previous RT in or near anticipated treatment field; pregnant; concurrent medical illnesses that precluded them from completing RT treatments	(9%) ovarian, 8 (8%) prostate, 37 (35%) other RT treatment setting: 44 (41%) primary, 16 (15%) locally recurrent, 46 (43%) oligometastatic Previous therapy: 56 (53%) surgery, 37 (35%) RT, 15 (14%) ablation Treatment site: 46 (38%) liver, 26 (21%) pancreas, 7 (6%) adrenal gland, 6 (5%) prostate, 6 (5%) pelvic wall, 22 (18%) other		
Bone cancers					
				○	•

Abbreviations. ECOG: Eastern Cooperative Oncology Group; Gy: Gray; MRI: magnetic resonance imaging; NCT: US National Clinical Trial; NR: not reported; RT: radiation therapy; SBRT: stereotactic body radiation therapy; SD: standard deviation.

Study Findings of Included Nonrandomized Studies

Breast Cancer

No eligible studies identified.

Prostate Cancer

Table C21. Evidence Tables for Nonrandomized and Registry-based Studies[a]

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
Andruska et al., 2022[22] National Cancer Database (2004 to 2015) NR	OS **Improved survival with SBRT without ADT vs. cRT without ADT: HR, 0.74 (95% CI, 0.61 to 0.89)** **Improved survival with SBRT without ADT vs. cRT with ADT: HR, 0.81 (95% CI, 0.67 to 0.99)** **Improved survival with SBRT without ADT vs. cRT with or without ADT: HR, 0.80 (95% CI, 0.65 to 0.98)** Compared with cRT with ADT, SBRT without ADT was associated with: • Reduced mortality in men aged 65 years and older (HR: 0.77; 95% CI: 0.62 to 0.96) ○ Lower, but not statistically significantly lower, mortality in men with Gleason 4 + 3	NR	NR

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
	disease (HR, 0.78; 95% CI, 0.59 to 1.04) ○ Lower, but not statistically significantly lower, mortality in men with no measured comorbidities (HR, 0.82; 95% CI, 0.66 to 1.02) ○ No difference in mortality for men aged younger than 65 years (HR, 1.04; 95% CI, 0.65 to 1.69) No difference in survival between SBRT without ADT vs. moderately fractionated RT: HR, 0.93 (95% CI, 0.62 to 1.40); analysis was underpowered No other outcomes of interest reported		
Bolzicco et al, 2013[23] 1 academic center in Italy NR	NA (harms only; noncomparative)	NA (harms only; noncomparative)	Mortality was not reported (assumed not observed) Acute toxicity: 62 (62%) • Usually resolved within 1 month • Urinary: 34% grade 1, 12% grade 2 • Rectal: 27% grade 1, 18% grade 2 Late toxicity: 9 (9%) • Urinary: 4% grade 1, 3% grade 2, 1% grade 3 • Rectal: 2% grade 1, 1% grade 2

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
Davis et al., 2015[24] RSSearch registry, including 27 sites and academic centers in US, Australia, and Turkey (2006 to 2015) NCT01885299	NA (harms only; noncomparative)	NA (harms only; noncomparative)	Mortality not reported Acute toxicity • Urinary frequency: 19% grade 1, 2% grade 2, 0 grades 3 to 5 • Urinary retention: 3% grade 1, 1% grade 2, 0 grades 3 to 5 • Cystitis: 3% grade 1, 1% grade 2, 0 grades 3 to 5 • Diarrhea: 4% grade 1, 1% grade 2, 0 grades 3 to 5 • Constipation: 1% grade 1, 0 grade 2, 0 grades 3 to 5 • Proctitis: 1% grade 1, 0 grade 2, 0 grades 3 to 5 • Fatigue: 2% grade 1, 0 grade 2, 0 grades 3 to 5 • Pain: 3% grade 1, 1% grade 2, 0 grades 3 to 5 Late toxicity • Urinary frequency: 25% grade 1, 8% grade 2, 0 grade 3, 0 grades 4 to 5 • Urinary retention: 4% grade 1, 2% grade 2, 0 grade 3, 0 grades 4 to 5 • Cystitis: 5% grade 1, 2% grade 2, 0 grade 3, 0 grades 4 to 5 • Diarrhea: 4% grade 1, 0 grade 2, 0 grade 3, 0 grades 4 to 5 • Constipation: 3% grade 1, 0 grade 2, 0 grade 3, 0 grades 4 to 5 • Proctitis: 3% grade 1, 2% grade 2, 0 grade 3, 0 grades 4 to 5 • Fatigue: 3% grade 1, 0 grade 2, 0 grade 3, 0 grades 4 to 5

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
			• Pain: 4% grade 1, 0.2% grade 2, 0.2% grade 3, 0 grades 4 to 5
Flushing Radiation 2006 to 2009[25,26] Single center in US NR	NA (harms only; noncomparative)	NA (harms only; noncomparative)	Mortality not reported (assumed not observed) At 10 years: • Acute grade 1 to 2 urinary toxicity: 179 (78%) • Acute grade 1 to 2 rectal toxicity: 136 (59%) • Acute grade 3 to 4 urinary or rectal toxicity: 0 • Late grade 2 urinary toxicity: 21 (9%) • Late grade 2 urinary toxicity: 7 (3%) • Late grade 2 rectal toxicity: 9 (4%) • Late grade 3 to 4 urinary or rectal toxicity: 0 • No difference between dose groups (35 Gy vs. 36.25 Gy) for toxicities At 7 years: • Acute grade 2 urinary or bowel toxicity: 4% • Late grade 2 urinary toxicity: 9% • Late grade 3 urinary toxicity: 2% • Higher dose (36.25 Gy) was marginally associated with grade 2 and significantly associated with grade 3 urinary toxicity ($P \leq .05$) • Late grade 2 bowel toxicity: 4% • Late grade 3 bowel toxicity: 0 • No association with dose
Flushing Radiation Winthrop 2006 to 2010 [27-29] Single academic center in US	NA (harms only; noncomparative)	NA (harms only; noncomparative)	At 6 years: • 26 patients died (none related to prostate cancer)

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
NR			• Acute grade 2 urinary toxicities: 14 (9%) • Acute grade 2 rectal toxicities: 11 (7%) • Late grade 2 urinary toxicities: 4% 35 Gy, 9% 36.25 Gy • Late grade 3 urinary toxicities: 0 35 Gy, 2% 36.25 Gy • Late grade 2 rectal toxicities: 2% 35 Gy, 5% 36.25 Gy • Late grade 3 rectal toxicities: 0 35 Gy, 0 36.25 Gy No significant difference between doses Late grade 3 to 4 GI toxicities: 0 At 7 years: • Acute grade 3 to 4 GI or GU toxicities: 0 • Late grade 3 GU toxicity: 2% • Late grade 3 to 4 GI toxicities: 0 In a related cohort of 304 men: • Acute grade 2 urinary toxicities: 4% 35 Gy, 5% 36.25 Gy • Acute grade 2 rectal toxicities: 4% 35 Gy, 4% 36.25 Gy • Late grade 2 urinary toxicities: 2% 35 Gy, 6% 36.25 Gy • Late grade 3 urinary toxicities: 0 35 Gy, 0.5% 36.25 Gy • Late grade 2 rectal toxicities: 0 35 Gy, 3% 36.25 Gy
Freeman et al., 2015[30]	NA (harms only; noncomparative)	NA (harms only; noncomparative)	Most common acute toxicity was grade 1 urinary symptoms Late grade 3 GI toxicity: 1 (< 1%)

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
Registry for Prostate Cancer Radiosurgery (RPCR; 2010 to 2013) NR			Late grade 3 GI toxicity: 0
Fuller et al, 2018[31,32] 18 centers, including academic and community centers, in US NCT00643617	NA (harms only; noncomparative)	NA (harms only; noncomparative)	1 patient died of prostate cancer, and 19 died from unrelated causes Acute GU toxicities: 35.1% grade 2, 1.1% grade 3 Acute GI toxicities: 6.9% grade 2, 0 grade 3 Late GU toxicities at 5 years: 12.7% grade 2, 0.4% grade 3 Late GI toxicities at 5 years: 3.4% grade 2, 0 grade 3 No differences between risk groups up to 5 years Cumulative incidence of grade 2 or higher toxicity: 16.3% at 5 years, 19.2% at 10 years Cumulative incidence of grade 2 GI toxicity: 4.1% at 5 years, 1.1% at 10 years; no grade 3 GI toxicity observed
Georgetown 2008 to 2011[33-36] Single academic center in US NR	NA (harms only; noncomparative)	NA (harms only; noncomparative)	Mortality was not reported (assumed not observed) At all time points, majority of men (N = 100) had no GI or GU toxicity. • Overall, highest GI grade toxicity was grade 2 in 5% at 1 month

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
			○ 5% experienced grade 2 bowel frequency/urgency at 1 month ○ No one experienced grade 2 proctitis or rectal bleeding • Overall, highest GU grade toxicity was grade 2 in 5% at 1 month ○ 1% experienced grade 3 hematuria at each time point from 6 to 24 months (requiring TURP) ○ No one experienced grade 2 dysuria ○ 2% had grade 2 incontinence at 1 month and 1% at 18 months ○ At each of 6, 12 and 24 months, 1% grade 2 urinary frequency/urgency, with 2% at 18 months ○ Urinary retention was most common grade 2 toxicity, ranging from 35% at 1 month to 16% at 12 and 18 months In cohort of 208 men, there were 2 acute grade 2 hematuria toxicities and 5 late grade 2 and 3 grade 3 hematuria toxicities No grade 4 or 5 hematuria toxicities observed 3-year incidence of grade 2 or higher hematuria toxicity: 2.4% **Having a procedure for benign prostate hyperplasia and use of alpha reductase**

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
			inhibitors was significantly associated with hematuria incidence (*P* < .01) No association for age, race, risk initial PSA, ADT, comorbidities, or anticoagulant use In a cohort of 269 men: • Acute grade 2 rectal bleeding: 0 • Late grade 2 rectal bleeding: 4 (1.5%) • Acute or late grade 3 or higher rectal bleeding: 0 In cohort of 216 men: • Grade 2 hematuria: 0 at all time points • Grade 3 hematuria: 3.8% at 6 months, 3.6% at 9 months, 0 at all other time points • Grade 2 dysuria: 3.4% at 18 months, 0 at all other time points • Grade 2 incontinence: 3.6% at 9 months, 3.6% at 24 months, 0 at all other time points • Grade 2 urinary frequency or urgency: 10.7% at 1 month, 3.7% at 3 months, 3.8% at 6 months, 14.3% at 9 months, 17.2% at 12 months, 10.3% at 18 months, 0 at 24 months • Grade 2 urinary retention: 55.6% at 1 month, 25.9% at 3 months, 26.9% at 6 months, 35.7% at 9 months, 55.2% at 12 months, 65.5% at 18 months, 35.7% at 24 months
Glowacki et al, 2015[37] Single center in Poland	NA (harms only; noncomparative)	NA (harms only; noncomparative)	Mortality not reported (assumed not observed)

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
NR			Acute GU toxicity: 54 (41%) grade 0, 61 (47%) grade 1, 14 (10%) grade 2, 3 (2%) grade 3, 0 grade 4 Acute GI toxicity: 95 (72%) grade 0, 33 (25%) grade 1, 4 (3%) grade 2, 0 grade 3, 0 grade 4 Late GU toxicity: 86 (83%) grade 0, 17 (16%) grade 1, 1 (< 1%) grade 2, 0 grade 3, 0 grade 4 Late GI toxicity: 92 (88%) grade 0, 8 (8%) grade 1, 3 (3%) grade 2, 1 (< 1%) grade 3, 0 grade 4 **Men with diabetes were significantly more likely to experience grade 2 or higher GU toxicity**; no association with hormone therapy or age No significant association with diabetes, hormone therapy or age
Glowacki et al, 2017[38] Single center in Poland NR	NR	NR	Mortality not reported Acute GU toxicity: 45 (41%) grade 0, 48 (44%) grade 1, 13 (12%) grade 2, 3 (3%) grade 3, 0 grade 4, SBRT; 23 (21%) grade 0, 35 (33%) grade 1, 46 (43%) grade 2, 3 (3%) grade 3, 0 grade 4, cRT Acute GI toxicity: 77 (71%) grade 0, 28 (26%) grade 1, 4 (3%) grade 2, 0 grade 3, 0 grade 4, SBRT; 47 (44%) grade 0, 40 (37%) grade 1, 19 (18%) grade 2, 1 (1%) grade 3, 0 grade 4, cRT

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
			No difference between groups other than: • Significantly higher rates of no toxicity in SBRT vs. cRT (GU, *P* =.002; GI, *P* = .0001) • Significantly lower grade 2 GU toxicity in SBRT group vs. cRT (12% vs. 43%; *P* = .00) • Significantly lower grade 2 GI toxicity in SBRT group vs. cRT (3% vs. 18%; *P* = .0004) No difference by marker status
Halpern et al., 2016[39] Surveillance, Epidemiology, and End Results Program (SEER)-Medicare (2004 to 2011) NR	NR	QoL **Significantly higher rates of erectile dysfunction with SBRT compared with other RT options (16.0% vs. 11.4%, 7.3%, 4.7% and 9.8%) at 1 year; *P* < .001** **Significantly lower rates of urinary incontinence with SBRT compared with BT options (15.6% SBRT; 32.2% BT; 32.9% combination; *P* < .001) at 1 year, but more than IMRT or proton beam therapy (13.1% and 6.9%; *P* < .001)** **Significantly higher rates of erectile dysfunction with SBRT compared with other RT options (23.3% vs. 18.8%, 12.3%, 10.8% and 17.7%) at 2 years; *P* < .001** **Significantly lower rates of urinary incontinence with SBRT**	No difference for GI complications at year 1 or 2

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
		compared with BT options (23.9% SBRT; 38.6% BT; 41.7% combination; *P* < .001) at 2 years, but more than IMRT or proton beam therapy (18.8% and 10.8%; *P* < .001)	
Johansson et al., 2019 [40] Single center in Sweden NR	NA (harms only; noncomparative)	NA (harms only; noncomparative)	27 (5%) died from prostate cancer, with 115 deaths overall At 5 years, incidence of GU AEs; 8% 0, 8% 1 and 11% 2, by baseline score At 5 years, prevalence of GU AEs; 2% 0, 7% 1 and 11% 2, by baseline score At 10 years, incidence of GU AEs; 13% 0, 11% 1 and 35% 2, by baseline score At 10 years, prevalence of GU AEs; 6% 0, 7% 1 and 11% 2, by baseline score At 5 years, incidence of GI AEs grade 3 and higher; 1% 0, 5% 1, by baseline score At 5 years, prevalence of GI AEs grade 3 and higher, 0 0, 0 1, by baseline score No progress of GI morbidity was observed between 5 and 10 years No difference in risk of AEs by age, or risk group **Significantly more likely to experience GI AEs with nodal RT** **Significantly less likely to experience GI AEs if a smoker**

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
			Significantly more likely to experience GI or GU AEs if TURP, or if score of 2 for GI or score of 1 for GU at baseline, or diabetes
Katz et al., 2012[41] Single academic center in US and 10 hospitals in Spain NR	NR	QoL Patients receiving SBRT had significantly higher urinary QoL throughout follow-up with largest difference at 1 month Patients undergoing surgery had significantly lower sexual QoL at all time points At 1 month, patients undergoing surgery had significantly higher QoL than those receiving SBRT	NR
Koskela et al., 2017[42] Not clear (assumed a single center), based in Finland NR	NA (harms only; noncomparative)	NA (harms only; noncomparative)	Grade 3 or higher acute GU toxicity: 0 Intermediate grade 3 GU toxicity: 4 (2%) Intermediate grade 4 GU toxicity: 0 Grade 3 or higher acute rectal toxicity: 0 Intermediate grade 4 rectal toxicity: 0 Grade 3 infectious toxicity: 3 (1%) Grade 4 infectious toxicity: 0
Lee et al., 2016[43] Single academic center in Korea NR	OS NR Disease control **At 5 years, biochemical failure-free survival: 100% SBRT; 80.8% cRT; *P* = .03**	NR	NR

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
Loblaw et al., 2017[44] 4 centers in Canada NR	OS At 6 years: 97.1% SBRT; 95.2% BT; *P* = .46 At 6 years: 95.0% SBRT; 97.1% EBRT; *P* = .65 Disease control At 6 years, biochemical failure-free survival: 97.1% SBRT; 93.4% BT; *P* = .23 **At 6 years, biochemical failure-free survival: 100% SBRT; 85.9% EBRT; *P* = .045**	NR	NR
Ma et al., 2022[45] 2 academic centers in US NCT03541850 SCIMITAR	NA (harms only; noncomparative)	NA (harms only; noncomparative)	Worse acute GU toxicity: 43% grade 1, 9% grade 2, 1% grade 3 Worse late GU toxicity: 40% grade 1, 9% grade 2, 1% grade 3 Worse acute GI toxicity: 57% grade 1, 5% grade 2, 1% grade 3 Worse late GI toxicity: 34% grade 1, 0% grade 2, 1% grade 3 **Any grade GU toxicity, elective node RT vs. no elective node RT: OR, 10.30 (95% CI, 2.56 to 41.43)** Any grade GU toxicity, time from prostatectomy to SBRT (1 month increase): OR, 1.00 (95% CI, 0.99 to 1.11)

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
			Any grade GU toxicity, pad at baseline vs. no pad use: OR, 2.78 (95% CI, 1.02 to 7.61) Any grade GU toxicity, baseline IPSS (1 unit increase): OR, 1.12 (95% CI, 1.00 to 1.25) Any grade GI toxicity, elective node RT vs. no elective node RT: OR, 3.09 (95% CI, 0.86 to 11.2) Any grade GI toxicity, prostate bed boost vs. no prostate bed use: OR, 0.37 (95% CI, 0.12 to 1.15) Any grade GI toxicity, baseline EPIC-26 bowel score (1 unit increase): OR, 0.95 (95% CI, 0.89 to 1.02)
Mantz, 2014[46] Single center (assumed) in US NR	NA (harms only; noncomparative)	NA (harms only; noncomparative)	Mortality not reported Acute grade 1 to 2 urinary toxicity: 32% at 1 month Late grade 1 to 2 urinary toxicity: 20% at 6 months
Meier et al., 2018[47] 21 centers in US, including 1 academic center NCT00643994	NA (harms only; noncomparative)	NA (harms only; noncomparative)	Overall, 15 patients died (4.9%) Acute GU toxicity: 182 (59%) grade 1, 79 (26%) grade 2, 0 grade 3 or higher Acute GI toxicity: 169 (55%) grade 1, 25 (8%) grade 2, 0 grade 3 or higher Acute fatigue: 87 (28%) grade 1, 11 (4%) grade 2, 0 grade 3 or higher

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
			Acute dermatitis: 5 (2%) grade 1, 0 grade 2, 0 grade 3 or higher Late GU toxicity: 87 (28%) grade 1, 38 (12%) grade 2, 4 (1%) grade 3, 0 grade 4 or 5 Late GI toxicity: 38 (12%) grade 1, 6 (2%) grade 2, 0 grade 3, 0 grade 4 or 5 Late fatigue: 4 (1%) grade 1, 0 grade 2, 0 grade 3, 0 grade 4 or 5 Late dermatitis: 0, any grade 7 patients (2%) diagnosed with bladder cancer, assessed as being unrelated to treatment
Miszczyk et al., 2017[48,49] Single center in Poland NR	NA (harms only; noncomparative)	NA (harms only; noncomparative)	Grade 2 or 3 GI toxicities: 0.5% at RT end, 2.0% at 1 month, 0.9% at 4 months, 0.7% at 8 months, 0.4% at 14 months, 0.7% at 20 months, 1.2% at 26 months, 0 at 32 months, 0 at 38 months Grade 2 or 3 GU toxicities: 6.5% at RT end, 4.4% at 1 month, 2.9% at 4 months, 0.7% at 8 months, 1.6% at 14 months, 1.4% at 20 months, 2.4% at 26 months, 2.5% at 32 months, 0 at 38 months No grade 4 toxicities observed
Monaco et al., 2022[50] Single center in US NR	NR	QoL No significant difference in urinary function across time, as measured by EPIC and IPSS, between SBRT and AS	No safety outcomes reported

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
		Treatment for urinary symptoms: 35% SBRT; 24% AS; *P* < .04 No significant difference in bowel function across time, as measured by EPIC and IPSS, between SBRT and AS No significant difference in sexual function across time, as measured by EPIC and IPSS, between SBRT and AS; **however more men experienced a decline in sexual function over time in SBRT group** No difference in PDE-5 inhibitor use between groups after treatment	
Oliai et al., 2016[51-53] 1 community hospital and 1 academic center in US NR	<u>OS</u> 5-year survival, when matched by treatment year, T-stage, age, Gleason score, pretreatment PSA, ADT use: 90.8% SBRT; 88.1% IMRT; *P* = .73 5-year survival, when matched by risk group. treatment year, age, ADT use: 96.7% SBRT; 87.1% IMRT; *P* = .30 <u>Disease control</u> 5-year freedom from biochemical failure, when matched by treatment year, T-stage, age, Gleason score,	NR	No deaths from prostate cancer in either group; all deaths in SBRT were unrelated to malignancy whereas 9 of 15 in IMRT group died of cancer-related causes (not associated with prostate cancer) Metastatic progression after biochemical failure: 3 of 6 SBRT; 3 of 9 IMRT No acute or late GU toxicities higher than grade 3 in either group • All grade 3 toxicities subsided at most recent follow-up • Grade 2 toxicities persisted in 14% of patients in SBRT group and 12% in IMRT group

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
	pretreatment PSA, ADT use: 88.7% SBRT; 95.5% IMRT; *P* = .17 5-year freedom from biochemical failure, when matched by risk group. treatment year, age, ADT use: 89.7% SBRT; 90.3% IMRT; *P* = .64 A similar analysis of 270 men (not propensity-score matched) but potentially same sample as a majority) also found no difference between groups at 5 years		No acute or late GI toxicities higher than grade 2 in either group • Grade 2 toxicities persisted in 3% of patients in SBRT group and 1% in IMRT group Grade 3 erectile dysfunction persisted in 6% of patients in SBRT group and 17% in IMRT group (analysis excluded patients on long-term ADT or with grade 3 erectile dysfunction at baseline) In a cohort of 270 men (possibly including 263 in primary publication), at last follow-up in 150 men treated with SBRT (median follow-up of 45.5 months) • Grade 2 GU toxicity, 16% • Grade 3 GU toxicity, 0 • Grade 2 GI toxicity, 2.7% • Grade 3 GI toxicity, 0 • Grade 2 erectile function toxicity, 35% • Grade 3 erectile function toxicity, 6% In a cohort of 270 men (possibly including 263 in primary publication), at last follow-up in 120 men treated with IMRT (median follow-up of 53.4 months) • Grade 2 GU toxicity, 12% • Grade 3 GU toxicity, 0 • Grade 2 GI toxicity, 2.5% • Grade 3 GI toxicity, 0 • Grade 2 erectile function toxicity, 14%

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
			• Grade 3 erectile function toxicity, 68%
Pan et al., 2018[54] MarketScan Commercial Claims and Encounters database (2008 to 2015) NR	NR	Costs **Mean radiation cost to payer: $49,504 SBRT; $57,244 IMRT; *P* < .001** **Mean radiation cost to patient: $1,015 SBRT; $1,560 IMRT; *P* < .001** Mean complication cost at 2 years: $3,084 SBRT; $2,079 IMRT; *P* = .25 Mean total health care cost at 2 years: $80,786 SBRT; $77,539 IMRT; *P* = .36 Other outcomes not reported	Mortality not reported Any urinary toxicity at 6 months: 27.5% SBRT; 25.0% IMRT Any urinary toxicity at 12 months: 36.1% SBRT; 35.1% IMRT Any urinary toxicity at 24 months: 48.4% SBRT; 46.5% IMRT Any urinary toxicity at 36 months: 50.7% SBRT; 53.0% IMRT Any urinary toxicity SBRT vs. IMRT: HR, 1.08 (95% CI, 0.91 to 1.29) **Urinary obstruction or retention SBRT vs. IMRT: HR, 1.50 (95% CI, 1.15 to 1.97)** **Urinary fistula SBRT vs. IMRT: HR, 6.68 (95% CI, 1.60 to 28.0)** No difference for incontinence, bleeding or irritation, or stricture Any bowel toxicity at 6 months: 3.9% SBRT; 2.8% IMRT Any bowel toxicity at 12 months: 8.6% SBRT; 7.4% IMRT Any bowel toxicity at 24 months: 14.9% SBRT; 15.4% IMRT Any bowel toxicity at 36 months: 22.7% SBRT; 18.2% IMRT

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
			Any bowel toxicity SBRT vs. IMRT: HR, 1.11 (95% CI, 0.81 to 1.53) No difference for bleeding or proctitis, ulcer, stricture or fistula, incontinence, proctectomy or hyperbaric oxygen, or erectile dysfunction
Pasquier et al., 2019[55] 7 centers in France and Italy, including academic centers NR	NA (harms only; noncomparative)	NA (harms only; noncomparative)	Mortality was not reported (assumed not observed) Grade 2 or higher GI toxicity: 0 Grade 2 or higher GI at 3 years: 1% (95% CI, 0.1% to 5.1%) Grade 2 or higher GU toxicity: 9 (5%) Grade 2 or higher GI at 3 years: 20.8% (95% CI, 3.1% to 29.7%) **Significantly more likely to experience late grade 1 or higher GU toxicity higher dose of initial RT (< 120 Gy); HR, 2.96 (95% CI, 1.35 to 6.5)** No association between risk of toxicity for treated volume, planning target volume, or type of initial RT (external RT, BT, or BT boost)
Patel et al., 2020[56] National Cancer Database (2004 to 2016) NR	OS At 6 years, unfavorable intermediate risk: 93.3%, SBRT; 90.9% EBRT; *P* = .40; aHR, 1.09 (95% CI, 0.68 to 1.74) At 6 years, high risk: 80.8%, SBRT; 80.4% EBRT; *P* = .21;	NR	NR

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
	aHR, 0.93 (95% CI, 0.76 to 1.14) No difference when analyzed by subgroup (excluding SBRT < 7 Gy per fraction; excluding EBRT < 74 Gy if < 2 Gy per fraction; aged < 65 years; no medical comorbidities) No other outcomes of interest reported		
Paydar et al., 2016[57] Single academic center in US NR	NA (harms only; noncomparative)	NA (harms only; noncomparative)	Mortality was not reported (assumed not observed) Acute GI bowel frequency/urgency grade 0: 51% at day 7, 65% at month 1, 89% at month 3 Acute GI bowel frequency/urgency grade 1: 26% at day 7, 32% at month 1, 11% at month 3 Acute GI bowel frequency/urgency grade 2: 23% at day 7, 3% at month 1, 0 at month 3 Acute GI proctitis grade 0: 79% at day 7, 85% at month 1, 98% at month 3 Acute GI proctitis grade 1: 21% at day 7, 15% at month 1, 2% at month 3 Acute GI proctitis grade 2: 0 at all time points Acute GI rectal bleeding grade 0: 86% at day 7, 91% at month 1, 97% at month 3

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
			Acute GI rectal bleeding grade 1: 14% at day 7, 9% at month 1, 3% at month 3 Acute GI rectal bleeding grade 2: 0 at all time points Highest GI grade 0: 43% at day 7, 54% at month 1, 84% at month 3 Highest GI grade 1: 34% at day 7, 43% at month 1, 16% at month 3 Highest GI grade 2: 23% at day 7, 3% at month 1, 0 at month 3 Cumulative incidence of acute grade 2 toxicity: 23% No acute grade 3 or higher toxicities
Pryor et al., 2019[58] 5 centers in Australia, including academic centers ACTRN12615000223538 PROMETHEUS	NA (harms only; noncomparative)	NA (harms only; noncomparative)	Mortality was not reported (assumed not observed) Acute grade 2 GI toxicity: 6 (4%) Acute grade 3 GI toxicity: 0 Acute grade 2 urinary toxicity: 36 (27%) Acute grade 3 GU toxicity: 0 Late grade 2 or higher GI toxicity: 2% at 6 months, 4% at 12, 2% at 18, and 0 at 24 and 36 months Cumulative incidence of late grade 2 or higher urinary toxicity: 25% Cumulative incidence of late grade 3 urinary toxicity: 2%

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
Rana et al., 2015[59] Single center in US NR	NA (harms only; noncomparative)	NA (harms only; noncomparative)	Mortality was not reported (assumed not observed) No grade 3 or 4 urinary or rectal toxicity Grade 2 urinary toxicity: 9.9% Grade 2 rectal toxicity: 3.0%
Ricco et al., 2017[60] National Cancer Database (2004 to 2013) NR	OS At 8 years: 77.23% SBRT; 79.38%; *P* = .65 No difference between treatments when limited to patients with PSA > 10 or a Gleason score > 7 No other outcomes reported	NR	NR
Tsang et al., 2021[61] Multicenter study in UK NR	OS NR Disease control Biochemical control rate at 3 years: 95% SBRT; 90% and 100%, depending on BT dose Biochemical control rate at 5 years: 92% SBRT; 69% and 95%, depending on BT dose **Biochemical control, 19 Gy BT vs. SBRT, over 84 months: HR, 3.47 (95% CI, 1.08 to 11.13) favoring SBRT**	NR	Mortality was not reported (assumed not observed) No GI toxicities higher than grade 3 in any group Cumulative incidence of grade 2 or higher GI toxicities at 3 years: 4% SBRT; 0 and 1%, depending on BT dose Cumulative incidence of grade 2 or higher GI toxicities at 5 years: 4% SBRT; 0 and 2%, depending on BT dose **GI toxicities were significantly higher in SBRT group (*P* < .05)**

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
	Biochemical control, 26 Gy BT vs. SBRT, over 84 months: HR, 0.60 (95% CI, 0.18 to 1.97) Similar results with multivariate analysis		Maximum prevalence of grade 3 GU toxicities seen at 6 months (3%) in BT group Cumulative incidence of grade 2 or higher GU toxicities at 3 years: 6% SBRT; 7% and 4%, depending on BT dose Cumulative incidence of grade 2 or higher GU toxicities at 5 years: 6% SBRT; 30% and 5%, depending on BT dose No significant differences between SBRT and BT (*P* = .37)
Werneburg et al., 2018[62] Single academic center in US NR	NR	QoL Urinary function, measured by EPIC and IPSS was similar for all 3 groups over 4 years; however, scores on both declined initially No difference when analyzed by hormone therapy status Bowel habit scores were significantly lower in SBRT group compared with AS, but improved and were similar in both groups at year 4 **Bowel habit score at year 2, SBRT vs. AS: MD, -5.38; *P* < .001** **Bowel habit score at year 3, SBRT vs. AS: MD, -5.20; *P* < .05**	NR

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
		Bowel habit score at year 4, SBRT vs. AS in men who received hormone therapy: MD, -7.75; *P* < .05 **Sexual function score at year 1, SBRT vs. AS: MD, -26.66; *P* < .0001** **Sexual function score at year 2, SBRT vs. AS: MD, -13.99; *P* < .0001** At years 3 and 4, there were no difference between groups for sexual function scores Sexual function scores remained lower in SBRT group, regardless of hormone therapy status Erectile dysfunction was similar in SBRT groups vs. AS other than for year 2 **Erectile dysfunction score at year 2, SBRT vs. AS: MD, -3.98; *P* < .01** **Sexual function scores, SBRT without hormone therapy vs. SBRT with hormone therapy: MD, 18.45; *P* < .01**	
Yu et al., 2014[63] Chronic Conditions Warehouse (2008 to 2011)	NR	NR Costs were reported, but are outside our date cutoff of 5 years for economic outcomes	**Over 6 months, claim indicative of GU toxicity: 15.6% SBRT; 12.6% IMRT; OR, 1.29 (95% CI, 1.05 to 1.53)**

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
NR			**Over 12 months, claim indicative of GU toxicity: 27.1% SBRT; 23.2% IMRT; OR, 1.23 (95% CI, 1.03 to 1.43)** **Over 24 months, claim indicative of GU toxicity: 43.9% SBRT; 36.3% IMRT; OR, 1.38 (95% CI, 1.12 to 1.63)** **Claim indicative of late GU toxicity 13 to 24 months after treatment: OR SBRT vs. IMRT, 1.33 (95% CI, 1.06 to 1.59)** **SBRT was also more likely to be significantly associated with claims for diagnostic procedures to investigate incontinence or obstruction and claims for urethritis, urethral strictures, and bladder outlet obstruction** **Over 6 months, claim indicative of GI toxicity: 5.8% SBRT; 4.1% IMRT; OR, 1.42 (95% CI, 1.00 to 1.85)** Over 12 months, claim indicative of GI toxicity: 12.2% SBRT; 11.6% IMRT; OR, 1.06 (95% CI, 0.82 to 1.29) Over 24 months, claim indicative of GI toxicity: 21.2% SBRT; 22.6% IMRT; OR, 0.92 (95% CI, 0.71 to 1.12) No significant difference between groups for other toxicities or any toxicities at 12 or 24 months. **At 6 months, SBRT was associated with higher rates of any toxicities (OR, 1.22; 95% CI, 1.02 to 1.41)**

Note. [a] Bold text indicates statistically significant findings.
Abbreviations. AE: adverse event; aHR: adjusted hazard ratio; AS: active surveillance; CI: confidence interval; cRT: conventional radiation therapy; EBRT: external beam radiation therapy; EPIC: Expanded Prostate Inventory Composite; GI: gastrointestinal; GU: genitourinary; IPSS: International Prostate Symptom Score; MD: mean difference; NA: not applicable; NR: not reported; OR: odds ratio; OS: overall survival; RT: radiotherapy: SBRT: stereotactic body radiation therapy; TURP: transurethral resection of prostate.

Lung Cancer

Table C22. Evidence Tables for Nonrandomized and Registry-based Studies[a]

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
Berkovic et al., 2020[64] Single academic center in Belgium NR	NA (harms only; noncomparative)	NA (harms only; noncomparative)	Acute grade 2 radiation pneumonitis: 2 (2%) Acute grade 3 radiation pneumonitis: 1 (1%) Late grade 3 radiation pneumonitis: 2 (2%) Late grade 4 radiation pneumonitis: 1 (1%) (subsequently died of possibly treatment related RT-induced pulmonary hemorrhage 3 months after SBRT)
Davis et al., 2015[65] RSSearch registry, including 18 sites and academic centers in US and Germany (2004 to 2014) NCT01885299	NA (harms only; noncomparative)	NA (harms only; noncomparative)	No acute or late grade 3 or higher toxicities Acute grade 2 cough: 1 (<1%) Late grade 2 cough: 1 (<1%) Late grade 2 dyspnea: 2 (2%) Late grade 2 pain: 1 (<%) Late grade 2 pneumonitis: 1 (<1%)
Duijm et al., 2018[66] 2 centers in Netherlands (1 academic) NR	NA (harms only; noncomparative)	NA (harms only; noncomparative)	Acute grade 2 esophageal toxicity: 7 (3%) Acute grade 3 and higher esophageal toxicity: 0 Late grade 2 esophageal toxicity: 0 Late grade 3 and higher esophageal toxicity: 0

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
Filippi et al., 2016[67] Single academic center in Italy NR	OS At 1 year, 89% SBRT; 96% surgery; At 2 years, 77% SBRT; 82% surgery; SBRT vs. surgery: aHR, 1.71 (95% CI, 0.82 to 3.54) PFS **Recurrence, SBRT vs. surgery: HR, 2.44 (95% CI, 1.51 to 3.94); aHR, 2.78 (95% CI, 1.67 to 4.62)**	NR	Grade 2 pulmonary toxicity: 14% in SBRT group Grade 2 radiological lung toxicity: 28% in SBRT group Grade 3 radiological lung toxicity: 14% in SBRT group Grade 3 chest wall pain: 4% in SBRT group Grade 2 skin toxicity: 4% in SBRT group In surgery group, no major complications and 1 death (< 1%) with 30 days
Fleming et al., 2017[68] Single center in US NR	OS **Median: 26.2 months SBRT; 9.0 months cRT; *P* < .001** PFS NR Disease control At 6 months, local failure: 5.8% SBRT; 31.5% cRT At 12 months, local failure: 19.5% SBRT; 43.2% cRT **Local control, SBRT vs. cRT; HR, 0.47 (95% CI, 0.30 to 0.76) univariate; HR, 0.54 (95% CI, 0.32 to 0.92) multivariate**	**NR**	NR
Guckenberger et al., 2009[69] Single academic center in Germany NR	NA (harms only; noncomparative)	NA (harms only; noncomparative)	Acute grade 2 pneumonitis: 19 (12%) Acute grade 3 pneumonitis: 1 (< 1%) Acute grade 2 pneumothorax: 2 (1%) Acute grade 3 pneumothorax: 0

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
			Acute grade 2 pleural effusion: 2 (1%) Acute grade 3 pleural effusion: 0 Late grade 2 dyspnea: 3 (2%) Late grade 3 dyspnea: 0 Late grade 2 pneumothorax: 2 (1%) Late grade 3 pneumothorax: 0 Late grade 2 esophageal ulceration: 0 Late grade 3 esophageal ulceration: 1 (< 1%) No grade 4 or 5 toxicities
Helou et al, 2017[70] Not clear NR	NA (harms only; noncomparative)	NA (harms only; noncomparative)	Grade 2 radiation pneumonitis: 8 (7%) Grade 3 radiation pneumonitis: 1 (< 1%) Grade 5 radiation pneumonitis: 1 (< 1%)
Jacobs et al., 2020[71] National Cancer Database (2004 to 2015) NR	OS **Death, SBRT vs. cRT: HR, 0.79 (95% CI, 0.71 to 0.87)** **Death, SBRT vs. HFRT: HR, 0.57 (95% CI, 0.50 to 0.66)** 2-year survival rates: 54.2% SBRT, 43.3% cRT, 34.0% HFRT 5-year survival rates: 22.0% SBRT, 18.7% cRT, 9.4% HFRT For primary lung tumors > 5cm • Death, SBRT vs. cRT: HR, 1.07 (95% CI, 0.71 to 1.61) • Death, SBRT vs. HFRT: HR, 0.59 (95% CI, 0.36 to 0.97) For tumors invading chest wall	NR	NR

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
	• Death, SBRT vs. cRT: HR, 1.02 (95% CI, 0.82 to 1.27) • Death, SBRT vs. HFRT: HR, 0.68 (95% CI, 0.52 to 0.90) For multifocal tumors in same lobe • Death, SBRT vs. cRT: HR, 0.81 (95% CI, 0.68 to 0.97) • Death, SBRT vs. HFRT: HR, 0.67 (95% CI, 0.51 to 0.87)		
Kanzaki et al., 2020[72] Single academic center in Japan NR	OS At 3 years: 52% SBRT; 77% PM; *P* = .10 PFS **At 3 years: 11% SBRT; 42% PM; *P* = .01** Disease control At 3 years, local control: 92% SBRT; 88% PM; *P* = .48	NR	NR (reported narratively but not by grade)
Lagerwaard et al., 2012[73] Single academic center in Netherlands NR	NA (harms only; noncomparative)	NA (harms only; noncomparative)	Grade 1 to 2 early side effects reported were fatigue (25%), cough (14%), local chest wall pain (11%), and dyspnea (10%) Late grade 3 or higher radiation pneumonitis: 4 (2%) Rib fractures: 5(3%)
Lee et al. 2018[74] 1 academic center in South Korea NR	OS SBRT vs. surgery: HR, 0.67 (95% CI, 0.19 to 2.35) univariate; HR, 1.58 (95% CI, 0.31 to 8.00) multivariate At 1 year, OS: 79.5% SBRT; 95.0% surgery; *P* = .53 At 2 years, OS: 68.2% SBRT; 81.8% surgery; *P* = .53	NR	Grade 2 radiation pneumonitis: 24% of SBRT group Grade 3 radiation pneumonitis: 5% of SBRT group Grade 2 rib fracture: 9% of SBRT group Grade 2 chest wall pain: 9% of SBRT group Grade 3 nausea: 3% of surgery group

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
	In SBRT group, patients with synchronous metastases had lower OS than people without (*P* = .03); but no differences between SBRT and surgery PFS SBRT vs. surgery: **HR, 0.46 (95% CI, 0.23 to 0.90) univariate;** HR, 0.80 (95% CI, 0.35 to 1.80) multivariate At 1 year, PFS: 23.8% SBRT; 51.1% surgery; *P* value NR At 2 years, PFS: 11.9% SBRT; 46.0% surgery; *P* value NR No difference between treatments in patients with or without synchronous metastases Disease control Local recurrence: 4 (19%) SBRT; 2 (7%) surgery At 1 year, local control: 83.5% SBRT; 96.6% surgery; *P* = .16 At 2 years, local control: 75.2% SBRT; 91.5% surgery; *P* = .16		
Lee et al., 2021[75] Single academic center in Korea NR	NA (harms only; noncomparative)	NA (harms only; noncomparative)	Acute grade 3 and higher cough (combined SBRT): 0 Acute grade 3 and higher dyspnea (combined SBRT): 0 Acute grade 3 and higher chest wall pain (combined SBRT): 0

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
			Chronic grade 3 and higher cough (combined SBRT): 1 of 80 (1.3%) Chronic grade 3 and higher dyspnea (combined SBRT): 4 of 80 (5.0%) Chronic grade 3 and higher chest wall pain (combined SBRT): 0 1 patient experienced chronic grade 5 dyspnea
Littau et al., 2022[76] National Cancer Database (2004 to 2016) NR	OS **Death, surgery vs. SBRT: HR, 0.35; 95% CI, 0.33 to 0.36** **Death, sublobar surgery vs. SBRT: HR, 0.51; 95% CI, 0.40 to 0.55** **Death, lobectomy vs. SBRT: HR, 0.32; 95% CI, 0.31 to 0.34** **Median overall survival: 57.5 months, SBRT; 98.7 months, surgery; *P* < .001** No other outcomes of interest reported	NR	NR
Lo et al., 2020[77] National Cancer Database (2004 to 2015) NR	OS **Mortality, SBRT vs. surgery: HR, 1.61 (95% CI, 1.36 to 1.92)** **Median survival: 34.6 months SBRT; 57.2 months surgery; *P* < .001** **5-year OS: 25% SBRT; 48% surgery: *P* < .0001**	NR	NR
Nelson et al., 2019[78] Single academic center in US	Disease control **Local recurrence, SBRT vs. surgery: HR, 3.28 (95% CI, 1.53 to 7.04)**	NR	NR

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
NR	At 2 years, local treatment failure: 29.4% SBRT; 14.1% surgery; *P* value NR (CIs overlap) At 5 years, local treatment failure: 37.3% SBRT; 18.4% surgery; *P* value NR (CIs overlap) Subgroup analysis did not identify any group in which SBRT provided significant improvement		
Osti et al., 2018[79] 1 academic center in Italy NR	NA (harms only; noncomparative)	NA (harms only; noncomparative)	Acute grade 3 pneumonitis: 6 (4%) Acute grade 3 dysphagia: 0 Acute grade 3 cough: 0 Acute grade 3 chest pain: 1 (< 1%) Acute grade 3 dyspnea: 0 Acute grade 3 skin erythema: 0 Acute grade 3 dysphagia: 0 Acute grade 5 pneumonitis: 1 (< 1%) Late grade 3 lung fibrosis: 11 (7%) Late grade 3 rib fracture: 2 (2%) No grade 4 toxicities (acute or late)
Rosen et al., 2016[80] National Cancer Database (2008 to 2012) NR	OS In first 7.5 months from diagnosis, lobectomy vs. SBRT: HR, 1.14 (0.86 to 1.50) **After 7.5 months from diagnosis, lobectomy vs. SBRT: HR, 0.38 (0.33 to 0.43)**	NR	NR

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
	Similar results seen when analyzed by T stage and when propensity matched **5-year survival: 29% SBRT; 59% surgery: *P* < .001** **Median survival: 39 months SBRT; 71 months surgery; *P* < .001**		
Scotti et al., 2019[81] 2 academic centers in Italy NR	OS In operable patients, SBRT vs. surgery: HR, 1.68 (95% CI, 0.72 to 3.90) PFS In operable patients, SBRT vs. surgery: HR, 1.57 (95% CI, 0.68 to 3.64)	NR	Nr
Sharma et al., 2019[82,83] Single center in Netherlands NR	NA (harms only; noncomparative)	NA (harms only; noncomparative)	No treatment-related death Acute grade 2 toxicities: < 5% Acute grade 3 toxicities: 5 (2%); 3, dyspnea, 1 chest pain, both 1 Late grade 2 cough: 7% Late grade 2 fatigue: 6% No grade 4 or 5 events
Takeda et al., 2010[84] Single center in Japan NR	NA (harms only; noncomparative)	NA (harms only; noncomparative)	Grade 2 radiation pneumonitis: 21 (16%) Grade 3 radiation pneumonitis: 7 (5%) No pretreatment clinical or dosimetric variables were associated with radiation pneumonitis; early graphical appearance of radiation pneumonitis significantly associated with severity
Wegner et al., 2020[85]	OS	NR	NR

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
National Cancer Database (2004 to 2015) NR	**Mortality, cRT vs. SBRT: HR, 1.21 (95% CI, 1.00 to 1.46); *P* = .046** **Median survival: 34.7 months SBRT; 23.7 months cRT; *P* = .02**		
Yamamoto et al. 2020[86] 68 institutions in Japan NR	NA (harms only; noncomparative)	NA (harms only; noncomparative)	10 (< 1%) patients died due to AEs from SBRT Grade 2 or higher lung AEs: 112 (11.7%) Grade 3 or higher lung AEs: 26 (2.5%) Grade 5 AEs: 10 (< 1%), comprising 3 grade 5 hemoptysis, 7 grade radiation pneumonitis

Note. [a] Bold text indicates statistically significant findings.
Abbreviations. AE: adverse events; aHR: adjusted HR; CI: confidence interval; cRT: conventional radiotherapy; HFRT: hypofractionated radiotherapy; HR: hazard ratio; NA: not applicable; NR: not reported; OS: overall survival; PFS: progression-free survival; PM: pulmonary metastasectomy.

Colorectal Cancer

No eligible studies identified.

Uterine Cancer

No eligible studies identified.

Melanoma

No eligible studies identified.

Renal Cancer

Table C23. Evidence Tables for Nonrandomized and Registry-based Studies[a]

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
Renal cancer			
Siva et al., 2022[87] International Radiosurgery Consortium of the Kidney (IROCK) NR	NA (harms only; noncomparative)	NA (harms only; noncomparative)	None of the 190 participants experienced grade 3 toxic effects or treatment-related deaths 1 patient developed a treatment-related acute grade 4 duodenal ulcer and late grade 4 gastritis after SBRT
Uhlig et al., 2020[88] National Cancer Database (2004 to 2015) NR	OS At 3 years: 76% SBRT; 87% TA; 84% CA; 88% PN At 5 years: 58% SBRT; 76% TA; 77% CA; 84% PN **PN vs. SBRT: HR, 0.29 (95% CI, 0.19 to 0.46) favoring PN** **CA vs. SBRT: HR, 0.40 (95% CI, 0.26 to 0.60) favoring CA** **TA vs. SBRT: HR, 0.46 (95% CI, 0.31 to 0.67) favoring TA**	NR	NR

Note. [a] Bold text indicates statistically significant findings.
Abbreviations. CA: cryoablation; CI: confidence interval; HR: hazard ratio; NR: not reported; OS: overall survival; PN: partial nephrectomy; SBRT: stereotactic body radiation therapy; TA: thermal ablation.

Pancreatic Cancer

Table C24. Evidence Tables for Nonrandomized and Registry-based Studies[a]

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
de Geus et al., 2017[89] National Cancer Database (2004 to 2012) NR	OS **Median, unmatched: 13.9 months SBRT; 9.9 months CT; 10.9 months cRT; 12.0 months IMRT; *P* < .001** **Median, matched: 13.9 months SBRT; 10.2 months CT; *P* < .001** **Median, matched: 13.9 months SBRT; 11.6 months cRT; *P* = .02** **Median, matched: 13.9 months SBRT; 12.2 months IMRT; *P* = .0492** Median, matched: 14.8 months SBRT with multi-agent CT; 12.9 months multi-agent CT alone; *P* = .09	NR	NR
Moningi et al., 2022[90] Surveillance, Epidemiology, and End Results (SEER) and Texas Cancer Registry, linked with Medicare; MarketScan Commercial Claims and Encounter database NR	NR	Health resource use and costs **Median 12-month total payments per patient (fee-for-service Medicare insurance coverage; IQR): $80,282 SBRT ($45,244 to $93,684); $57,502 for CT ($34,179 to $84,888); $66,366 cRT ($60,645 to $118,298); *P* < 0.001** **Median payments per patient (under employer-based insurance coverage; IQR): $212,579 SBRT ($144,177 to $303,268) $127,438 CT ($76,001 to $194,98); $172,547 cRT ($117,987 to $248,735); *P* < .001**	**GI bleed, SBRT vs. CT: HR, 4.13 (95% CI, 2.58 to 6.61)** **GI stricture, SBRT vs. CT: HR, 1.58 (95% CI, 1.18 to 2.21)** In older patients **Gastric bleeding with ulcer or perforation: 11.4% SBRT; 3.1% CT; 8.1% cRT; *P* < .01 across all 3;** *P* = .24 SBRT vs. cRT **Duodenal bleeding with ulcer or perforation: 14.3% SBRT; 4.2% CT;**

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
			13.0% cRT; *P* < .01 across all 3; *P* = .71 SBRT vs. cRT **Other intestinal bleeding with ulcer or perforation: NR SBRT; NR CT; 1.2% cRT; *P* = .03 across all 3;** *P* = .06 SBRT vs. cRT Duodenal stricture: 14.3% SBRT; 8.5% CT; 10.5% cRT; *P* = .07 across all 3; *P* = .23 SBRT vs. cRT **Biliary stricture: 42.9% SBRT; 28.4% CT; 31.8% cRT; *P* < .01 across all 3; *P* = .02 SBRT vs. cRT** **Biliary fistula: NR SBRT; NR CT; 0.7% cRT; *P* < .01 across all 3;** *P* = .05 SBRT vs. cRT In younger patients **Gastric bleeding with ulcer or perforation: 7.9% SBRT; 2.4% CT; 7.8% cRT; *P* < .01 across all 3;** *P* = .95 SBRT vs. cRT **Duodenal bleeding with ulcer or perforation: 6.9% SBRT; 3.0% CT; 7.9% cRT; *P* < .01 across all 3;** *P* = .73 SBRT vs. cRT

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
			Other intestinal bleeding with ulcer or perforation: 0 SBRT;0.4% CT; 1.3% cRT; *P* = .02 across all 3; *P* = .63 SBRT vs. cRT **Duodenal stricture: 7.9% SBRT; 4.3% CT; 6.8% cRT; *P* = .01 across all 3;** *P* = .67 SBRT vs. cRT **Biliary stricture: 28.7% SBRT; 20.3% CT; 24.6% cRT; *P* = .01 across all 3;** *P* = .36 SBRT vs. cRT **Biliary fistula: 1% SBRT; 0.1% CT; 0.5% cRT; *P* = .03 across all 3;** *P* = .41 SBRT vs. cRT
Zhong et al., 2017[91] National Cancer Database (2004 to 20123 NR	OS **At 2 years, unmatched: 20.3% SBRT; 16.3% cRT; HR, 0.84 (95% CI, 0.75 to 0.93) favoring SBRT** **At 2 years, matched: 21.7% SBRT; 16.5% cRT; *P* = .001** **Median: 13.9 months SBRT; 11.6 months cRT; *P* < 001** **Significantly better survival with SBRT for people aged 69 and younger, tumor stages T3 or T4, nodal stage N1, tumor size of 3 cm or less, no comorbidities, no surgery and CT use**	NR	NR

Note. [a] *Bold text indicates statistically significant findings.*
Abbreviations. cRT: conventional RT; CT: chemotherapy; GI: gastrointestinal; IMRT: intensity-modulated radiotherapy; IQR; interquartile range; NCT: US National Clinical Trial; NR: not reported; SBRT: stereotactic body radiation therapy.

Head and Neck Cancer

Table C25. Evidence Tables for Nonrandomized and Registry-based Studies[a]

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
Al-Mamgani et al., 2013[92] Single center in Netherlands NR	OS OS at 3 years: 81% SBRT; 83% BT; *P* = .83 Progression and PFS Disease-free survival at 3 years: 92% SBRT; 86% BT; *P* = .15	Disease control Local control at 3 years: 97% SBRT; 94% BT; *P* = .33 Local control, T1 tumors at 3 years: 100% SBRT; 96% BT; *P* = .16 Local control, T2 tumors at 3 years: 95% SBRT; 92% BT; *P* = .51 Local failure: 4% SBRT; 6% BT; *P* value not reported Quality of life Quality of life deteriorated in both groups, with worst around end of treatment, but returned to baseline levels at around 3 to 6 months after treatment No difference between groups at any time point	Acute grade 3 toxicity: 23% SBRT; 31% BT; *P* = .14 Acute grade 3 dysphagia: 17% SBRT; 20% BT; *P* = .47 Late grade 3 toxicity: 5% SBRT; 4% BT; *P* = .70
Ozyigit et al., 2011[93]	OS Cancer-specific survival at 2 years: 64% SBRT; 47% conformal RT; *P* = .40	Disease control	**Late grade 3 or higher toxicity: 21% SBRT; 48% conformal RT; *P* = .04**

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
Single academic center in Turkey NR		Local control at 2 years: 82% SBRT; 80% conformal RT; *P* = .57	Grade 3 and higher toxicities included cranial neurophathy, carotid blow-out syndrome, and brain necrosis in SBRT group; brain necrosis, trismus, cranial neuropathy, and carotid blow-out syndrome in conformal RT group Fatal complications: 12.5% SBRT; 14.8% conformal RT; *P* = .80
Vargo et al., 2018[94] 8 academic centers in US NR	OS **At 2 years: 16.3% SBRT; 35.4% IMRT; *P* < .001** Median: 7.8 months SBRT; 13.3 months IMRT No difference in multivariate analysis (HR, 0.88; 95% CI, 0.70 to 1.10) In patients with unresectable tumors with an intertreatment interval >2 years or those with ≤ 2 years and without feeding tube or tracheostomy dependence (RPA Class II) had improved survival with IMRT when compared with SBRT (18.6% SBRT; 39.1% IMRT; *P* < .001)	Disease control **Cumulative incidence of locoregional failure: 57.0% SBRT; 45.4% IMRT; *P* = .01** No difference in multivariate analysis (HR, 1.15; 95% CI, 0.89 to 1.50) **Patients in RPA Class 2 also had less locoregional failure with IMRT than with SMRT (*P* = .006)**	Acute grade 3 or higher toxicity: 11.7% SBRT; 16.6% IMRT; *P* = 15 **Acute grade 4 or higher toxicity: 0.5% SBRT; 5.1% IMRT; *P* < .01 (fistula development, intensive care unit admission, or life-threatening bleeding)** Acute grade 5 deaths: 0.5% SBRT; 1.8% IMRT; *P* = .42 (bleeding) Late grade 3 or higher toxicity: 11.6% SBRT; 12.4% IMRT: *P* = 69 Cumulative incidence of progression or death: 79.2% SBRT; 73.1% IMRT
Yamazaki et al., 2017[95,96] 3 centers, including an academic center, in Japan NR	OS At 1 year: 55% SBRT; 51% IMRT; 68% charged particle RT; *P* = .15; HR, 1.49 (95% CI, 0.86 to 2.57) **When matched: HR, 0.35 (95% CI, 0.13 to 0.94) favoring charged particle RT**	Disease control Local control at 1 year: 67.1% photon RT (SBRT or IMRT); 66.9% charged particle RT; *P* value NR (CIs overlap)	**Grade 3 or higher toxicity: 21% SBRT; 23% IMRT; 46% charged particle RT; *P* = .04; HR univariate, 2.71 (95% CI, 1.15 to 6.39);** HR multivariate, 1.2 (95% CI, 0.42 to 3.41) There were 13 (9%: 10 bleeding, 1 ulceration, 1 mucositis, 1 trismus and abscess) grade 5 toxicities in photon RT group, whereas 4 (15%: 2 bleeding, 1 skin/bone necrosis and infection, 1 soft

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
			tissue necrosis and infection) in charged particle RT group

Note. [a] *Bold text indicates statistically significant findings.*
Abbreviations. BT: brachytherapy; CI: confidence interval; HR: hazard ratio; IMRT: intensity-modulated radiation therapy; OS: overall survival; PFS: progression-free survival; RT: radiation therapy; SBRT: stereotactic body radiation therapy.

Ovarian Cancer

No eligible studies identified.

Liver Cancer

Table C26. Evidence Tables for Nonrandomized and Registry-based Studies[a]

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
Andratschke et al., 2018[97] 17 centers in Germany and Switzerland NR	NA (harms only; noncomparative)	NA (harms only; noncomparative)	Acute grade 1 to 2 toxicity: 23% (fatigue, nausea, diarrhea) Acute grade 3 toxicity: < 1% (gastric ulcer) Late grade 1 to 2 toxicity: 10% Acute grade 3 toxicity: 1% (radiation hepatitis, liver fibrosis, consecutive varicosis and bleeding, necrotic reaction of metastases) No grade 4 or 5 toxicities
Berber et al., 2013[98] 4 academic centers in US NR	NA (harms only; noncomparative)	NA (harms only; noncomparative)	Any grade 2 toxicity: 3 (2%) Any grade 3 toxicity: 5 (3%) No grade 4 or 5 toxicities

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
Bettinger et al., 2019[99] 15 centers, including academic centers across Germany, UK, Italy, Switzerland, Japan, and South Korea NR	<u>OS</u> Median OS, unmatched: 17.0 months SBRT; 8.8 months sorafenib; *P* value NR **Median OS, matched: 16.0 months SBRT; 9.6 months sorafenib; HR, 0.53 (95% CI, 0.36 to 0.77)** **In univariate and multivariate analysis, SBRT was significantly associated with survival vs. sorafenib (HR, 0.57; 95% CI, 0.40 to 0.81, univariate; HR, 0.53; 95% CI, 0.36 to 0.77, multivariate)** **Similar pattern seen in patients with extrahepatic metastases and portal vein thrombosis** (although no difference for portal vein thrombosis after matching) <u>Progression and PFS</u> **Median PFS, unmatched: 9.0 months SBRT; 4.0 months sorafenib; *P* < .001** **Median PFS, matched: 9.0 months SBRT; 6.0 months sorafenib; HR, 0.59 (95% CI, 0.42 to 0.86)**	NR	In sorafenib group: • Any grade hand-foot skin reaction: 281 (31%); 104 grade 2, 73 grade 3, 2 grade 4 • Any grade diarrhea: 354 (39%); 102 grade 2, 99 grade 3, 10 grade 4 • Any grade obstipation: 16 (2%); 5 grade 2, 0 grade 3, 0 grade 4 • Any grade fatigue: 264 (29%); 96 grade 2, 59 grade 3, 5 grade 4 • Any grade weight loss: 171 (19%); 54 grade 2, 14 grade 3, 5 grade 4 • Any grade hypertension: 120 (13%); 50 grade 2, 17 grade 3, 0 grade 4 • Any grade mucositis: 42 (5%); 18 grade 2, 6 grade 3, 0 grade 4 • Any grade nausea and vomiting: 68 (7%); 26 grade 2, 5 grade 3, 0 grade 4 In SBRT group: • Any grade fatigue: 1 (1%); 0 grade 2, 0 grade 3, 0 grade 4 • Any grade increase in ALT/AST: 0; 0 grade 2, 0 grade 3, 0 grade 4 • Any grade increase in bilirubin: 9 (7%); 2 grade 2, 7 grade 3, 0 grade 4 • Any grade increase in alkaline phosphatase: 2 (2%); 2 grade 2, 0 grade 3, 0 grade 4 • Any grade increase in γ-glutamyl transferase: 3 (3%); 2 grade 2, 1 grade 3, 0 grade 4 • Any grade duodenitis or gastrointestinal bleeding: 3 (3%); 2 grade 2, 1 grade 3, 0 grade 4 • Any grade liver abscess: 1 (< 1%); 0 grade 2, 0 grade 3, 1 grade 4 • Any grade RILD: 1 (< 1%); 0 grade 2, 1 grade 3, 0 grade 4

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
			• Any grade hepatic decompensation: 3 (3%); 0 grade 2, 2 grade 3, 1 grade 4 • Any grade cholangitis: 1 (< 1%); 0 grade 2, 1 grade 3, 0 grade 4
Bujold et al., 2013[100-102] Single academic center in Canada NCT00914355 and NCT00152906	NA (harms only; noncomparative)	NA (harms only; noncomparative)	No grade 3 liver toxicity (other than 2 patients who did not complete treatment) No classic RILD observed Any grade 3 toxicity: 27 (27%) Any grade 4 toxicity: 3 (3%) Any grade 5 toxicity: 7 (7%) Grade 3 fatigue: 1 (1%) Grade 3 AST/ALT: 11 (11%) Grade 3 bilirubin: 3 (3%) Grade 4 bilirubin: 2 (2%) Grade 3 creatinine: 1 (1%) Grade 3 hemoglobin: 2 (2%) Grade 3 leukocytes: 1 (1%) Grade 3 platelets: 9 (9%) Grade 5 cholangitis: 1 (1%) Grade 3 gastritis/bleed: 1 (1%) Grade 5 gastritis/bleed: 1 (1%) Grade 3 liver failure: 1 (1%) Grade 4 liver failure: 1 (1%) Grade 5 liver failure: 5 (5%) Grade 3 nausea/vomiting: 1 (1%)

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
			Grade 3 chest wall pain: 1 (1%) At 3 months, Child-Turcotte-Pugh deterioration: 46% by score, 29% by class At 12 months, Child-Turcotte-Pugh deterioration: 17% by score, 6% by class Dose was significantly associated with increased toxicity; however no longer significant on univariate and multivariate analysis On univariate analysis, baseline Child-Pugh score and baseline albumin-bilirubin score, SBRT liver dose were significantly associated with toxicity On multivariate analysis, baseline albumin-bilirubin score, SBRT liver dose remained significantly associated with toxicity When combined with a cohort from another center: • 15.9% of 214 evaluable patients experienced a worsening Child-Pugh score • 21.2% of 241 evaluable patients had a worsening in albumin-bilirubin grade • Grade 3 and higher biochemical: 73 (25%) • Grade 3 and higher biliary: 3 (1%); 1 grade 4 and 1 grade 5 toxicity • Grade 3 and higher luminal gastrointestinal: 4 (1%); 1 grade 5 toxicity • Grade 3 and higher ascites: 23 (8%); all grade 3 • No classic RILD
Hara et al., 2019[103] Two centers (1 academic) in Japan NR	OS At 3 years, unmatched: 63.6% SBRT; 72.2% RFA; *P* = .11 At 3 years, matched: 70.4% SBRT; 69.1% RFA; *P* = .86	NR	Child-Pugh deterioration of 2 or more: 8.2% SBRT; 10.2% RFA; *P* = .23 According to Child-Pugh class and liver failure death, SBRT-HFRT group had significantly worse outcomes (*P* < .01)

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
	At 3 years, cancer-specific mortality, unmatched: 18.8% SBRT; 10.5% RFA; *P* = .07 At 3 years, cancer-specific mortality, matched: 11.8% SBRT; 12.8% RFA; *P* = .99 At 3 years, liver failure mortality, unmatched: 7.1% SBRT; 10.4% RFA; *P* = .48 At 3 years, liver failure mortality, matched: 7.6% SBRT; 9.2% RFA; *P* = .52 At 3 years, nonspecific mortality, unmatched: 10.5% SBRT; 7.4% RFA; *P* = .37 At 3 years, nonspecific mortality, unmatched: 10.3% SBRT; 8.9% RFA; *P* = .70 Disease control **At 3 years, local recurrence, unmatched: 5.3% SBRT; 12.9% RFA; *P* < .001** **Significantly lower for SBRT for HCC attached to vessels and those adjacent to vessels** **At 3 years, local recurrence, matched: 6.4% SBRT; 20.2% RFA; *P* < .01**		In RFA group, 1 case of grade 5 hemorrhagic gastric ulcer and 1 case of grade 5 peritonitis No grade 5 toxicities in SBRT group

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
	At 3 years, intrahepatic recurrence, unmatched: 59.3% SBRT; 57.6% RFA; *P* = .64		
Honda et al., 2013[104] Single academic center in Japan NR	OS At 1 year: 100% TACE-SBRT; 88.9% TACE At 2 years: 100% TACE-SBRT; 73.6% TACE At 3 years: 100% TACE-SBRT; 66.1% TACE; *P* = .47 Median OS: not reached for TACE-SBRT (no deaths); 40.9 months In treatment-naïve patients, disease-free survival: • At 1 year: 71.4% TACE-SBRT; 24.8% TACE • At 2 years: 42.0% TACE-SBRT; 14.2% TACE • At 3 years: 0 TACE-SBRT; 7.0% TACE; *P* = .03 overall Median disease-free survival: 15.2 months TACE-SBRT; 4.2 months TACE Disease control **Complete response: 29 (96.3%) TACE-SBRT; 1 (3.3%) TACE; *P* < .001**	NR	Grade 2 leukocytopenia: 8 (27%) TACE-SBRT; 8 (21%) TACE Grade 3 leukocytopenia: 2 (7%) TACE-SBRT; 0 TACE Grade 2 thrombocytopenia: 8 (27%) TACE-SBRT; 8 (21%) TACE Grade 3 thrombocytopenia: 1 (3%) TACE-SBRT; 3 (8%) TACE Grade 2 low hemoglobin: 3 (10%) TACE-SBRT; 2 (5%) TACE Grade 3 low hemoglobin: 0 TACE-SBRT; 0 TACE Grade 2 hyperbilirubinemia: 3 (10%) TACE-SBRT; 2 (5%) TACE Grade 3 hyperbilirubinemia: 0 TACE-SBRT; 2 (5%) TACE Grade 2 high serum transaminases: 0 TACE-SBRT; 5 (13%) TACE Grade 3 high serum transaminases: 0 TACE-SBRT; 0 TACE Grade 2 high serum alkaline phosphatase: 0 TACE-SBRT; 4 (10%) TACE Grade 3 high serum alkaline phosphatase: 0 TACE-SBRT; 0 TACE No grade 4 toxicities

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
Jacob et al., 2015[105] Single academic center in US NR	OS No 30-day mortality in either group 90-day mortality: 0, TACE-SBRT; 7 (6%) TACE; *P* = .35 **Median survival: 33 months, TACE-SBRT; 20 months, TACE; *P* = .02** Disease control **Local recurrence: 4 (10.8%) TACE-SBRT; 32 (25.8%) TACE; *P* = .04**	NR	1 patient died within 4 weeks of SBRT (pulmonary sepsis) Grade 2 gastrointestinal toxicity: 1 (3%) TACE-SBRT Grade 3 gastrointestinal toxicity: 1 (3%) TACE-SBRT Grade 2 bone and soft tissue toxicity: 1 (3%) TACE-SBRT No grade 2 or higher hematologic or hepatic toxicities in TACE-SBRT group
Jeong et al., 2021[106,107] Single center in South Korea NR	OS **At 4 years: 64.1% SBRT; 78.1% RFA; *P* = .01** OS over 4 years, multivariate analysis: HR, 1.46 (95% CI, 0.85 to 2.52) Progression and PFS Local progression by lesion: 4.1% SBRT; 6.3% RFA; *P* = .53 Progression over 4 years: HR, 0.46 (95% CI, 0.15 to 1.45) Disease control Intrahepatic recurrence: 27.6% SBRT; 36.7% RFA; *P* = .53 Intrahepatic recurrence over 4 years: HR, 0.82 (95% CI, 0.56 to 1.18) Perivascular location was a significant negative prognostic	NR	In comparative analysis of SBRT and RFA (N = 266): • 1 patient died due to hepatic failure of unknown cause at 4 months after SBRT • No grade 2 or higher fatigue in either group • No grade 2 or higher anorexia in either group • No grade 3 or higher nausea in either group; 3 cases of grade 2 nausea (3%) in SBRT group • No grade 2 or higher vomiting in either group • No grade 3 or higher AST/ALT elevation in either group; 7 cases of grade 2 AST/ALT elevation (4%) in RFA group • No grade 2 or higher alkaline phosphatase elevation in either group • No grade 3 or higher bilirubin elevation in either group; 5 cases of grade 2 bilirubin elevation (6%) in SBRT group and 5 cases (3%) in RFA group • In SBRT group, 1 case of grade 2 rib fracture and 1 case of grade 3 biliary stricture • In RFA group, 1 case of grade 4 intra-abdominal hemorrhage and 1 case of grade 2 diaphragmatic injury In noncomparative analysis of SBRT (N =290): • Grade 2 non-classic RILD: 29 (10%) • Grade 3 non-classic RILD: 6 (2%)

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
	factor in people treated with RFA but not in those treated with SBRT		• Grade 4 non-classic RILD: 2 (< 1%) • Grade 2 anorexia: 11 (4%) • Grade 3 anorexia: 1 (< 1%) • Grade 2 nausea: 9 (3%) • Grade 3 biliary stricture in people with a centrally located tumor: 5 (9%) • No grade 5 toxicities
Ji et al., 2022[108] Single academic center in Hong Kong NR	OS At 1 year: 88.2% SBRT; 100% RFA At 2 years: 85.7% SBRT; 75.0% RFA; *P* = .58 across both years PFS At 1 year: 50.0% SBRT; 44.7% RFA At 2 years: 13.6% SBRT; 7.9% RFA; *P* = .81 across both years Disease control CR: 18 (82%) SBRT; 34 (89%) RFA; *P* = .40 At a median of 26 months follow-up: • Local tumor control rate: 20 (91%) SBRT; 36 (95%) RFA; *P* = .57 • Intrahepatic recurrence: 10 (45%) SBRT; 20 (53%) RFA; *P* = .59 • Extrahepatic recurrence: 6 (27%) SBRT; 0 RFA; *P* < .001 • Intrahepatic recurrence and extrahepatic recurrence: 1 (5%) SBRT; 1 (3%); *P* = .67	NR	In first week after treatment: • Overall complications: 5 (23%) SBRT; 8 (21%) RFA; *P* = .88 • Fever: 5 (23%) SBRT; 8 (21%) RFA; *P* = .88 • Liver failure; 0 SBRT; 0 RFA • Biliary complication • Intrahepatic vascular complication; 0 SBRT; 0 RFA; 0 SBRT; 0 RFA • Renal failure; 0 SBRT; 0 RFA • Severe complications; 0 SBRT; 0 RFA • Hospital mortality: 0 SBRT; 0 RFA During follow-up, patients in both groups died of liver failure and of hepatorenal syndrome and gastrointestinal bleeding in RFA groups (numbers NR)

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
	• Median time to tumor recurrence (range): 16 months (2 to 33) SBRT; 14 months (1 to 33) RFA; *P* = .93		
Jun et al, 2018[109] 4 centers in South Korea, including 3 academic centers NR	OS At 1 year: 98.8% SBRT-TACE; 99.7% TACE At 3 years: 89.1% SBRT-TACE; 83.3% TACE At 5 years: 80.7% SBRT-TACE; 71.0% TACE; *P* < .21 overall SBRT-TACE vs, TACE: HR, 0.72 (95% CI, 0.38 to 1.38) univariate PFS **At 1 year: 56.5% SBRT-TACE; 42.2% TACE** **At 3 years: 32.3% SBRT-TACE; 21.6% TACE; *P* = .02 overall** **SBRT-TACE vs, TACE: HR, 0.67 (95% CI, 0.48 to 0.99) univariate;** HR, 0.69 (95% CI, 0.48 to 1.00, multivariate **In patients with < 2 HCCs, SBRT-TACE was also associated with better PFS (HR, 0.59; 95% CI, 0.39 to 0.89)** Disease control **At 1 year, local control: 91.1% SBRT-TACE; 69.9% TACE**	NR	Child-Pugh deterioration of 2 or more: 9.4% SBRT-TACE; 5.5% TACE; *P* = .12 Elevated liver transaminases: 9.4% SBRT-TACE; 4.8% TACE; *P* = .24

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
	At 3 years, local control: 89.9% SBRT-TACE; 48.8% TACE **At 5 years, local control: 89.9% SBRT-TACE; 48.8% TACE; *P* < .001 overall**		
Kibe et al., 2022[110] Single center in Japan NR	NA (harms only; noncomparative)	NA (harms only; noncomparative)	No treatment-related death observed Acute grade 2 AST toxicity: 4 (2%) Acute grade 3 AST toxicity: 0 Acute grade 2 ALT toxicity: 2 (1%) Acute grade 3 ALT toxicity: 0 Acute grade 2 total bilirubin toxicity: 15 (9%) Acute grade 3 total bilirubin toxicity: 0 Acute grade 2 albumin toxicity: 7 (4%) Acute grade 3 albumin toxicity: 1 (< 1%) Acute grade 2 platelets toxicity: 24 (14%) Acute grade 3 platelets toxicity: 5 (3%) No acute grade 4 or 5 hematological toxicities No grade 3 or higher nonhematological hepatic or gastrointestinal acute toxicities Nonclassic RILD: 4 (2%)
Kim et al., 2020[111] 7 centers in Korea, Taiwan, China, and Hong Kong NR	OS **Before matching, at 2 years, mortality, RFA vs. SBRT: 25.7% SBRT; 18.9% RFA; HR, 1.57 (95% CI, 1.36 to 1.81)**	NR	Any acute grade 3 or higher toxicity: 8 (2%) SBRT; 41 (3%) RFA Acute grade 3 to 4 nausea: 1 (< 1%) SBRT; 0 RFA Acute grade 3 to 4 abdominal pain: 2 (< 1%) SBRT; 0 RFA

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
	After matching, at 2 years, mortality, RFA vs. SBRT: 22.4% SBRT; 28.9% RFA; HR, 0.86 (95% CI, 0.70 to 1.06) Disease control **Cumulative local recurrence rate: 19.4% SBRT; 23.7% RFA; *P* < .001** **Local control, RFA vs. SBRT: HR, 0.45 (95% CI, 0.35 to 0.58) favoring SBRT** **Similar results seen after matching** **In subgroup analysis, SBRT was associated with superior local control in small tumors (≤ 3 cm) irrespective of location, large tumors located in subphrenic region, and those that progressed after TACE**		Acute grade 3 to 4 duodenal ulcer: 3 (< 1%) SBRT; 0 RFA Acute grade 3 to 4 biliary fistula: 1 (< 1%) SBRT; 5 (< 1%) RFA Acute grade 3 to 4 hepatic failure: 0 SBRT; 34 (2%) RFA Acute grade 3 to 4 intra-abdominal hemorrhage: 1 (< 1%) SBRT; 1 (< 1%) RFA Acute grade 3 to 4 pleural hemorrhage: 0 SBRT; 1 (< 1%) RFA Any late grade 3 to 4 toxicity: 0 SBRT; 15 (1%) RFA Late grade 3 to 4 biliary fistula: 0 SBRT; 5 (< 1%) RFA Late grade 3 to 4 pleural effusion: 0 SBRT; 10 (< 1%) RFA **Change in Child-Pugh score of more than 2: 11.2% SBRT; 4.7% RFA; *P* < .001**
Kimura et al., 2018[112] 2 centers in Japan (1 academic center) NR	OS At 1 year: 100% SBRT; 94.8% SBRT-TACE At 2 years: 78.6% SBRT; 80.3% SBRT-TACE; *P* = .66 across both years PFS At 1 year: 74.4% SBRT; 61.3% SBRT-TACE At 2 years: 49.0% SBRT; 42.9% SBRT-TACE; *P* = .19 across both years	NR	Incidence of grade 3 or higher toxicities was 17.9% in SBRT alone group and 18.9% in combination group (*P* = .90). Grade 3 elevated bilirubin: 0 SBRT; 6 (5%) SBRT-TACE (2 post SBRT and 4 post TACE) Grade 3 elevated AST/ALT: 0 SBRT; 12 (10%) SBRT-TACE (1 post SBRT and 11 post TACE) Grade 3 decreased platelets: 3 (11%) SBRT; 33 (27%) SBRT-TACE (16 post SBRT and 17 post TACE) Grade 4 decreased platelets: 1 (4%) SBRT; 2 (2%) SBRT-TACE (2 post SBRT and 0 post TACE)

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
	Disease control At 1 year, local PFS: 100% SBRT; 95.6% SBRT-TACE At 2 years, local PFS: 71.4% SBRT; 80.8% SBRT-TACE; *P* = .97 across both years At 1 year, local control: 100% SBRT; 99.2% SBRT-TACE At 2 years, local control: 95.4% SBRT; 98.5% SBRT-TACE; *P* = .42 across both years		Grade 3 decreased albumin: 0 SBRT; 2 (2%) SBRT-TACE (2 post SBRT and 0 post TACE) Grade 3 ascites: 0 SBRT; 3 (2%) SBRT-TACE (3 post SBRT and 0 post TACE) Grade 3 portal vein thrombosis: 1 (4%) SBRT; 1 (1%) SBRT-TACE (1 post SBRT and 0 post TACE) Grade 3 other toxicities: 1 (4%) SBRT; 3 (2%) SBRT-TACE (2 post SBRT and 1 post TACE) No radiation pneumonitis
Lock et al., 2022[113] Single academic center in Canada NR	NA (harms only; noncomparative)	NA (harms only; noncomparative)	Mean toxicity change (SD), 0 to 3 months: 0.30 (1.03) Mean toxicity change (SD), 0 to 6 months: 0.32 (1.20) Mean Child-Pugh score change (SD), 0 to 3 months: -1.55 (2.31)
Loi et al., 2021[114] Single center in Italy NR	NA (harms only; noncomparative)	NA (harms only; noncomparative)	Acute toxicity: 37 (26%) Grade 2 toxicity was recorded in 4 cases, consisting of persistent nausea or favoring abdominal pain, requiring medical intervention Grade 3 adverse event, consisting of acute liver failure and ascites requiring paracentesis, was reported in 1 patient Lower dose therapy (median 103 vs. 120 Gy), Child-Pugh score B, BCLC stages B to C were associated with an increased incidence of acute toxicity; **however, in logistic regression, only BCLC stages B to C remained associated with increased acute toxicity (HR, 2.9; 95% CI, 1.10 to 7.65)** Late toxicity: 11 (8%; liver impairment)

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
			Grade 2 liver toxicity in 4 patients; grade 3 deterioration with ascites and mild encephalopathy was seen in 2 patients No gastrointestinal bleeding or biliary tract stricture were observed No variable was statistically correlated with occurrence of late toxicity
Mahadevan et al., 2018[115] RSSearch registry, including 25 sites and academic centers in US, Germany, and Australia (2005 to 2017) NCT01885299	NA (harms only; noncomparative)	NA (harms only; noncomparative)	No grade 3 toxicity reported
Méndez Romero et al., 2021[116] 13 centers, including academic centers, in the Netherlands and Belgium NR	NA (harms only; noncomparative)	NA (harms only; noncomparative)	Grade 3 abdominal pain: 2 Grade 3 bile duct stenosis: 3 Grade 3 chest wall pain: 2 Grade 3 cholecystitis: 2 Grade 3 fatigue: 2 Grade 3 fibrosis deep connective tissue: 1 Grade 3 flank pain: 1 Grade 3 fracture: 1 Grade 3 hematoma: 1 Grade 3 nausea: 2 Grade 3 pneumothorax: 1

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
			Grade 3 portal vein thrombosis: 1 Grade 3 vomiting: 1 Grade 4 gallbladder perforation: 1 Grade 4 gastric perforation: 1 Grade 5 hepatobiliary disorders: 1 No association between dose, age, or tumor diameter with toxicities
Munoz-Schuffenegger et al., 2021[117] Single center in Canada NR	NA (harms only; noncomparative)	NA (harms only; noncomparative)	All patients completed SBRT as planned During follow up period, 6 patients developed gastrointestinal bleeding (2- to 8-months post SBRT), and 2 of bleeds were from tissues outside irradiated volume leaving 4 patients with gastrointestinal bleeding likely related to previous SBRT
Nabavizadeh et al., 2021[118] Single academic center in US NR	OS At 1 year: 74% TACE-SBRT; 89% TACE-TA At 2 years: 49% TACE-SBRT; 77% TACE-TA **Over 2 years, TACE-SBRT vs. TACE-TA: sHR, 2.55 (95% CI, 1.80 to 3.61) favoring TACE-TA** In subgroup of patients with BCLC stage A HCC and Child-Pugh score A cirrhosis, no difference between groups PFS At 1 year: 65% TACE-SBRT; 85% TACE-TA	NR	**Treatment-related hepatotoxicity: 27% TACE-SBRT; 9% TACE-TA; *P* = .01**

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
	At 2 years: 50% TACE-SBRT; 76% TACE-TA **Over 2 years, TACE-SBRT vs. TACE-TA: sHR, 1.85 (95% CI, 1.25 to 2.76) favoring TACE-TA** Disease control At 1 year, local control: 99% TACE-SBRT; 90% TACE-TA At 2 years, local control: 94% TACE-SBRT; 87% TACE-TA; *P* = .28 across both years		
Nieuwenhuizen et al., 2021[119] AmCORE (2007 to 2020) NR	OS **SBRT vs. TA: HR, 1.29 (95% CI, 1.12 to 1.49) favoring TA** At 1 year: 84% SBRT; 94% TA At 2 years: 61% SBRT; 80% TA At 3 years: 37% SBRT; 65% TA At 5 years: 19% SBRT; 41% TA Limiting to treatment naïve patients or patients with small tumors did not change results PFS **Local tumor PFS, SBRT vs. TA: HR, 1.58 (95% CI, 1.31 to 1.90) favoring TA** No difference between groups for distant PFS (HR, 1.07; 95% CI, 0.93 to 1.22)	NR	90-day mortality: 0 SBRT; 0 TA Grade 3 events: 0 SBRT; 9 (6%) TA; *P* = .06 **Any AE: 30.9% SBRT; 11.8% TA; *P* = .001**

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
	Limiting to treatment naïve patients or patients with small tumors did not change results Disease control **Local control was significantly worse in SBRT group (HR, 1.60, 95% CI 1.23 to 2.08)**		
Oladeru et al., 2016[120] Surveillance, Epidemiology, and End Results Program (SEER)-Medicare (2004 to 2011) NR	OS Median survival: 14 months, SBRT; 12 months, SIRT; *P* = .29 OS, SBRT vs. SIRT: HR, 0.72 (95% CI, 0.49 to 1.07) Median disease-free survival: 14 months, SBRT; 14 months, SIRT; *P* = .21 Disease-free survival: SBRT vs. SIRT: HR, 0.70 (95% CI, 0.46 to 1.05)	NR	NR
Parikh et al., 2018[121] Surveillance, Epidemiology, and End Results Program (SEER)-Medicare (2004 to 2011) NR	OS At 1 year: 78.1% SBRT; 79.4% RFA At 3 years, RFA associated with significantly improved survival vs. SBRT (*P* <.001) **SBRT vs. RFA, unmatched, multivariate: HR, 1.80 (95% CI, 1.15 to 2.82) favoring RFA** SBRT vs. RFA, matched, multivariate: HR, 1.28 (95% CI, 0.60 to 2.72)	Resource use and costs 90-day post treatment hospitalization: NR SBRT; 27.2% RFA; *P* = .06 See Table C29 for costs	NR

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
	Progression NR		
Rajyaguru et al., 2018[122] National Cancer Database (2004 to 2013) NR	OS **At 5 years: 19.3% SBRT; 29.8% RFA; HR, 0.67 (95% CI, 0.55 to 0.81) favoring RFA** **Similar results in subgroup analyses**	NR	NR
Sapisochin et al., 2017[123] Single center in Canada NR	OS At 1 year: 83% SBRT; 86% TACE; 86% RFA At 3 years: 61% SBRT; 61% TACE; 72% RFA At 5 years: 61% SBRT; 56% TACE; 61% RFA; *P* = .40 over 5 years Mortality post-transplant was also similar between groups (*P* = .70) Progression NR Disease control **At 1 year, recurrence: 7% SBRT; 18% TACE; 8% RFA** **At 3 years, recurrence: 26% SBRT; 28% TACE; 13% RFA** **At 5 years, recurrence: 26% SBRT; 35% TACE; 14% RFA; *P* = .03 over 5 years** **Recurrence: 23.2% SBRT; 30.4% TACE; 13.3% RFA; *P* = .004**	NR	**Impairment of liver function: 14 (38.9%) SBRT; 18 (19.4%) TACE; 31 (13.0%) RFA; *P* = .001** **Fatigue: 2 (5.6%) SBRT; 22 (23.7%) TACE; 5 (2.1%) RFA; *P* < .001** **Vomiting/nausea: 3 (8.3%) SBRT; 10 (10.8%) TACE; 4 (1.7%) RFA; *P* = .001** **Pain: 1 (2.8%) SBRT; 50 (53.8%) TACE; 51 (21.5%) RFA; *P* < .001** Other: 2 (5.6%) SBRT; 13 (14.0%) TACE; 14 5.9%) RFA; *P* = .06 No patient was “delisted” due to treatment toxicity
Sebastian et al., 2019[124]	OS	NR	NR

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
National Cancer Database (2004 to 2014) NR	Median OS: 48 months SBRT; 20 months TARE; 14 months cRT **SBRT vs. TARE, univariate: HR, 0.40 (95% CI, 0.22 to 0.74), favoring SBRT** **SBRT vs. cRT, univariate: HR, 0.37 (95% CI, 0.20 to 0.68), favoring SBRT** **SBRT vs. TARE, multivariate: aHR, 0.42 (95% CI, 0.21 to 0.84), favoring SBRT** **SBRT vs. cRT, multivariate: aHR, 0.44 (95% CI, 0.21 to 0.91), favoring SBRT** **Similar results after adjusting for propensity weighting**		
Stintzing et al., 2019[125] Single center in Germany NR	NA (harms only; noncomparative)	NA (harms only; noncomparative)	Grade 2 nausea: 2 (1%); both among first treated patients Grade 3 gastric ulcers: 2 (1%)
Voglhuber et al., 2021[126] Single academic center in Germany NR	NA (harms only; noncomparative)	NA (harms only; noncomparative)	Acute grade 2 fatigue: 13 (11%) Acute grade 2 nausea: 8 (7%) Acute grade 2 vomiting: 5 (4%) Acute grade 2 abdominal pain: 2 (2%) Acute grade 2 diarrhea: 2 (2%) Acute grade 2 fever/chills/sweating: 2 (2%) Acute grade 2 radiogenic hepatitis: 1 (< 1%)

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
			Acute grade 2 radiation pneumonitis: 2 (2%) Acute grade 2 weight loss: 1 (< 1%) Acute grade 2 constipation: 1 (< 1%) Acute grade 2 cholestasis/biliary stenosis: 1 (< 1%) Acute grade 2 erythema/radiodermatitis: 1 (< 1%) Acute grade 2 thoracic/rib pain: 1 (< 1%) Acute grade 3 subileus/corpostasis: 1 (< 1%) Acute grade 3 esophagus stenosis: 1 (< 1%) Late grade 2 fatigue: 9 (8%) Late grade 2 abdominal pain: 8 (7%) Late grade 2 weight loss: 3 (3%) Late grade 2 constipation: 3 (3%) Late grade 2 nausea: 2 (2%) Late grade 2 vomiting: 2 (2%) Late grade 2 loss of appetite: 2 (2%) Late grade 2 radiation liver-parenchymal abnormalities: 2 (2%) Late grade 2 thoracic/rib pain: 2 (2%) Late grade 2 diarrhea: 1 (< 1%) Late grade 2 flatulence: 1 (< 1%) Late grade 2 cholestasis/biliary stenosis: 1 (< 1%) Late grade 2 cholangitis: 1 (< 1%) Late grade 2 hyperpigmentation/scarring: 1 (< 1%)

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
			Late grade 2 dry cough: 1 (< 1%) Late grade 2 numbness in irradiation field: 1 (< 1%) Late grade 3 cholestasis/biliary stenosis: 4 (4%) Late grade 3 abdominal pain: 2 (2%) Late grade 3 cholangitis: 2 (2%) Late grade 3 liver failure/encephalopathy: 1 (< 1%) Late grade 3 liver abscess: 1 (< 1%)
Wahl et al., 2016[127] Single academic center in US NR	OS At 1 year: 74.1% SBRT; 69.6% RFA At 2 years: 46.3% SBRT; 52.9% RFA; *P* ≥ .05 overall Progression and PFS At 1 year, freedom from local progression: 97.4% SBRT; 83.6% RFA At 2 years, freedom from local progression: 83.8% SBRT; 80.2% RFA **Local progression, RFA vs. SBRT, univariate: HR, 2.63 (95% CI, 1.20 to 5.75) favoring SBRT** **Local progression, RFA vs. SBRT, multivariate: HR, 3.84 (95% CI, 1.62 to 9.09) favoring SBRT** **No difference between groups for tumors < 2 cm, but SBRT significantly better in larger tumors**	NR	Grade 3 and higher toxicities: 5% SBRT; 11% RFA; *P* = .31 In SBRT group, grade 3 and higher toxicities were radiation-induced liver disease (n = 1), GI bleeding (n = 1), and worsening ascites (n = 1); no deaths were observed related to SBRT treatment In RFA group, grade 3 and higher toxicities were pneumothorax (n = 1), sepsis (n = 2), duodenal and colonic perforation (n = 2), and bleeding (n = 3) and resulted in 2 deaths within 1 month of treatment At 1 year, late grade 3 and higher biliary toxicity: 3.3% SBRT; 2.3% RFA; *P* = .70 At 2 years, late grade 3 and higher biliary toxicity: 3.3% SBRT; 6.0% RFA; *P* = .38 At 1 year, late grade 3 and higher luminal gastrointestinal toxicity: 5.4% SBRT; 3.4% RFA; *P* = .49 At 2 years, late grade 3 and higher luminal gastrointestinal toxicity: 8.3% SBRT; 6.4% RFA; *P* = .66 No late grade 5 toxicities in either group

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
			Child-Pugh scores worsened by 0.2 and 0.5 for RFA- and SBRT-treated patients (*P* = .17), **and 12 months after treatment, Child-Pugh scores worsened by 0.3 and 1.2 (*P* = .005)** In a multivariate model, SBRT was not significantly associated with worsening (OR, 1.02; *P* = .97); nor was SBRT dose associated with worsening Child-Pugh scores
Wang et al., 2021[128] Single academic center in Japan NR	OS At 1 year: 95.2% SBRT; 90.5% RFA At 2 years: 87.3% SBRT; 73.7% RFA At 5 years: 78.4% SBRT; 46.3% RFA; *P* = .09 over 5 years HCC-related death overall: 1 SBRT; 4 RFA Progression and PFS Median time to progression: 13.9 months, SBRT; 8.3 months, RFA; *P* = .11 At 1 year, PFS: 66.7% SBRT; 52.4% RFA At 2 years, PFS: 31.4% SBRT; 28.6% RFA; *P* = .31 over both years Disease control At 1 year, intrahepatic recurrence: 33.3% SBRT; 29.5% RFA; *P* = .97 At 1 year, local recurrence: 0 SBRT; 25.7% RFA; *P* = .06	NR	Child-Pugh deterioration of 2 or more: 23.8% SBRT; 33.3% RFA; *P* > .05 No grade 3 or higher events in either group

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
Wong et al., 2019[129] 2 centers (1 academic) in Hong Kong NR	OS Median survival: 23.9 months TACE + SBRT; 10.4 months TACE **At 1 year: 67.2% TACE + SBRT; 43.9% TACE** **At 2 years: 47.1% TACE + SBRT; 24.2% TACE** **At 3 years: 47.1% TACE + SBRT; 13.3% TACE; *P* = .003 overall** **TACE + SBRT vs. SBRT: HR, 0.55 (95% CI, 0.37 to 0.82) favoring combination** **Similar results in multivariate analysis** **All deaths (34) in TACE + SBRT group and 86% of deaths (91) in TACE were cancer-related** PFS Median PFS: 7.6 months TACE + SBRT; 5.7 months TACE **At 1 year: 32.5% TACE + SBRT; 21.4% TACE** **At 2 years: 20.1% TACE + SBRT; 12.1% TACE** **At 3 years: 15.1% TACE + SBRT; 5.1% TACE; *P* = .01 overall** **TACE + SBRT vs. SBRT: HR, 0.62 (95% CI, 0.42 to 0.90) favoring combination**	NR	At 1 month, Child-Pugh A: 93.9% TACE + SBRT; 86.7% TACE; *P* = .17 No patients developed classical RILD TACE + SBRT was associated with more fatigue and hematological abnormality in hemoglobin, platelet and white cell count TACE patients had more renal and liver impairment and were more likely to have fever Grade 2 fatigue: 18 (37%) TACE + SBRT; 6 (6%) TACE Grade 2 fever: 3 (6%) TACE + SBRT; 0 TACE Grade 2 bilirubin: 6 (12%) TACE + SBRT; 16 (17%) TACE Grade 3 or higher bilirubin: 6 (12%) TACE + SBRT; 7 (7%) TACE Grade 2 albumin: 9 (18%) TACE + SBRT; 34 (35%) TACE Grade 2 AST: 6 (12%) TACE + SBRT; 16 (17%) TACE Grade 3 or higher AST: 5 (10%) TACE + SBRT; 32 (33%) TACE Grade 2 INR: 0 TACE + SBRT; 2 (2%) TACE Grade 3 or higher INR: 0 TACE + SBRT; 1 (1%) TACE Grade 2 platelet: 8 (16%) TACE + SBRT; 4 (4%) TACE Grade 3 or higher platelet: 4 (8%) TACE + SBRT; 3 (3%) TACE Grade 2 white cell count: 8 (16%) TACE + SBRT; 4 (4%) TACE

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
	Similar results in multivariate analysis Disease control Never had radiological control: 1 (2%) TACE + SBRT; 42 (43%) TACE		Grade 3 or higher white cell count: 7 (14%) TACE + SBRT; 1 (1%) TACE Grade 2 hemoglobin: 6 (12%) TACE + SBRT; 0 TACE Grade 3 or higher hemoglobin: 3 (6%) TACE + SBRT; 0 TACE Grade 2 creatinine: 0 TACE + SBRT; 5 (5%) TACE Grade 3 or higher creatinine: 0 TACE + SBRT; 3 (3%) TACE
Wong et al., 2021[130] Single academic in Hong Kong NCT03950102	OS At 1 year: 84.9% SBRT; 88.1% TACE; 80.4% HIFU At 2 years: 76.4% SBRT; 72.7% TACE; 60.8% HIFU At 3 years: 73.0% SBRT; 65.6% TACE; 54.9%; *P* = .29 overall Progression and PFS No difference in recurrence-free survival between groups at 1, 2, and 3 years **At 1 year, progression: 10.8% SBRT; 45.0% TACE; 47.6% HIFU** **At 2 years, progression: 18.5% SBRT; 50.6% TACE; 62.8% HIFU** **At 3 years, progression: 18.5% SBRT; 54.9% TACE; 62.8% HIFU; *P* < .001 overall** Disease control	NR	No 30-day mortality after bridging therapy in any of 3 groups Readmission within 30 days of bridging therapy: 5% SBRT; 8% TACE; 9% HIFU; *P* = .70 Grade 2 fatigue: 3% SBRT; 2% TACE; 0 HIFU Grade 2 fever: 2% SBRT; 6% TACE; 5% HIFU **Grade 2 bilirubin: 40% SBRT; 41% TACE; 19% HIFU** **Grade 3 or higher bilirubin: 3% SBRT; 18% TACE; 3% HIFU; *P* = .03 overall** Grade 2 albumin: 17% SBRT; 31% TACE; 20% HIFU Grade 3 or higher albumin: 3% SBRT; 0 TACE; 0 HIFU Grade 2 AST: 5% SBRT; 1% TACE; 0 HIFU Grade 2 INR: 13% SBRT; 21% TACE; 9% HIFU **Grade 2 platelets: 27% SBRT; 25% TACE; 25% HIFU** **Grade 3 or higher platelets: 57% SBRT; 41% TACE; 27% HIFU; *P* < .001 overall** **Grade 2 white blood cell count: 35% SBRT; 19% TACE; 20% HIFU**

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
	At 3 months, local control: 91.7% SBRT; 69.6% TACE; 72.3% HIFU; *P* = .03 **At 6 months, local control: 96.0% SBRT; 67.3% TACE; 59.5% HIFU; *P* = .03** **At 9 months, local control: 90.0% SBRT; 50.0% TACE; 51.9% HIFU; *P* = .009** **At 12 months, local control: 92.3% SBRT; 43.5% TACE; 33.3% HIFU; *P* = .02** **At 3 months, CR: 27.8% SBRT; 8.9% TACE; 12.8% HIFU; *P* ≤ .05** **At 6 months, CR: 48.0% SBRT; 16.3% TACE; 18.9% HIFU; *P* ≤ .05** **At 9 months, CR: 50.0% SBRT; 18.4% TACE; 18.5% HIFU; *P* ≤ .05** **At 12 months, CR: 53.8% SBRT; 17.4% TACE; 13.3% HIFU; *P* ≤ .05** **At 3 months, objective response: 63.9% SBRT; 35.7% TACE; 36.2% HIFU; *P* = .01** **At 6 months, objective response: 80.0% SBRT; 38.8% TACE; 32.4% HIFU; *P* < .001** **At 9 months, objective response: 80.0% SBRT; 39.5% TACE; 29.6% HIFU; *P* = .002**		**Grade 3 or higher white blood cell count: 17% SBRT; 4% TACE; 5% HIFU; *P* = .003 overall** Grade 2 hemoglobin: 5% SBRT; 21% TACE; 10% HIFU Grade 3 or higher hemoglobin: 3% SBRT; 2% TACE; 2% HIFU Grade 2 creatinine: 5% SBRT; 4% TACE; 3% HIFU

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
	At 12 months, objective response: 76.9% SBRT; 39.1% TACE; 26.7% HIFU; *P* = .02 In SBRT group, 4 patients were "delisted" because HCC was assessed as having been treated		

Note. [a] Bold text indicates statistically significant findings.
Abbreviations. aHR: adjusted hazard ratio; ALT: alanine aminotransferase; AST: aspartate aminotransferase; CI: confidence interval; CR: complete response or remission; HIFU: high-intensity focused ultrasound; HR: hazard ratio; NA: not applicable; NR: not reported; OS: overall survival; PFS: progression-free survival; RFA: radiofrequency ablation; RILD: RT-induced liver disease RT: radiation therapy; SBRT; stereotactic body radiation therapy; SD: standard deviation; sHR: subdistribution hazard ratio TACE: transarterial chemoembolization; TARE: transarterial radioembolization.

Cervical Cancer

No eligible studies identified.

Esophageal Cancer

No eligible identified.

Oligometastatic Cancer

Table C27. Evidence Tables for Nonrandomized and Registry-based Studies[a]

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
Bouman-Wammes et al., 2017[131] Single center in Netherlands NR	OS NR Progression and PFS NR Disease control	NR	No grade 3 or higher toxicities in SBRT group

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
	Once ADT started, time to castration resistance: 31.5 months SBRT; 26.9 months no SBRT; *P* = .54 **Median time to ADT: 17.3 months SBRT; 4.2 months no SBRT; *P* < .001** **Mean time between diagnosis of metastasis until progression of disease during ADT use; 66.6 month SBRT; 36.4 months no SBRT; *P* = .02)**		
Bowden et al., 2020[132] Single center in Australia ACTRN12618000566235 TRANSFORM	NA (harms only; noncomparative)	NA (harms only; noncomparative)	No grade 3 toxicities related to SBRT
Chalkidou et al., 2021[133] 17 centers in England NR	NA (harms only; noncomparative)	NA (harms only; noncomparative)	Grade 3 fatigue: 28 (2%) Grade 3 increased bilirubin: 8 (1%) Grade 3 cough: 7 (< 1%) Grade 3 bone pain: 6 (< 1%) Grade 3 urinary frequency: 0 Grade 3 nausea: 3 (< 1%) Grade 3 gastrointestinal hemorrhage: 3 (< 1%) Grade 3 increased alanine aminotransferase: 3 (< 1%) Grade 3 spinal fracture: 2 (< 1%) Grade 3 diarrhea: 2 (< 1%) Grade 3 pneumonitis: 2 (< 1%)

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
			Grade 3 dysphagia: 2 (< 1%) Grade 3 pericarditis: 2 (< 1%) Grade 3 vomiting: 2 (< 1%) Grade 3 urinary incontinence: 1 (< 1%) Grade 3 hematuria: 1 (< 1%) Grade 3 fever: 1 (< 1%) Grade 3 duodenal or gastric ulcer: 1 (< 1%) Grade 4 increased bilirubin: 7 (< 1%) Grade 4 increased alanine aminotransferase: 2 (< 1%) Grade 4 pericarditis: 1 (< 1%) Grade 4 urinary retention: 1 (< 1%)
De Bleser et al., 2019[134] 15 centers, including academic centers, across Europe NR	OS NR Progression and PFS **Metastasis-free survival: 68% SBRT; 77% ENRT; *P* = .01** **In patients with 1 node, SBRT vs. ENRT: HR, 0.50 (95% CI, 0.30 to 0.85) favoring ENRT** In patients with > 1 node: HR, 0.92 (95% CI, 0.54 to 1.59 Disease control 3-year castration-free survival: 88% SBRT; 87% ENRT; *P* = .05	NR	Acute grade 2 genitourinary toxicity: 1 (< 1%) SBRT; 2 (1%) ENRT Acute grade 2 gastrointestinal toxicity: 0 SBRT; 3 (2%) ENRT Acute grade 3 genitourinary toxicity: 0 SBRT; 1 (< 1%) ENRT Late grade 2 genitourinary toxicity: 1 (< 1%) SBRT; 7 (4%) ENRT Late grade 2 gastrointestinal toxicity: 2 (< 1%) SBRT; 6 (3%) ENRT Late grade 2 other toxicity: 0 SBRT; 3 (2%) ENRT

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
	Local progression: 16% SBRT; 5% ENRT; *P* < .001 **Lymph node progression observed more frequently following SBRT than following ENRT (*P* < .001), especially in pelvis (*P* < .001)** Bone, prostate, or visceral progression similar between both groups (*P* ≥ .05) **Relapse following SBRT (177 patients) was significantly higher than following ENRT (74 patients; *P* < .001)**		Late grade 3 genitourinary toxicity: 0 SBRT; 3 (2%) ENRT **ENRT associated with significantly higher acute toxicity (*P* = .002) and late toxicity (*P* < .001)**
Franzese et al., 2021[135] Multiple centers in Italy NR	NA (harms only; noncomparative)	NA (harms only; noncomparative)	Acute grade 2 pain: 2 (2%) Acute grade 2 cough: 2 (< 1%) Acute grade 2 dyspnea: 1 (< 1%) Acute grade 2 nausea: 1 (< 1%) Acute grade 2 diarrhea: 1 (< 1%) Late grade 2 pain: 2 (< 1%) Late grade 2 dysphagia: 1 (< 1%) Late grade 2 fibrosis: 1 (< 1%) No grade 3 or higher toxicities No association between site of SBRT or use of systemic therapy during SBRT and toxicity
Hurmuz et al., 2020[136] Multiple centers in Turkey TROD-09-002	OS At 2 years: 87.7% SBRT; 87.3% cRT; *P* = .91 PFS	NR	No grade 3 or higher toxicities Any acute grade 2 toxicity: 10.8% Any acute grade 2 toxicity: 1.7%

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
	At 2 years: 86.2% SBRT; 54.9% cRT; *P* < .001		
Macchia et al., 2020[137] Multiple centers, including academic centers, in Italy MITO RT1	NA (harms only; noncomparative)	NA (harms only; noncomparative)	Acute grade 2 pain: 5 (8%) Acute upper gastrointestinal disorders: 5 (8%) Acute lower gastrointestinal disorders: 3 (5%) Acute pulmonary toxicity: 1 (2%) Late pulmonary toxicity: 2 (11%) No grade 3 or higher toxicities reported
Milano et al., 2008[138,139] Single academic center in US NR	NA (harms only; noncomparative)	NA (harms only; noncomparative)	No grade 4 or 5 toxicity Grade 3 toxicity: 1 (< 1%); nonmalignant pleural and pericardial effusion after SBRT for lung and mediastinal tumors
Nicosia et al., 2020[140] Multiple centers, including academic centers, in Italy and Germany NR	NA (harms only; noncomparative)	NA (harms only; noncomparative)	No grade 2 or higher toxicities observed
Olsen et al., 2022[141] 6 centers in Canada NCT02933242 SABR-5	NA (harms only; noncomparative)	NA (harms only; noncomparative)	Any grade 2 toxicity: 14.2% Any grade 3 toxicity: 4.2% Any grade 4 toxicity: 0 Any grade 5 toxicity: < 1% Any grade 2 or higher pain: 25 (7%); 5 grade 3, 0 grade 4, 0 grade 5

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
			Any grade 2 or higher diarrhea: 1 (1%); 1 grade 3, 0 grade 4, 0 grade 5 Any grade 2 or higher constipation: 2 (1%); 0 grade 3, 0 grade 4, 0 grade 5 Any grade 2 or higher pneumonitis: 5 (1%); 0 grade 3, 0 grade 4, 0 grade 5 Any grade 2 or higher rib fracture: 5 (1%); 0 grade 3, 0 grade 4, 0 grade 5 Any grade 2 or higher spine fracture: 7 (2%); 4 grade 3, 0 grade 4, 0 grade 5 Any grade 2 or higher neuropathy: 6 (2%); 0 grade 3, 0 grade 4, 0 grade 5 Any grade 2 or higher other toxicity: 39 (10%); 10 grade 3, 0 grade 4, 1 grade 5 Any grade 2 or higher toxicity by site: 16 (9%) lung, 22 (15%) bone, 16 (19%) spine, 10 (13%) lymph node, 6 (21%) liver, 4 (27%) adrenal No difference by type of disease (oligometastatic vs. progressive), or number of treated metastases (1 vs. > 1) 1 grade 5 event (death) possibly associated with SBRT Incidence of grade 2 or higher toxicity: 15.2% year 1, 4.3% year 2, 3.0% year 3, 3.7% year 4, 0 year 5 Incidence of grade 3 or higher toxicity: 2.9% year 1, 2.5% year 2, 1.5% year 3, 0 year 4, 0 year 5

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
Ost et al., 2016[142] Multicenter study (sites not clear) NR	NA (harms only; noncomparative)	NA (harms only; noncomparative)	No grade 3 toxicity observed
Poon et al., 2020[143] 6 high-volume academic centers in US, Canada, Australia, and Italy NR	NA (harms only; noncomparative)	NA (harms only; noncomparative)	All acute toxicities occurred in < 1% of patients: • 1 grade 3 bile duct stenosis • 3 grade 3 cough • 1 grade 3 dermatitis • 1 grade 3 dysphagia • 2 grade 3 dyspnea • 2 grade 3 esophagitis • 5 grade 3 fatigue • 2 grade 3 fracture • 1 grade 3 hemorrhage • 6 grade 3 pain • 5 grade 3 pneumonitis • 1 grade 4 pneumonitis • 1 grade 5 pneumonitis All late toxicities occurred in < 1% of patients: • 1 grade 4 bile duct stenosis • 1 grade 5 bile duct stenosis • 1 grade 3 brachial plexopathy • 1 grade 3 bronchial stricture • 5 grade 3 cough • 3 grade 3 dyspnea • 1 grade 3 esophagitis • 4 grade 3 fracture • 2 grade 3 liver abscess • 7 grade 3 pain • 8 grade 3 pneumonitis • 1 grade 3 radiculitis

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
			1 patient died of bile duct stenosis, related to SBRT
Sogono et al., 2021[144] Single center in Australia NR	NA (harms only; noncomparative)	NA (harms only; noncomparative)	Grade 3 or 4 toxicity: 12 (3%); dyspnea, radiculopathy, fractures No grade 5 toxicity
Sutera et al., 2019[145] Single academic center in US NCT01345552	NA (harms only; noncomparative)	NA (harms only; noncomparative)	Acute grade 2 and higher toxicity: 7.5% Acute grade 3 and higher toxicity: 2.0%; grade 3 dyspnea, grade 3 dermatitis, and grade 3 anemia Late grade 2 and higher toxicity: 1.4% Late grade 3 and higher toxicity: 1.4%; grade 3 ureter obstruction and grade 4 small bowel obstruction
Triggiani et al., 2017[146] 9 centers, including academic centers, in Italy NR	NA (harms only; noncomparative)	NA (harms only; noncomparative)	No grade 3 or higher toxicity observed

Note. [a] *Bold text indicates statistically significant findings.*
Abbreviations. ADT: androgen deprivation therapy; CI: confidence interval; cRT: conventional RT; ENRT: elective nodal radiation therapy; HR: hazard ratio; NA: not applicable; OS: overall survival; PFS: progression-free survival; SBRT: stereotactic body radiation therapy.

Other Cancers

Table C28. Evidence Tables for Nonrandomized and Registry-based Studies[a]

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
Adrenal cancer			
Franzese et al., 2021[147] 3 centers, including academic centers, in Italy NR	NA (harms only; noncomparative)	NA (harms only; noncomparative)	No grade 3 or higher events reported 1 (0.7%) patient, affected by adrenal gland metastases from melanoma treated with single fractions of 10 Gy, had a hemorrhage from lesion after SBRT
Large tumors			
Grozman et al., 2021[148] Single academic center in Sweden NR	NA (harms only; noncomparative)	NA (harms only; noncomparative)	Grade 3 toxicity (as maximum): 24 (15%); pneumonia or radiation pneumonitis (n = 9), fatigue (n = 4), dyspnea (n = 3), thoracic pain (n = 3), abdominal pain (n = 2), diarrhea (n = 2), appearance of a liver abscess and radiation induced brachial plexopathy (n = 1) Grade 4 toxicity (as maximum): 4 (2%); radiation pneumonitis or pneumonia (n = 2), esophago-tracheal fistula (n = 1) and gastric perforation (n = 1) Grade 5 toxicity (as maximum): 10 (6%); hemoptysis (n = 4), radiation pneumonitis or pneumonia (n = 4), GI bleeding (n = 1), duodenal perforation (n = 1)
Mixed cancers			
McCammon et al., 2009[149] Single academic center in US NR	NA (harms only; noncomparative)	NA (harms only; noncomparative)	Grade 3 events: 7 (5%) Grade 4 events: 1 (< 1%) 3 grade 3 pneumonitis; grade 3 dermatitis (n NR); grade 3 higher soft-tissue or muscle inflammation or fibrosis (n NR) 2 patients developed vertebral fractures within radiation field most likely attributable to treatment

Citation Setting NCT or Other Trial ID	Survival and Disease Control	Other Outcomes	Safety
Yoon et al., 2021[150] Single academic center in US NR	NA (harms only; noncomparative)	NA (harms only; noncomparative)	Acute grade 3 toxicities: 1 (1%) Acute grade 4 or 5 toxicities: 0 No association between acute toxicities by grade and BED dose Late grade 3 toxicities: 5 (5%) Late grade 4 toxicities: 2 (2%); sepsis from a perirectal abscess after treatment to a rectal mass and sepsis from a peribiliary abscess Late grade 5 toxicities: 0 No association between late toxicities by grade and BED dose

Note. [a] *Bold text indicates statistically significant findings.*
Abbreviations. BED: biologically-equivalent dose; NA: not applicable; NCT: US National Clinical Trial; NR: not reported; SBRT: stereotactic body radiation therapy.

Economic Studies

Table C29. Study Characteristics and Evidence Tables for Economic Studies[a]

Citation Country	Design Intervention Comparator(s)	Population Analytic Assumptions	Main Findings
Prostate cancer			
Pan et al., 2018[54] US	See Table C18 for details	See Table C18 for details	Costs **Mean radiation cost to payer: $49,504 SBRT; $57,244 IMRT; *P* < .001** **Mean radiation cost to patient: $1,015 SBRT; $1,560 IMRT; *P* < .001** Mean complication cost at 2 years: $3,084 SBRT; $2,079 IMRT; *P* = .25

Citation Country	Design Intervention Comparator(s)	Population Analytic Assumptions	Main Findings
			Mean total health care cost at 2 years: $80,786 SBRT; $77,539 IMRT; *P* = .36 Other outcomes not reported

Parikh et al., 2020[151]
US
	Cost-effectiveness analysis (Markov model)
	• Upfront metastasis-directed therapy, follwed by salvage abiraterone acetate plus prednisone (AAP) with ADT followed by salvage docetaxel with ADT (strategy 1)
	• Upfront AAP with ADT, followed by salvage docetaxel with ADT (strategy 2)
	• Upfront docetaxel with ADT, followed by salvage AAP with ADT (strategy 3)
		Men with oligorecurrent hormone-sensitive prostate cancer
		• Baseline utility for metastatic, hormone-sensitive prostate cancer, 0.90
		• Baseline utility for metastatic, castrate-resistant prostate cancer, 0.83
		• Disutility by treatment
		  ○ Androgen deprivation therapy, -0.06
		  ○ Docetaxel, -0.041
		  ○ Abiraterone acetate plus prednisone, -0.017
		  ○ SBRT, 0
			Aat 10 years, by strategy
			• Strategy 1
			  ○ Cost, $141,148
			  ○ Effectiveness, 4.63 QALYs
			  ○ Net monetary benefit, $322,240
			• Strategy 2
			  ○ Cost, $166,807
			  ○ Effectiveness, 4.89 QALYs
			  ○ Net monetary benefit, $322,018
			• Strategy 3
			  ○ Cost, $136,154
			  ○ Effectiveness, 4.00 QALYs
			  ○ Net monetary benefit, $263,407
			In the probabilistic sensitivity analysis using a Monte Carlo simulation (1,000,000 simulations), strategy 1 was the cost-effective strategy in 53.6% of simulations. The probabilistic sensitivity analysis revealed 95% CIs for cost ($75,914 to $179,862, $124,431 to $223,892, and $103,298 to $180,617) and utility in QALYs (3.85 to 6.12, 3.91 to 5.86, and 3.02 to 5.22) for strategies 1, 2, and 3, respectively

Lung cancer			
Kim et al., 2019[152] US	Cost-effectiveness analysis (Markov state transition model) • SBRT plus maintenance therapy • Maintenance therapy alone	People with oligometastatic stage IV NSCLC, grouped by mutation status • Median survival, 21 to 40 months depending on mutation status • Median PFS without SBRT, 4.6 to 18 months depending on mutation status	Total costs for SBRT (3 fractions): $12,794.86 Total costs for SBRT (5 fractions): $16,176.00 Total costs for maintenance therapy: range, $845 for 6 cycles of platinum-based chemotherapy to $60,000 for hospice care of 4 weeks or more

Citation Country	Design Intervention Comparator(s)	Population Analytic Assumptions	Main Findings
		• Median PFS with SBRT, 12 to 25 months depending on mutation status • Median complication probability with SBRT, 16% to 30% depending on mutation status • Median complication probability with maintenance alone, 13% to 25% depending on mutation status • Median hospital stay for complications with treatment, 2 days SBRT and 1 day for maintenance alone • Utility of 0.75 at time of treatment • Utility, 0.80 after treatment without progression • Utility, 0.60 after treatment with progression • Utility, 0.30 for terminal or hospice care • Disutility, -0.30 from complication or toxicity	In base case analysis: • In EGFR or ALK-positive cohort, SBRT plus maintenance therapy costed $64,511 more than maintenance therapy alone while gaining 0.11 QALYs, resulting in an ICER of $564,186 per QALY gained. • For PDL-1-positive cohort, cost difference was $56,066 with 0.17 QALYs gained, resulting in an ICER of $299,248 per QALY gained with SBRT plus maintenance therapy. • In mutation-negative cohort, SBRT plus maintenance therapy costed $30,075 more than maintenance therapy alone while gaining 0.23 QALYs, resulting in an ICER of $128,424 per QALY gained. In one-way sensitivity analysis, none of parameters, when varied, caused SBRT plus maintenance therapy to be a cost-effective option. In probabilistic sensitivity analysis, SBRT plus maintenance therapy was favored in 31% of model iterations and maintenance therapy alone favored in 69% at a WTP threshold of $100,000 per QALY gained for both EGFR/ALK mutation-positive and PDL-1-positive cohorts. In mutation-negative cohort, if cost of maintenance therapy was reduced by 25% or more, ICER would be below $50,000 per QALY gained, and if median survival when treated with SBRT was more than 1.5 times that of maintenance therapy alone, ICER would be below $100,000 per QALY gained. Probabilistic sensitivity analysis demonstrated that SBRT plus maintenance was favored in 45% of model iterations and maintenance therapy alone

Citation Country	Design Intervention Comparator(s)	Population Analytic Assumptions	Main Findings
			favored in 55% at a WTP threshold of $100,000 per QALY gained. SBRT therefore was assessed as not being cost-effective at a WTP threshold of $100,000 when added to maintenance therapy for people with oligometastatic NSCLC.[152]
Pancreatic cancer			
Moningi et al., 2022[90] US	See Table C16 for details	See Table C16 for details	Health resource use and costs **Median 12-month total payments per patient (fee-for-service Medicare insurance coverage; IQR): $80,282 SBRT ($45,244 to $93,684); $57,502 for CT ($34,179 to $84,888); $66,366 cRT ($60,645 to $118,298); *P* < 0.001** **Median payments per patient (under employer-based insurance coverage; IQR): $212,579 SBRT ($144,177 to $303,268) $127,438 CT ($76,001 to $194,98); $172,547 cRT ($117,987 to $248,735); *P* < .001**
Head and neck cancer			
Kim et al., 2018[153] US	Cost-effectiveness analysis (Markov state transition model) • Platinum-based chemotherapy alone • Chemotherapy plus cetuximab • SBRT alone • SBRT plus cetuximab • IMRT plus chemotherapy	People with unresectable locally recurrent previously irradiated head and neck cancers • Median survival, 7 months for chemotherapy alone, 10 months for other treatment options • Median PFS, 2.0 to 9.4 months depending on treatment strategy • Median acute toxicities of grade 3 or higher, 5% to 30% depending on treatment strategy	Total costs for SBRT (5 fractions): $16,500 Total costs for other options: range, $4,290 for 6 cycles of platinum-based chemotherapy to $69,590 for 18 cycles of cetuximab The common base line therapy was chemotherapy alone (least costly and least effective). No treatment strategy was cost-effective at WTP threshold of $100 000 per QALY gained. • SBRT alone had an ICER of $150,866 per QALY gained. • SBRT plus cetuximab had an ICER of $219,509 per QALY gained.

Citation Country	Design Intervention Comparator(s)	Population Analytic Assumptions	Main Findings
		• Median late toxicities of grade 3 or higher, 5% to 15% depending on treatment strategy • Median hospital stay for toxicity, 2 to 12 days depending on toxicity • Utility, 0.60 for treatment • Utility, 0.70 for no progression • Utility, 0.50 for disease progression • Utility, 0.35 for toxicities from chemotherapy • Utility, 0.1 to 0.5 for acute or late toxicities	• IMRT plus chemotherapy was absolutely dominated (i.e., less effective and more costly than SBRT alone and SBRT plus cetuximab). • Chemotherapy plus cetuximab (current standard of care) was least cost-effective therapy among all other therapies. If median survival was 11 months or longer, SBRT alone strategy was lower than $100,000 per QALY gained. If median survival was 13 months or longer, SBRT plus cetuximab was lower than $100,000 per QALY gained. No variation in tumor progression utility values caused a strategy to meet WTP threshold. Probabilistic sensitivity analysis demonstrated that chemotherapy alone was favored in 65% of model iterations, in 16% for SBRT alone, 15% for IMRT plus chemotherapy, 6% for SBRT plus cetuximab, and in 0.5% of model iterations for chemotherapy plus cetuximab at $100,000 WTP threshold.
Liver cancer			
Parikh et al., 2018[121] US	See Table C18 for details	See Table C18 for details	Total costs for SBRT: $51,746 Total costs for RFA: $85,106 Rates of 90-day hospitalization were higher in RFA group, but results were not statistically significant (27.2% in RFA group; *P* = .06). When costs were compared: • Total costs were significantly lower in SBRT group ($51,746 SBRT vs. $85,016 RFA; *P* = .02) • Inpatient costs were significantly lower in SBRT group ($23,360 SBRT vs. $54,053 RFA; *P* = .02)

Citation Country	Design Intervention Comparator(s)	Population Analytic Assumptions	Main Findings
			• 90-day outpatient costs were significantly higher in SBRT group ($15,478 SBRT vs. $5,760 RFA; *P* < .001) • No difference between SBRT and RFA for outpatient costs, Part D medication costs, 90-day overall costs, 90-day inpatient costs, or in median cost per median life-year gained ($38,810 SBRT vs. $40,777; *P* value not reported). The full sample bootstrap median ICER was $61,164 (95% CI, $420,299 to 367,960), meaning SBRT was not cost-effective compared with RFA in overall population; however, 85.5% of bootstrap ICER estimates were lower than WTP threshold of $100,000.
Oligometastatic cancer			
Kumar et al., 2021[154] US	Cost-effectiveness analysis (Markov model) • SBRT • Standard care	People with oligometastatic disease • Utility stable disease, 0.77 • Utility progression, 0.62 • Disutility grade 4 toxicity, -0.16 SBRT, -0.073 standard of care • Grade 5 toxicity, 0 • Death, 0 • Survival with SBRT, HR, 0.57 (95% CI, 0.30 to 1.10) • Survival with SBRT, HR, 0.47 (95% CI, 0.30 to 0.76) • Probability of grade 2 to 4 toxicity, 0.29 SBRT, 0.09 standard of care	Total costs of SBRT: $12,242 Monthly costs of standard care: $8,039 From health care sector perspective, base case analysis found SBRT increased overall cost of treatment by $54,260 from $405,901 with standard therapy to $460,161 with SBRT. From societal perspective, SBRT increased overall cost of treatment by $72,799 from $472,544 with standard therapy to $545,343 with SBRT. SBRT increased effectiveness by 1.88 QALYs, from 2.96 QALY on standard therapy to 4.84 QALY with SBRT. The ICER for SBRT compared with standard therapy was $28,906 per QALY (health care sector perspective) and $38,783 per QALY (societal

Citation Country	Design Intervention Comparator(s)	Population Analytic Assumptions	Main Findings
			perspective); both were considered cost-effective at a WTP threshold of $100,000 per QALY. Probabilistic sensitivity analyses demonstrated SBRT was a cost-effective treatment option 99.8% (health care sector perspective) or 98.7% (societal perspective) of time.
Mehrens et al., 2021[155] US	Cost-effectiveness analysis (partitioned survival model) • SBRT • Standard care	People with oligometastatic disease • Survival with standard of care, 0.88 in 1st year to 0.18 in 6th year • Survival with SBRT, 0.88 in 1st year to 0.42 in 6th year • PFS with standard of care, 0.19 in 1st year to 0 in 6th year • Survival with SBRT, 0.50 in 1st year to 0.18 in 6th year • Utility oligometastatic disease, 0.82 • Utility polymetastatic disease, 0.59 • Adverse events disutility, -0.002 SBRT, -0.0008 standard of care	Cumulative SBRT costs: $11,700 Costs of standard of care: $11,070 palliative RT, $19,174 end of life costs In base case analysis of total study population over trial duration of 6 years, SBRT led to an increased effectiveness of 0.78 QALY at increased costs of $1,133, with an ICER of $1,446 per QALY. When additional long-term data were applied, SBRT led to an increased effectiveness of 1.34 QALY at additional costs of $52,180. Results were sensitive to systemic therapy costs, with higher costs of oligometastatic disease and lower costs of polymetastatic disease leading to unfavorable ICER values and lower costs for therapy of oligometastatic state and higher costs of polymetastatic state leading to favorable ICERs. SBRT remained cost-effective even when costs for SBRT and salvage SBRT were increased up to around 8 times for study duration and for long-term survival. Overall, SBRT was cost-effective in 100% of Monte Carlo simulation runs.

Note. [a] *Bold text indicates statistically significant findings.*
Abbreviations. ADT: androgen deprivation therapy; ALK: anaplastic lymphoma kinase; CI: confidence interval; EGFR: epidermal growth factor receptor; HR:

hazard ratio; ICER: incremental cost-effectiveness ratio; IMRT: intensity-modulated radiation therapy; NR: not reported; NSCLC: non-small cell lung cancer; PDL: programmed death ligand-1; PFS: progression-free survival, QALY: quality-adjusted life year; RFA: radiofrequency ablation; RT: radiation therapy; SBRT: stereotactic body radiation therapy.

Appendix D. Risk-of-Bias Assessments

Table D1. Risk-of-Bias: Randomized Controlled Trials

Study	Randomization	Allocation Concealment	Intervention	Outcomes	Investigator & Participant Masking	Outcome Assessor Masking	Intention to Treat Analysis	Statistical Analysis	Other Biases	Interest Disclosure	Funding	Overall Risk-of-Bias Assessment Comments
Altorki et al., 2021[7]	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	**Moderate**
Brand et al, 2019[1]	Yes	Yes	Yes	Yes	No	No	Yes	No	No	Yes	Yes	**Moderate**
Kim et al., 2022[10]	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	**Moderate**
Kwan et al., 2022[3]	No	No	Yes	Yes	No	No	Unclear	Yes	No	Yes	Yes	**Moderate**
Lukka et al., 2018[4]	Yes	Yes	Yes	Yes	No	No	Unclear	Yes	No	Yes	Yes	**Moderate**
McBride et al., 2021[11]	No	No	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	**Moderate**
Nguyen et al., 2019[21]	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	**Moderate**
Ost et el., 2017[12]	Yes	No	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	**Moderate**
Palma et al., 2019[14]	Yes	No	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	**Moderate**
Phillips et al., 2020[19]	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	**Moderate**
Theelen et al., 2019[9]	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	**Moderate**
Widmark et al., 2019[5]	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	**Moderate**

Table D2. Risk-of-Bias: Comparative Nonrandomized Studies

All noncomparative nonrandomized studies were assessed as being at high risk-of-bias, because of lack of comparator.

Study	Participant Selection	Intervention Exposure	Appropriate Comparator	Outcomes	Outcome Assessor Masking	Confounding	Statistical Analysis	Other Biases	Interest Disclosure	Funding	Overall Risk-of-Bias Assessment Comments
Al-Mamgani et al., 2013[92]	Yes	Yes	Yes	Yes	No	No	No	No	Yes	No	**High**
Andruska et al., 2022[22]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	**Low**
Bettinger et al., 1015[99]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	No	**Moderate**
Bouman-Wammes et al., 2017[131]	Yes	Yes	Yes	Yes	No	No	No	No	Yes	No	**High**
De Bleser et al., 2019[134]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	No	**Moderate**
de Geus et al., 2017[89]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	**Low**
Filippi et al., 2016[67]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	No	No	**Moderate**
Fleming et al., 2017[68]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	**Moderate**
Glowacki et al., 2017[38]	Yes	Yes	Yes	Yes	No	No	No	No	No	No	**High**
Halpern et al., 2016[39]	Yes	Yes	Yes	Yes	No	No	No	No	Yes	Yes	**High**
Hara et al., 2019[103]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	No	**Moderate**
Honda et al., 2013[104]	Yes	Yes	Yes	Yes	No	No	No	No	Yes	No	**High**
Hurmuz et al., 2920[136]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	No	**Moderate**
Jacob et al., 2015[105]	Yes	Yes	Yes	Yes	No	No	No	No	Yes	No	**High**
Jacobs et al., 2020[71]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	No	**Low**
Jeong et al., 2021[106]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	**Moderate**
Ji et al., 2022[108]	Yes	Yes	Yes	Yes	No	No	No	No	Yes	Yes	**High**
Jun et al., 2018[109]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	**Moderate**
Kanzaki et al., 2020[72]	Yes	Yes	Yes	Yes	No	No	No	No	Yes	Yes	**High**
Katz et al., 2012[41]	No	Yes	Yes	Yes	No	No	No	No	Yes	No	**High**
Kim et al., 2020[111]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	**Moderate**
Kimura et al. 2018[112]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	**Moderate**

Study	Participant Selection	Intervention Exposure	Appropriate Comparator	Outcomes	Outcome Assessor	Confounding	Statistical Analysis	Other Biases	Interest Disclosure	Funding	Overall Risk-of-Bias Assessment Comments
Lee et al., 2016[43]	Yes	Yes	Yes	Yes	No	No	No	No	Yes	Yes	**High**
Lee et al., 2018[74]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	No	**Moderate**
Littau et al., 2022[76]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	No	**Low**
Lo et al., 2020[77]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	**Moderate**
Loblaw et al., 2017[44]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	No	**Moderate**
Monaco et al., 2022[50]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	No	**Moderate**
Moningi et al., 2022[90]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	**Low**
Nabavizadeh et al., 2021[118]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	**Moderate**
Nelson et al., 2019[78]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	**Moderate**
Nieuwenhuizen et al., 2021[119]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	**Moderate**
Oladeru et al., 2016[120]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	No	**Low**
Oliai et al., 2016[51]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	**Moderate**
Ozyigit et al., 2011[93]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	No	**Moderate**
Pan et al., 2018[54]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	No	**Low**
Parikh et al., 2018[121]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	No	**Low**
Patel et al., 2020[56]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	**Low**
Rajyaguru et al., 2018[122]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	No	**Low**
Ricco et al., 2017[60]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	**Low**
Rosen et al., 2016[80]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	**Low**
Santos et al., 2021[156]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	**Low**
Sapisochin et al., 2017[123]	Yes	Yes	Yes	Yes	No	No	No	No	Yes	Yes	**High**
Scotti et al., 2109[81]	Yes	Yes	Yes	Yes	No	No	No	No	Yes	No	**High**
Sebastian et al., 2019[124]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	No	**Low**
Tsang et al., 2021[61]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	No	**Moderate**

Study	Participant Selection	Intervention Exposure	Appropriate Comparator	Outcomes	Outcome Assessor	Confounding	Statistical Analysis	Other Biases	Interest Disclosure	Funding	Overall Risk-of-Bias Assessment Comments
Uhlig et al., 2020[88]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	**Low**
Vargo et al., 2018[94]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	No	**Moderate**
Wahl et al., 2016[127]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	**Moderate**
Wang et al., 2021[128]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	No	**Moderate**
Wegner et al., 2020[85]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	No	**Low**
Werneburg et al., 2018[62]	Yes	Yes	Yes	Yes	No	No	No	No	No	Yes	**High**
Wong et al., 2019[129]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	**Moderate**
Wong et al., 2021[130]	No	Yes	Yes	Yes	No	No	No	No	No	Yes	**High**
Yamazaki et al.,2017[95]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	No	**Moderate**
Yu et al., 2014[63]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	**Low**
Zhong et al., 2017[91]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	No	**Low**

Table D3. Risk-of-Bias: Economic Modeling Studies

Part 1

Citation	Target Population	Perspective	Time Horizon	Discount Rate	Comparators	Modeling	Effectiveness
Kim et al., 2018[153]	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Kim et al., 2019[152]	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Kumar et al., 2021[154]	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Mehrens et al., 2021[155]	Yes	Not clear	Yes	Yes	Yes	Yes	Yes
Parikh et al., 2020[151]	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Part 2

Citation	Outcomes	Resource Use/Costs	Uncertainty	Results	Interest Disclosure	Funding Source	Overall Risk-of-Bias Assessment Comments
Kim et al., 2018[153]	Yes	Yes	Yes	Yes	No	No	Low
Kim et al., 2019[152]	Yes	Yes	Yes	Yes	Yes	No	Low
Kumar et al., 2021[154]	Yes	Yes	Yes	Yes	Yes	Yes	Low
Mehrens et al., 2021[155]	Yes	Yes	Yes	Yes	Yes	No	Low
Parikh et al., 2020[151]	Yes	Yes	Yes	Yes	No	Yes	**Low**

Table D4. Methodological Quality: Guidelines

Guideline Developer, Year	Rigor of Development: Evidence	Rigor of Development: Recommendations	Editorial Independence	Scope & Purpose	Stakeholder Involvement	Clarity & Presentation	Applicability	Overall Assessment
Prostate cancer								
American Society for Radiation Oncology and American Urological Association (ASTRO/AUA), 2022[157-159]	Yes	Yes	Not clear	Yes	Yes	Yes	Yes	**Good**
Prostate Cancer Guidelines Panel, 2022 [160]	Yes	Yes	Not clear	Yes	Yes	Yes	Yes	**Good**
Australian and New Zealand Faculty of Radiation Oncology	Not clear	Not clear	Not clear	Yes	No	Yes	Yes	**Poor**

Guideline Developer, Year	Rigor of Development: Evidence	Rigor of Development: Recommendations	Editorial Independence	Scope & Purpose	Stakeholder Involvement	Clarity & Presentation	Applicability	Overall Assessment
Genito-Urinary Group (FROGG), 2018[161]								
Lung cancer								
American Society of Clinical Oncology (ASCO), 2021[162]	Yes	Yes	Not clear	Yes	Yes	Yes	Yes	**Good**
Society of Interventional Radiology (SIR), 2021[163]	Not clear	Not clear	Not clear	Yes	Not clear	Yes	Yes	**Moderate**
European Society for Medical Oncology (ESMO), 2020 (update of 2018)[164,165]	Not clear	Not clear	Not clear	Yes	Not clear	Yes	Yes	**Moderate**
National Institute for Health and Care Excellence (NICE), 2018[166]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	**Good**
Colorectal cancer								
American Society of Clinical Oncology (ASCO), 2022 [167]	Yes	Yes	Not clear	Yes	Yes	Yes	Yes	**Good**
European Society for Medical Oncology (ESMO), 2022[168]	Not clear	Not clear	Not clear	Yes	Not clear	Yes	Yes	**Moderate**
National Institute for Health and Care Excellence (NICE), 2021[169]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	**Good**

Guideline Developer, Year	Rigor of Development: Evidence	Rigor of Development: Recommendations	Editorial Independence	Scope & Purpose	Stakeholder Involvement	Clarity & Presentation	Applicability	Overall Assessment
Gynecological cancer								
European Society of Gynaecological Oncology (ESGO), 2018[170]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	**Good**
European Society of Gynaecological Oncology (ESGO), 2020[171]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	**Good**
Melanoma								
European Society for Medical Oncology (ESMO), 2019[172]	Not clear	Not clear	Not clear	Yes	Not clear	Yes	Yes	**Moderate**
Renal cancer								
National Comprehensive Cancer Network (NCC), 2022[173]	No	Yes	Not clear	Yes	Not clear	Yes	Yes	**Moderate**
European Association of Urology (EAU), 2022[174]	Yes	Yes	Not clear	Yes	Yes	Yes	Yes	**Good**
American Urology Association (AUA), 2021[175,176]	Yes	Yes	Not clear	Yes	Yes	Yes	Yes	**Good**
European Society for Medical Oncology (ESMO), 2019[177]	Not clear	Not clear	Not clear	Yes	Not clear	Yes	Yes	**Moderate**
Pancreatic cancer								
American Society for Radiation Oncology (ASTRO), 2019[178]	Yes	Yes	Not clear	Yes	Yes	Yes	Yes	**Good**

Guideline Developer, Year	Rigor of Development: Evidence	Rigor of Development: Recommendations	Editorial Independence	Scope & Purpose	Stakeholder Involvement	Clarity & Presentation	Applicability	Overall Assessment
Liver cancer								
American College of Radiology (ACR), 2022[179]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	**Good**
American Society for Radiation Oncology (ASTRO), 2022[180]	Yes	Yes	Not clear	Yes	Yes	Yes	Yes	**Good**
European Society for Medical Oncology (ESMO), 2022[181]	Not clear	Not clear	Not clear	Yes	Not clear	Yes	Yes	**Moderate**
European Society for Medical Oncology (ESMO), 2018 [182]	Not clear	Not clear	Not clear	Yes	Not clear	Yes	Yes	**Moderate**
Nonspine bone cancer								
European Society for Medical Oncology (ESMO), 2021[183]	Not clear	Not clear	Not clear	Yes	Not clear	Yes	Yes	**Moderate**
Spanish Society of Radiation Oncology (SEOR), 2022[184]	No	No	Not clear	No	No	Yes	Yes	**Poor**
Testicular cancer								
European Society for Medical Oncology (ESMO), 2022[185]	Not clear	Not clear	Not clear	Yes	Not clear	Yes	Yes	**Moderate**

Appendix E. GRADE Quality of Evidence

Table E1. GRADE Profile: Effectiveness and Toxicity of Stereotactic Body Radiation for Prostate Cancer

Number of Participants and Studies	Risk-of-Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Comments	Effect	Overall Certainty of Evidence Rating
SBRT vs. cRT for intermediate-to-high-risk localized prostate cancer								
Overall survival								
N = 1,200 1 RCT[5]	No serious	Not assessable (single study)	No serious	Very serious (downgraded 2 levels)	Not assessed	No additional comments	5-year overall survival: HR, 1.11; 95% CI, 0.73 to 1.69	⨁⨁◯◯ LOW
Progression-free survival								
N = 1,200 1 RCT[5]	No serious	Not assessable (single study)	No serious	Serious (downgraded 1 level)	Not assessed	No additional comments	5-year failure-free survival (biochemical or clinical failure: aHR, 1.00 (95% CI, 0.76 to 1.33)	⨁⨁⨁◯ MODERATE
Disease-control								
N = 1,200 1 RCT[5]	Serious (downgraded 1 level)	Not assessable (single study)	No serious	Very serious (downgraded 2 levels)	Not assessed	Downgraded for blinding related to this outcome	Local failure: HR, 0.94; 95% CI, 0.40 to 2.22 Distant failure: HR, 0.99; 95% CI, 0.63 to 1.54 Use of ADT at 5 years: HR, 1.12; 95% CI, 0.79 to 1.59	⨁◯◯◯ VERY LOW
Quality of life								
Not reported								
SBRT vs. other forms of RT for localized prostate cancer (all risk groups)								
Overall survival								
N = 75,749 5 comparative NRSs[22,44,51,56,60]	No serious	No serious	No serious	No serious	Not assessed	No additional comments	Men with localized prostate cancer (all risk groups) treated with SBRT had similar or improved overall survival when compared with	⨁⨁◯◯ LOW

Number of Participants and Studies	Risk-of-Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Comments	Effect	Overall Certainty of Evidence Rating
							other treatment options, including cRT, IMRT and brachytherapy; ; studies reported at different times using different statistics, precluding any summary statistics (see detailed findings)	
Progression-free survival								
Not reported								
Disease-control								
N = 1,190 4 comparative NRSs[43,44,51,61]	No serious	No serious	No serious	No serious	Not assessed	No additional comments	Men with localized prostate cancer (all risk groups) treated with SBRT had similar or improved disease control when compared with other treatment options, including cRT, IMRT and brachytherapy, , with biochemical control rates of around 89% to 100% at 5 years.	⊕⊕◯◯ LOW
Quality of life								
N = 2,154 3 RCTs[1,3,5]	Serious (downgraded 1 level)	No serious	No serious	Serious (downgrade 1 level)	Not assessed	Downgraded for blinding related to this outcome and precision not assessable	Men with localized prostate cancer (all risk groups) treated with SBRT had a similar quality of life to men treated with other forms of RT; however, specific symptoms affecting quality of life may vary between treatments.	⊕⊕◯◯ LOW

Number of Participants and Studies	Risk-of-Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Comments	Effect	Overall Certainty of Evidence Rating
SBRT vs. other forms of RT for localized prostate cancer (all risk groups)								
Toxicity								
N = 2,409 4 RCTs[1,3-5]	Serious (downgraded 1 level)	No serious	No serious	No serious	Not assessed	Downgraded for blinding related to this outcome	Rates of toxicities of grade 3 or higher were relatively infrequent in SBRT for localized prostate cancer (around 1% to 2%), and were similar to those of other RTs.	⊕⊕⊕◯ MODERATE
N = 67,968 5 comparative NRSs[38,51,54,61,63]	No serious	No serious	No serious	No serious	Not assessed	No additional comments	Overall, grade 3 toxicities were rare (up to 6% depending on the specific toxicity and the time point) and no grade 4 or 5 events were reported when SBRT was used for localized prostate cancer (all risk groups). There may be some evidence that SBRT is associated with increased urinary retention or obstruction, urinary fistula, and more GI and GU toxicity than IMRT and greater GI toxicity than brachytherapy.	⊕⊕◯◯ LOW

Abbreviations. ADT: androgen deprivation therapy; aHR: adjusted hazard ratio; CI; confidence interval; cRT: conventional radiation therapy; GIL gastrointestinal; GU: genitourinary; HR: hazard ratio; IMRT: intensity-modulated radiation therapy; NRS: nonrandomized study; RCT: randomized controlled trial; SBRT: stereotactic body radiation therapy.

Table E2. GRADE Profile: Effectiveness and Toxicity of Stereotactic Body Radiation for Lung Cancer

Number of Participants and Studies	Risk-of-Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Comments	Effect	Overall Certainty of Evidence Rating
SBRT vs. surgery or no SBRT for operable early-stage NSCLC								
Overall survival								
N = 41,583 3 comparative NRSs[76,80,81]	No serious	Serious (downgraded 1 level)	No serious	No serious	Not assessed	No additional comments	SBRT was associated with significantly worse outcomes than surgery for operable early-stage NCSLC; surgery was associated with around a 60 to 65% lower risk of mortality. However, 1 study did find that in patients who were medically operable, SBRT and lobectomy may be equally effective.	⊕◯◯◯ VERY LOW
Progression-free survival								
N = 187 1 comparative NRS[81]	Serious (downgraded 1 level)	Not assessable (single study)	No serious	Very serious (downgraded 2 levels)	Not assessed	No additional comments	In patients who were medically operable, SBRT and lobectomy may be equally effective (HR, 1.57; 95% CI, 0.68 to 3.64)	⊕◯◯◯ VERY LOW
Disease-control								
N = 60 1 RCT[7]	Serious (downgraded 1 level)	Not assessable (single study)	No serious	No serious	Not assessed	Downgraded for blinding related to this outcome	In people with potentially resectable early-stage NCSLC, SBRT in combination with durvalumab was associated with significantly higher odds of having a major pathological response (OR, 16.0; 95% CI, 3.2 to 79.6) or a partial radiographic response (46.7% SBRT with durvalumab vs. 3.3% durvalumab; *P* = .001) than durvalumab alone.	⊕⊕⊕◯ MODERATE

Number of Participants and Studies	Risk-of-Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Comments	Effect	Overall Certainty of Evidence Rating
Quality of life								
Not reported								
SBRT vs. RT for inoperable stage II								
Overall survival								
N = 4,401 1 comparative NRS[71]	No serious	Not assessable (single study)	No serious	No serious	Not assessed	No additional comments	SBRT appears to be associated with improved survival than cRT (HR, 0.79; 95% CI, 0.71 to 0.87) or hypofractionated radiotherapy (HR, 0.57; 95% CI, 0.50 to 0.66) for inoperable stage II NSCLC.	⊕⊕◯◯ LOW
Progression-free survival								
Not reported								
Disease-control								
Not reported								
Quality of life								
Not reported								
SBRT vs. no SBRT for advanced NCSLC								
Overall survival								
N = 78 1 RCT[9]	No serious	Not assessable (single study)	No serious	Serious (downgraded 1 level)	Not assessed	No additional comments	People with advanced NSCLC treated with SBRT after pembrolizumab or pembrolizumab alone had a similar overall survival (median: 15.9 months SBRT vs. 7.6 months control; HR, 0.66; 95% CI, 0.37 to 1.18) However, in subgroup analyses, men (HR, 0.42; 95%CI, 0.19 to 0.96; *P* = .04) and smokers (HR,	⊕⊕⊕◯ MODERATE

Number of Participants and Studies	Risk-of-Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Comments	Effect	Overall Certainty of Evidence Rating
							0.48; 95% CI, 0.25 to 0.93; *P* = .03) had significantly improved survival with SBRT compared with pembrolizumab alone.	
Progression-free survival								
N = 78 1 RCT[9]	Serious (downgraded 1 level)	Not assessable (single study)	No serious	Serious (downgraded 1 level)	Not assessed	Downgraded for blinding related to this outcome	People with advanced NSCLC treated with SBRT after pembrolizumab or pembrolizumab alone had a similar PFS (HR, 0.71; 95% CI, 0.42 to 1.18).	⊕⊕◯◯ LOW
Disease-control								
Not reported								
Quality of life								
Not reported								
SBRT vs. surgery or cRT for lung metastases								
Overall survival								
N= 483 4 comparative NRSs[9,67,68,72,74]	No serious	No serious	No serious	No serious	Not assessed	No additional comments	In people with lung metastases, SBRT and surgery may be associated with similar overall survival (median survival at 2 years of around 68% to 77% in the SBRT group versus 82% in the surgery group); however, SBRT may be associated with improved survival when compared with cRT (median survival of 26 months in the SBRT group versus 9 months in the cRT group; *P* < .001)..	⊕⊕◯◯ LOW

Number of Participants and Studies	Risk-of-Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Comments	Effect	Overall Certainty of Evidence Rating
Progression-free survival								
N = 301 3 comparative NRSs[67,72,74]	No serious	Serious (downgraded 1 level)	No serious	No serious	Not assessed	No additional comments	People with lung metastases treated with SBRT had significantly worse PFS than people treated with surgery (around 3 times more likely to have progression). However, results were mixed with 1 study showing no difference between SBRT and surgery.	⨁◯◯◯ VERY LOW
Disease-control								
N = 694 4 comparative NRSs[68,72,74,78]	No serious	Serious (downgraded 1 level)	No serious	No serious	Not assessed	No additional comments	Results were mixed with SBRT being associated with both similar and lower levels of local control than surgery for lung metastases. SBRT, however, was significantly associated with improved local control when compared with cRT. Studies reported at different times using different statistics, precluding any summary statistics (see detailed findings).	⨁◯◯◯ VERY LOW
Quality of life								
Not reported								
SBRT vs. surgery or cRT for LCNEC of lung								
Overall survival								
N = 3,963 2 comparative NRSs[77,85]	No serious	No serious	No serious	No serious	Not assessed	No additional comments	In people with LCNEC of lung, SBRT may be associated with improved survival when compared with cRT (HR, 0.83;	⨁⨁◯◯ LOW

Number of Participants and Studies	Risk-of-Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Comments	Effect	Overall Certainty of Evidence Rating
							95% CI, 0.68 to 1.00)[a], but worse outcomes when compared with surgery (HR, 1.61; 95% CI, 1.36 to 1.92).	
Progression-free survival								
Not reported								
Disease-control								
Not reported								
Quality of life								
Not reported								
SBRT vs. surgery and other RT for any lung cancer								
Toxicity								
N = 138 2 RCTs[7,9]	Serious (downgraded 1 level)	No serious	No serious	No serious	Not assessed	Downgraded for blinding related to this outcome	Grade 3 and higher events occurred in around 3% to 11% of SBRT group; most common being dyspnea and pneumonia, pancreatitis, and fatigue.	⊕⊕⊕◯ MODERATE
N = 221 2 comparative NRSs[67,74]	No serious	No serious	No serious	No serious	Not assessed	No additional comments	Grade 3 toxicities were not common with SBRT, and included lung toxicity (including radiation pneumonitis) and chest wall pain; ranging from 3% to 14% depending on the specific toxicity.	⊕⊕◯◯ LOW

Note. [a] Inverted for consistency Abbreviations. CI: confidence interval; cRT: conventional radiation therapy; HR: hazard ratio; LCNEC: large-cell neuroendocrine carcinoma; NRS: nonrandomized study; NSCLC: non-small cell lung cancer; PFS: progression-free survival; RCT: randomized controlled trial; SBRT: stereotactic body radiation therapy;

Table E3. GRADE Profile: Effectiveness and Toxicity of Stereotactic Body Radiation for Melanoma

Number of Participants and Studies	Risk-of-Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Comments	Effect	Overall Certainty of Evidence Rating
SBRT with nivolumab and ipilimumab vs. nivolumab and ipilimumab for Merkel cell carcinoma								
Overall survival								
N = 50 1 RCT[10]	No serious	Not assessable (single study)	No serious	Very serious (downgraded 2 levels)	Not assessed	No additional comments	No difference between groups by immunotherapy status: • Naïve to treatment: HR, 2.12; 95% CI, 0.13 to 34.23 Previous treatment: HR, 2.15; 95% CI, 0.83 to 5.57	⨁⨁◯◯ LOW
Progression-free survival								
N = 50 1 RCT[10]	No serious	Not assessable (single study)	No serious	Very serious (downgraded 2 levels)	Not assessed	No additional comments	No difference between groups by immunotherapy status: • Naïve to treatment: HR, 1.77; 95% CI, 0.11 to 28.38 Previous treatment: HR, 1.60; 95% CI, 0.68 to 3.75	⨁⨁◯◯ LOW
Disease-control								
N = 50 1 RCT[10]	Serious (downgraded 1 level)	Not assessable (single study)	No serious	Serious (downgraded 1 level)	Not assessed	Downgraded for blinding related to this outcome	Response: 50% vs. 72%; *P* = .26	⨁⨁◯◯ LOW
Quality of life								
Not reported								
Toxicity								
N = 50 1 RCT[10]	Serious (downgraded 1 level)	Not assessable (single study)	No serious	Serious (downgraded 1 level)	Not assessed	Downgraded for blinding related to this outcome	8 (16%) discontinued protocol treatment due to toxicity.	⨁⨁◯◯ LOW

Number of Participants and Studies	Risk-of-Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Comments	Effect	Overall Certainty of Evidence Rating
							No deaths were attributed to treatment. Grade 3 events occurred in 24% of SBRT group and 28% in control group; grade 4 events occurred in 8% and 12% by group.	

Abbreviations. CI: confidence interval; HR: hazard ratio; RCT: randomized controlled trial.

Table E4. GRADE Profile: Effectiveness and Toxicity of Stereotactic Body Radiation for Renal Cell Carcinoma

Number of Participants and Studies	Risk-of-Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Comments	Effect	Overall Certainty of Evidence Rating
SBRT vs. cRT in stage I RCC								
Overall survival								
N = 91,965 1 comparative NRS[88]	No serious	Not assessable (single study)	No serious	No serious	Not assessed	No additional comments	In people with stage I RCC, SBRT was associated with a significantly worse overall survival than people treated with ablation or surgery[88]: • Partial nephrectomy vs. SBRT: HR, 0.29 (95% CI, 0.19 to 0.46) • Cryoablation vs. SBRT: HR, 0.40 (95% CI, 0.26 to 0.60) • Radiofrequency ablation or microwave ablation vs. SBRT: HR, 0.46 (95% CI, 0.31 to 0.67)	⊕⊕◯◯ LOW
Progression-free survival								
Not reported								

Number of Participants and Studies	Risk-of-Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Comments	Effect	Overall Certainty of Evidence Rating
Disease-control								
Not reported								
Quality of life								
Not reported								
Toxicity								
N = 190 1 noncomparative NRS[87]	Serious (down-graded 1 level)	Not assessable (single study)	No serious	Serious (down-graded 1 level)	Not assessed	No additional comments	Fewer than 1% of participants experienced a grade 3 or higher toxicity	⨁◯◯◯ VERY LOW

Abbreviations. CI: confidence interval; HR: hazard ratio; NRS: nonrandomized study; RCC: renal cell carcinoma; SBRT: stereotactic body radiation therapy.

Table E5. GRADE Profile: Effectiveness and Toxicity of Stereotactic Body Radiation for Pancreatic Cancer

Number of Participants and Studies	Risk-of-Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Comments	Effect	Overall Certainty of Evidence Rating
SBRT vs. CT or IMRT for unresected pancreatic cancer								
Overall survival								
N = 14,331 1 comparative NRS[89]	No serious	Not assessable (single study)	No serious	No serious	Not assessed	No additional comments	In people with unresected pancreatic cancer treated with SBRT had significantly better overall survival than people treated with CT (13.9 months SBRT vs. 10.2 months CT; *P* < .001) or IMRT (13.9 months SBRT vs. 12.2 months IMRT; *P* = .049). However, there was no difference in overall survival between SBRT with multi-agent CT and multi-agent CT alone (14.8 months SBRT with multi-agent CT vs. 12.9 months multi-agent CT alone; *P* = .09).	⨁⨁◯◯ LOW

Number of Participants and Studies	Risk-of-Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Comments	Effect	Overall Certainty of Evidence Rating
Progression-free survival								
Not reported								
Disease-control								
Not reported								
Quality of life								
Not reported								
SBRT vs. cRT for locally advanced pancreatic cancer								
Overall survival								
N = 8,450 1 comparative NRS[91]	No serious	Not assessable (single study)	No serious	No serious	Not assessed	No additional comments	People with locally advanced pancreatic cancer treated with SBRT had significantly better overall survival than people treated with cRT at 2 years (HR, 0.84; 95% CI, 0.75 to 0.93), with a significantly longer median survival.	⨁⨁◯◯ LOW
Progression-free survival								
Not reported								
Disease-control								
Not reported								
Quality of life								
Not reported								
Toxicity								
N = 5,624 1 comparative NRS[90]	No serious	Not assessable (single study)	No serious	No serious	Not assessed	No additional comments	In people with nonmetastatic, unresectable pancreatic cancer, SBRT was associated with significantly more GI bleeds than CT alone (HR, 4.13; 95% CI, 2.58 to 6.61) and GI strictures (HR, 1.58; 95% CI, 1.18 to 2.21). However, risk varied by age, with SBRT being associated with similar rates of GI complications to cRT in younger people.	⨁⨁◯◯ LOW

Abbreviations. CI: confidence interval; cRT: conventional radiation therapy; CT: chemotherapy; GI: gastrointestinal; HR: hazard ratio; IMRT: intensity-modulated radiation therapy; NRS: nonrandomized study; SBRT: stereotactic body radiation therapy.

Table E6. GRADE Profile: Effectiveness and Toxicity of Stereotactic Body Radiation for Head and Neck Cancer

Number of Participants and Studies	Risk-of-Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Comments	Effect	Overall Certainty of Evidence Rating
SBRT vs. brachytherapy in early-stage oropharyngeal cancer								
Overall survival								
N = 250 1 comparative NRS[92]	No serious	Not assessable (single study)	No serious	No serious	Not assessed	No additional comments	SBRT boost or brachytherapy boost after cRT were associated with a similar overall survival at 3 years (81% SBRT vs. 83% BT; *P* = .83).	⨁⨁◯◯ LOW
Progression-free survival								
N = 250 1 comparative NRS[92]	No serious	Not assessable (single study)	No serious	No serious	Not assessed	No additional comments	SBRT boost or brachytherapy boost after cRT were associated with a similar disease-free survival at 3 years (92% SBRT vs. 86% BT; *P* = .15).	⨁⨁◯◯ LOW
Disease-control								
N = 250 1 comparative NRS[92]	No serious	Not assessable (single study)	No serious	No serious	Not assessed	No additional comments	SBRT boost or brachytherapy boost after cRT were associated with a similar local control rate at 3 years (97% SBRT vs. 94% BT; *P* = .33).	⨁⨁◯◯ LOW
Quality of life								
N = 250 1 comparative NRS[92]	No serious	Not assessable (single study)	No serious	No serious	Not assessed	No additional comments	No significant difference in quality of life in patients with early-stage oropharyngeal cancer boosted with SBRT or brachytherapy after cRT.	⨁⨁◯◯ LOW
SBRT vs. other treatment options for recurrent or metastatic head and neck cancer								
Overall survival								
N = 62 1 RCT[11]	No serious	Not assessable (single study)	No serious	Serious (downgraded 1 level)	Not assessed	Imprecision not assessable	No difference between nivolumab in combination with SBRT or nivolumab alone (at 12 months, 54.4% SBRT vs. 50.2% control; *P* = .75).	⨁⨁⨁◯ MODERATE

Number of Participants and Studies	Risk-of-Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Comments	Effect	Overall Certainty of Evidence Rating
N = 641 3 comparative NRSs[93-95]	No serious	No serious	No serious	No serious	Not assessed	No additional comments	SBRT appears to be associated with a significantly worse overall survival than charged particle RT (HR, 0.35; 95% CI, 0.13 to 0.94), but a similar cancer-specific survival to IMRT (HR, 0.88; 95% CI, 0.70 to 1.10) and conformal RT (at 2 years, 64% SBRT vs. 47% conformal RT; *P* = .40).	⨁⨁◯◯ LOW
Progression-free survival								
N = 62 1 RCT[11]	No serious	Not assessable (single study)	No serious	Serious (downgraded 1 level)	Not assessed	Imprecision not assessable	No difference between nivolumab in combination with SBRT or nivolumab alone (at 12 months, 54.4% SBRT vs. 50.2% control; *P* = .75).	⨁⨁⨁◯ MODERATE
Disease-control								
N = 62 1 RCT[11]	No serious	Not assessable (single study)	No serious	Very serious (downgraded 2 levels)	Not assessed	Imprecision not assessable	No difference between nivolumab in combination with SBRT or nivolumab alone (at 12 months, OR, 0.80; 95% CI, 0.24 to 2.61).	⨁⨁◯◯ LOW
N = 641 3 comparative NRSs[93-95]	No serious	No serious	No serious	No serious	Not assessed	No additional comments	SBRT appears to be associated with similar levels of disease control to IMRT (HR, 1.15; 95% CI, 0.89 to 1.50), conformal RT (at 2 years, 82% SBRT; 80% conformal RT; *P* = .57), and charged particle RT (at 1 year, 67% SBRT vs. 67% charged particle RT; *P* value not reported)	⨁⨁◯◯ LOW
Quality of life								
Not reported								

Number of Participants and Studies	Risk-of-Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Comments	Effect	Overall Certainty of Evidence Rating
SBRT vs. other options for early and recurrent head and neck cancers								
Toxicity								
N = 62 1 RCT[11]	No serious	Not assessable (single study)	No serious	Serious (downgraded 1 level)	Not assessed	Imprecision not assessable	No difference between nivolumab in combination with SBRT or nivolumab alone (grade 3, and higher 9.7% SBRT vs. 13.3% control; *P* = .70).	⊕⊕⊕◯ MODERATE
N = 891 4 comparative NRSs[92-95]	No serious	No serious	No serious	No serious	Not assessed	No additional comments	SBRT had a favorable toxicity profile, with similar or fewer toxicities than other treatment options (brachytherapy, conformal RT, IMRT, charged particle RT); however, grade 5 events were relatively high, with 1 study reporting 12.5% grade 5 events in SBRT group.	⊕⊕◯◯ LOW

Abbreviations. CI: confidence interval; cRT: conventional radiation therapy; IMRT: intensity-modulated radiation therapy; NRS: nonrandomized study; OR: odds ratio; RCT: randomized controlled trial; RT: radiation therapy; SBRT: stereotactic body radiation therapy.

Table E7. GRADE Profile: Effectiveness and Toxicity of Stereotactic Body Radiation for Liver Cancer

Number of Participants and Studies	Risk-of-Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Comments	Effect	Overall Certainty of Evidence Rating
SBRT vs. RFA for early-stage HCC								
Overall survival								
N = 4,892 4 comparative NRSs[103,121,122,128]	No serious	Serious (downgraded 1 level)	No serious	No serious	Not assessed	No additional comments	In people with early-stage HCC, results were mixed. SBRT may be associated with similar overall survival to RFA (at 5 years, 78.4% vs. 46.3%; *P* = .09 over the 5 years);	⊕◯◯◯ VERY LOW

Number of Participants and Studies	Risk-of-Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Comments	Effect	Overall Certainty of Evidence Rating
							however, 1 study showed that SBRT may be associated with worse survival than RFA at 5 years (HR, 0.67; 95% CI, 0.55 to 0.81).	
Progression-free survival								
N = 98 1 comparative NRS[128]	No serious	Not assessable (single study)	No serious	Serious (not assessable)	Not assessed	No additional comments	In people with early-stage HCC, SBRT after RFA may be associated with similar PFS to repeated RFA (at 2 years, 31.4% vs. 28.6%; *P* = .31).	⨁◯◯◯ VERY LOW
Disease-control								
N = 472 2 comparative NRSs[103,128]	No serious	No serious	No serious	No serious	Not assessed	No additional comments	In people with early-stage HCC, SBRT may be associated with similar rates of intrahepatic recurrence (at 3 years, 59.3% RT vs. 57.6% RFA; *P* = .64) and local recurrence (0 SBRT vs. 25.7% RFA; *P* = .06).	⨁⨁◯◯ LOW
Quality of life								
Not reported								
SBRT vs. TACE and RFA in small HCCs								
Overall survival								
N = 683 4 comparative NRSs[104,106,109,112]	No serious	No serious	No serious	Serious (downgraded 1 level)	Not assessed	No additional comments	In people with small HCCs, SBRT, alone or in combination with TACE is associated with a similar overall survival to TACE alone, TACE in combination with TACE, or to RFA.	⨁◯◯◯ VERY LOW

Number of Participants and Studies	Risk-of-Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Comments	Effect	Overall Certainty of Evidence Rating
							Studies reported at different times using different statistics, precluding any summary statistics (see detailed findings).	
Progression-free survival								
N = 615 3 comparative NRSs[106,109,112]	No serious	No serious	No serious	No serious	Not assessed	No additional comments	In people with small HCCs, SBRT is associated with a similar PFS to RFA. SBRT in combination with TACE is associated with similar or improved PFS to TACE alone or SBRT alone. Studies reported at different times using different statistics, precluding any summary statistics (see detailed findings).	⨁⨁◯◯ LOW
Disease-control								
N = 683 4 comparative NRSs[104,106,109,112]	No serious	Serious (downgraded 1 level)	No serious	No serious	Not assessed	No additional comments	In people with small HCC, SBRT added to TACE appears to be associated with improved local control, but results are mixed. Studies reported at different times using different statistics, precluding any summary statistics (see detailed findings).	⨁◯◯◯ VERY LOW
Quality of life								
Not reported								

Number of Participants and Studies	Risk-of-Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Comments	Effect	Overall Certainty of Evidence Rating
SBRT vs. other treatments for unresectable HCC								
Overall survival								
N = 3,338 8 comparative NRSs[105,108,111,118-120,127,129]	No serious	No serious	No serious	No serious	Not assessed	No additional comments	In people with unresectable HCC, SBRT, alone or in combination with TACE, appears to be associated with similar or improved survival compared with TACE alone, RFA, or SIRT. When compared with TA, SBRT appears to be associated with a lower survival rate. Studies reported at different times using different statistics, precluding any summary statistics (see detailed findings).	⨁⨁◯◯ LOW
Progression-free survival								
N = 889 5 comparative NRSs[108,118-120,129]	No serious	No serious	No serious	No serious	Not assessed	No additional comments	In people with unresectable HCC, SBRT, alone or in combination with TACE, appears to be associated with similar or improved PFS compared with TACE alone, RFA, or SIRT. When compared with TA, SBRT appears to be associated with a lower PFS. Studies reported at different times using different statistics, precluding any summary statistics (see detailed findings below).	⨁⨁◯◯ LOW

Number of Participants and Studies	Risk-of-Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Comments	Effect	Overall Certainty of Evidence Rating
Disease-control								
N = 3,149 8 comparative NRSs[105,108,111,118,119,127,129]	No serious	No serious	No serious	No serious	Not assessed	No additional comments	In people with unresectable HCC, SBRT, alone or in combination with TACE, may have similar or improved rates of disease control and recurrence when compared with RFA or TACE alone. When compared with TA, results are mixed, with 1 study showing no difference and 1 showing a significant decrease in local control with SBRT. Studies reported at different times using different statistics, precluding any summary statistics (see detailed findings below).	⊕⊕◯◯ LOW
Quality of life								
Not reported								
SBRT vs. sorafenib for advanced HCC								
Overall survival								
N = 1,023 1 comparative NRS[99]	No serious	Not assessable (single study)	No serious	No serious	Not assessed	No additional comments	In people with advanced HCC, SBRT was associated with improved survival when compared with sorafenib (HR, 0.53; 95% CI, 0.36 to 0.77).	⊕⊕◯◯ LOW
Progression-free survival								
N = 1,023 1 comparative NRS[99]	No serious	Not assessable (single study)	No serious	Serious (downgraded 1 level)	Not assessed	No additional comments	In people with advanced HCC, SBRT was associated with improved PFS when	⊕◯◯◯ VERY LOW

Number of Participants and Studies	Risk-of-Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Comments	Effect	Overall Certainty of Evidence Rating
							compared with sorafenib (HR, 0.59; 95% CI, 0.42 to 0.86).	
Disease-control								
Not reported								
Quality of life								
Not reported								
SBRT vs. other treatment as bridging therapy for people on waiting list for liver transplantation due to HCC								
Overall survival								
N = 744 2 comparative NRSs[123,130]	No serious	Not assessable (single study)	No serious	No serious	Not assessed	No additional comments	SBRT, as bridge therapy, appears to be associated with a similar overall survival to other options for bridge therapy (TACE, RFA, or HIFU) ; at around 61% to 73% at 3 years).	⨁⨁◯◯ LOW
Progression-free survival								
N = 150 1 comparative NRS[130]	No serious	Not assessable (single study)	No serious	Serious (downgraded 1 level)	Not assessed	No additional comments	SBRT, as bridge therapy, appears to be associated with improved PFS when compared with TACE or HIFU (progression at 3 years, 18.5% SBRT vs. 54.9% TACE vs. 62.8% HIFU; *P* < .001).	⨁◯◯◯ VERY LOW
Disease-control								
N = 744 2 comparative NRSs[123,130]	No serious	Not assessable (single study)	No serious	Serious (downgraded 1 level)	Not assessed	No additional comments	SBRT, as bridge therapy, appears to be associated with a better disease control than other options for bridge therapy (TACE or HIFU) but may be associated with worse disease control than	⨁◯◯◯ VERY LOW

Number of Participants and Studies	Risk-of-Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Comments	Effect	Overall Certainty of Evidence Rating
							RFA. Studies reported at different times using different statistics, precluding any summary statistics (see detailed findings below).	
Quality of life								
Not reported								
SBRT vs. TARE or cRT for unresectable intrahepatic cholangiocarcinoma								
Overall survival								
N = 141 1 comparative NRS[124]	No serious	Not assessable (single study)	No serious	No serious	Not assessed	No additional comments	SBRT was associated with improved survival compared with TARE (HR, 0.40; 95% CI, 0.22 to 0.74) or cRT (HR, 0.37; 95% CI, 0.20 to 0.68).	⨁⨁◯◯ LOW
Progression-free survival								
Not reported								
Disease-control								
Not reported								
Quality of life								
Not reported								
SBRT vs. other treatments for HCC								
Toxicity								
N = 6,071 16 comparative NRSs[99,103-106,108,109,111,112,118,119,123,127-130]	No serious	No serious	No serious	No serious	Not assessed	No additional comments	Rates of toxicities of grade 3 or higher were relatively infrequent in SBRT, and were similar to those of other RTs or treatment options. SBRT may be associated with some increased toxicities, but it is also associated with some	⨁⨁◯◯ LOW

Number of Participants and Studies	Risk-of-Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Comments	Effect	Overall Certainty of Evidence Rating
							decreased toxicities when compared with other options. Rates of toxicities varied by type of toxicity and time frame.	

Abbreviations CI: confidence interval; cRT: conventional radiation therapy; HCC: hepatocellular carcinoma; HIFU: high-intensity focused ultrasound; HR: hazard ratio; NRS: nonrandomized study; PFS: progression-free survival; RFA: radiofrequency ablation; SBRT: stereotactic body radiation therapy; TA: thermal ablation; TACE: transarterial chemoembolization.

Table E8. GRADE Profile: Effectiveness and Toxicity of Stereotactic Body Radiation for Oligometastatic Cancer

Number of Participants and Studies	Risk-of-Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Comments	Effect	Overall Certainty of Evidence Rating
SBRT vs. standard of care for oligometastatic cancer (primaries mostly adrenal, bone, liver, and lung)								
Overall survival								
N = 99 1 RCT[14]	No serious	Not assessable (single study)	No serious	Serious (downgraded 1 level)	Not assessed	No additional comments	At 5 years, no difference between groups (HR, 0.57; 95% CI, 0.30 to 1.10) At 6 years, improved survival with SBRT (HR, 0.47; 95% CI, 0.27 to 0.81)	⊕⊕⊕◯ MODERATE
Progression-free survival								
N = 99 1 RCT[14]	Serious (downgraded 1 level)	Not assessable (single study)	No serious	No serious	Not assessed	Downgraded for blinding related to this outcome	At 5 years, improved PFS with SBRT (HR, 0.47; 95% CI, 0.30 to 0.76) At 6 years, improved PFS with SBRT (HR, 0.48; 95% CI, 0.31 to 0.76)	⊕⊕⊕◯ MODERATE

Number of Participants and Studies	Risk-of-Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Comments	Effect	Overall Certainty of Evidence Rating
Disease-control								
N = 99 1 RCT[14]	Serious (downgraded 1 level)	Not assessable (single study)	No serious	Serious (downgraded 1 level)	Not assessed	Downgraded for blinding related to this outcome and imprecision not assessable	SBRT is associated with improved disease control (absence of progression, 75% SBRT vs. 49% standard of care; *P* = .001; lesional control by location).	⊕⊕◯◯ LOW
Quality of life								
N = 99 1 RCT[14]	Serious (downgraded 1 level)	Not assessable (single study)	No serious	Serious (downgraded 1 level)	Not assessed	Downgraded for blinding related to this outcome and imprecision not assessable	People with a controlled primary tumor and 1 to 5 oligometastatic lesions treated with SBRT or standard of care had a similar quality of life at each subsequent follow-up.	⊕⊕◯◯ LOW
SBRT vs. observation for oligometastatic prostate cancer								
Overall survival								
N = 116 2 RCTs[12,19]	No serious	No serious	No serious	Very serious (downgraded 2 levels)	Not assessed	No additional comments	In a pooled analysis of 2 RCTs, median for overall survival was not reached in either group, with similar overall survival between groups (HR, 0.53; 95% CI, 0.13 to 2.11).	⊕⊕◯◯ LOW
Progression-free survival								
N = 116 2 RCTs[12,19]	Serious (downgraded 1 level)	No serious	No serious	Serious (downgraded 1 level)	Not assessed	Downgraded for blinding related to this outcome	SBRT may be associated with similar or improved PFS (11.9 months MDT vs. 5.9 months surveillance; HR, 0.44; 95% CI, 0.29 to 0.66), and other measures of disease-related	⊕⊕◯◯ LOW

Number of Participants and Studies	Risk-of-Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Comments	Effect	Overall Certainty of Evidence Rating
							survival (ADT-free and castration-resistant prostate cancer-free survival).	
Disease-control								
N = 54 1 RCT[19]	Serious (downgraded 1 level)	Not assessable (single study)	No serious	Serious (downgraded 1 level)	Not assessed	Downgraded for blinding related to this outcome and imprecision not assessable	Men treated with SBRT had higher complete response (28% SBRT vs. 8% observation) and partial response rates (43% vs. 39% observation) at 6 months; however, no formal statistical testing was reported.	⊕⊕◯◯ LOW
Quality of life								
N = 116 2 RCTs[12,19]	Serious (downgraded 1 level)	No serious	No serious	Serious (downgraded 1 level)	Not assessed	Downgraded for blinding related to this outcome and imprecision not assessable	No difference between groups.	⊕⊕◯◯ LOW
SBRT vs. RT or no SBRT for oligometastatic prostate cancer								
Overall survival								
N = 506 1 comparative NRS[136]	No serious	Not assessable (single study)	No serious	No serious	Not assessed	No additional comments	Men with oligometastatic or oligorecurrent prostate cancer treated with SBRT or cRT had a similar overall survival at 2 years (87.7% SBRT vs. 87.3% cRT; *P* = .91).	⊕⊕◯◯ LOW
Progression-free survival								
N = 682 2 comparative NRSs[134,136]	No serious	No serious	No serious	Serious (downgraded 1 level) No serious	Not assessed	Imprecision not assessable	SBRT appears to be associated with a worse metastasis-free survival when compared with elective nodal	⊕◯◯◯ VERY LOW

Number of Participants and Studies	Risk-of-Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Comments	Effect	Overall Certainty of Evidence Rating
							RT but similar or improved PFS when compared with cRT.	
Disease-control								
N = 239 2 comparative NRSs[131,134]	No serious	No serious	No serious	Serious (downgraded 1 level) No serious	Not assessed	Imprecision not assessable	SBRT appears to be associated with worse outcomes (local and lymph node progression, relapse) when compared with elective nodal RT (68% SBRT vs. 77% with elective nodal RT; *P* = .01) but similar or improved outcomes (time to ADT or castration-resistance) when compared with no SBRT.	⨁◯◯◯ VERY LOW
Quality of life								
Not reported								
SBRT vs. other treatment for oligometastatic cancer (primary sites included prostate, breast, lung, and other sites)								
Toxicity								
N = 215 3 RCTs[12,14,19]	Serious (downgraded 1 level)	No serious	No serious	Serious (downgraded 1 level)	Not assessed	Downgraded for blinding related to this outcome and imprecision not assessable	No grade 3 and higher toxicities were seen in 2 of the 3 trials, , but some SBRT-related deaths were observed.	⨁⨁◯◯ LOW
N = 745 3 comparative NRSs[131,134,136]	No serious	No serious	No serious	Serious (downgraded 1 level)	Not assessed	Imprecision not assessable	No grade 3 and higher toxicities were reported, lower than those experienced with elective nodal RT (up to 2%).	⨁◯◯◯ VERY LOW

Abbreviations ADT: androgen deprivation therapy; CI: confidence interval; HR: hazard ratio; NRS: nonrandomized study; RCT: randomized controlled trial; RT: radiation therapy; SBRT: stereotactic body radiation therapy.

Table E9. GRADE Profile: Effectiveness and Toxicity of Stereotactic Body Radiation for Adrenal Cancer

Number of Participants and Studies	Risk-of-Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Comments	Effect	Overall Certainty of Evidence Rating
SBRT vs. other treatment options for adrenal cancer								
Overall survival								
No eligible comparative studies								
Progression-free survival								
No eligible comparative studies								
Disease-control								
No eligible comparative studies								
Quality of life								
No eligible comparative studies								
Toxicity								
No eligible comparative studies								

Abbreviations. SBRT: stereotactic body radiation therapy.

Table E10. GRADE Profile: Effectiveness and Toxicity of Stereotactic Body Radiation for Large Tumors

Number of Participants and Studies	Risk-of-Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Comments	Effect	Overall Certainty of Evidence Rating
SBRT vs. other treatment options for large tumors								
Overall survival								
No eligible comparative studies								
Progression-free survival								
No eligible comparative studies								
Disease-control								
No eligible comparative studies								
Quality of life								
No eligible comparative studies								

Number of Participants and Studies	Risk-of-Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Comments	Effect	Overall Certainty of Evidence Rating
Toxicity								
No eligible comparative studies								

Abbreviations. SBRT: stereotactic body radiation therapy.

Table E11. GRADE Profile: Effectiveness and Toxicity of Stereotactic Body Radiation for Mixed Cancers

Number of Participants and Studies	Risk-of-Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Comments	Effect	Overall Certainty of Evidence Rating
SBRT vs. other treatment options for mixed cancers								
Overall survival								
No eligible comparative studies								
Progression-free survival								
No eligible comparative studies								
Disease-control								
No eligible comparative studies								
Quality of life								
No eligible comparative studies								
Toxicity								
No eligible comparative studies								

Abbreviations. SBRT: stereotactic body radiation therapy.

Table E12. GRADE Profile: Effectiveness and Toxicity of Stereotactic Body Radiation for Bone Cancer

Number of Participants and Studies	Risk-of-Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Comments	Effect	Overall Certainty of Evidence Rating
SBRT vs. cRT for bone cancer								
Overall survival								
N = 160 1 RCT[21]	No serious	Not assessable (single study)	No serious	Serious (downgraded 1 level)	Not assessed	Imprecision not assessable	People with radiologically confirmed painful bone metastases (mostly nonspine) treated with SBRT or MFRT had a similar overall survival (median, 6.7 months in both groups).	⊕⊕⊕◯ MODERATE
Progression-free survival								
Not reported								
Disease-control								
N = 160 1 RCT[21]	Serious (downgraded 1 level)	Not assessable (single study)	No serious	Very serious (downgraded 2 levels)	Not assessed	Downgraded for blinding related to this outcome	When compared with MFRT, SBRT was found to be noninferior for both local failure (HR, 0.18; 95% CI, 0.02 to 1.47).	⊕◯◯◯ VERY LOW
Quality of life								
N = 160 1 RCT[21]	Serious (downgraded 1 level)	Not assessable (single study)	No serious	Serious (downgraded 1 level)	Not assessed	Downgraded for blinding related to this outcome and imprecision not assessable	No significant difference in quality of life for patients treated with SBRT or with MFRT.	⊕⊕◯◯ LOW

Number of Participants and Studies	Risk-of-Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Comments	Effect	Overall Certainty of Evidence Rating
Toxicity								
N = 160 1 RCT[21]	Serious (downgraded 1 level)	Not assessable (single study)	No serious	Serious (downgraded 1 level)	Not assessed	Downgraded for blinding related to this outcome and imprecision not assessable	No significant difference in toxicities for patients treated with SBRT or with MFRT. SBRT was associated with around 1% grade 3 or higher toxicities, and up to 10% for fatigue grade 3 and higher.	⨁⨁◯◯ LOW

Abbreviations. CI: confidence interval; MFRT: multifraction radiation therapy; SBRT: stereotactic body radiation therapy.

Cost-Effectiveness

Table E13. GRADE Profile: Cost-Effectiveness of Stereotactic Body Radiation Therapy by Cancer Type

Number of Participants and Studies	Risk-of-Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Comments	Effect	Overall Quality of Evidence Rating
SBRT vs. IMRT for prostate cancer								
Outcome: cost-effectiveness								
N = 3 hypothetical cohorts 1 economic modelling study[151]	No serious	Not assessable (single study)	Serious (downgraded 1 level)	Some serious	Not assessed	Oligometastatic hormone-resistant prostate cancer	Upfront SBRT may be a cost-effective option for people who wish to avoid systemic therapy; however, it was the cost-effective strategy in only 53.6% of microsimulations at a WTP of $100,000 per QALY	⨁⨁◯◯ LOW
Outcome: costs								
N = 12,128 1 comparative NRS[54]	No serious	Not assessable (single study)	Serious (downgraded 1 level)	No serious	Not assessed	Localized cancer in younger men only	Similar costs to payer and patient for SBRT and IMRT. No difference between treatments in complication costs or overall health care costs at 2 years.	⨁◯◯◯ VERY LOW
SBRT plus maintenance therapy vs maintenance therapy for lung cancer								
Outcome: cost-effectiveness								
N = 3 hypothetical cohorts 1 economic modelling study[152]	No serious	Not assessable (single study)	Serious (downgraded 1 level)	No serious	Not assessed	Oligometastatic NSCLC only, by mutation status	SBRT was assessed as not being cost-effective at a WTP threshold of $100,000 when added to maintenance therapy for people with oligometastatic NSCLC.	⨁⨁⨁◯ MODERATE
SBRT vs. cRT or chemotherapy for pancreatic cancer								
Outcome: cost-effectiveness								
Not reported								

Number of Participants and Studies	Risk-of-Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Comments	Effect	Overall Quality of Evidence Rating
Outcome: costs								
N = 5,624 1 comparative NRS[90]	No serious	Not assessable (single study)	Serious (downgraded 1 level)	No serious	Not assessed	Nonmetastatic, unresectable pancreatic cancer	Health care payments were greatest for SBRT when compared with cRT or chemotherapy under US Medicare ($P < .001$) and employer-based insurance ($P < .001$).	⊕◯◯◯ VERY LOW
SBRT plus maintenance therapy vs salvage therapies for head and neck cancer								
Outcome: cost-effectiveness								
N = 1 hypothetical cohort 1 economic modelling study[153]	No serious	Not assessable (single study)	Serious (downgraded 1 level)	No serious	Not assessed	Locoregional previously irradiated head and neck cancer	None of treatment strategies were cost-effective. However, SBRT-based re-irradiation has potential to be cost-effective, as model was sensitive to median survival.	⊕⊕⊕◯ MODERATE
SBRT vs. RFA for liver cancer								
Outcome: cost-effectiveness								
N = 440 1 comparative NRS[121]	No serious	Not assessable (single study)	Serious (downgraded 1 level)	No serious	No serious	No additional comments	SBRT was not cost-effective compared with RFA in overall population of people with early-stage HCC. However, 85.5% of bootstrap ICER estimates were lower than WTP threshold of $100,000.	⊕⊕⊕◯ MODERATE
SBRT vs. standard care for oligometastatic cancer								
Outcome: cost-effectiveness								
N = 2 hypothetical cohorts based	No serious	No serious	Serious (downgraded 1 level)	No serious	Not assessed	Analysis based on a single trial	The addition of SBRT increased costs and improved quality adjusted survival, overall leading to a cost-effective treatment	⊕⊕⊕◯ MODERATE

Number of Participants and Studies	Risk-of-Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Comments	Effect	Overall Quality of Evidence Rating
on SABR-COMET data 2 economic modelling studies[154,155]							strategy for patients with oligometastatic cancer.	
SBRT vs. other forms of RT for bone cancer								
Outcome: costs								
N = 40,993 cases 1 comparative NRS	No serious	Not assessable (single study)	Serious (downgraded 1 level)	No serious	Not assessed	No indication how many were nonspine metastases	For people with bone metastases, cost of SBRT was significantly higher for both professional and technical fees ($679 lower provider costs and $6,422 lower technical costs for external beam RT; $36 lower provider costs and $2,534 lower technical costs for IMRT; *P* < .001).	⊕◯◯◯ VERY LOW

Abbreviations. cRT: conventional radiation therapy; HCC: hepatocellular carcinoma; ICER: incremental cost-effectiveness ratio; IMRT: intensity-modulated radiation therapy; NCSLS: non-small cell lung cancer; NRS: nonrandomized study; RFA: radiofrequency ablation; RT: radiation therapy; SBRT: stereotactic body radiation therapy WTP: willingness-to-pay.

Appendix F. MAUDE and Medical Device Recall Reports

Table F1. Reports on Stereotactic Body Radiation Therapy From Manufacturer and User Facility Device Experience (MAUDE) Database

See attachment for results from US FDA Manufacturer and User Facility Device Experience (MAUDE) database, (pages F1-F659).

Table F2. Reports on Stereotactic Body Radiation Therapy From FDA Medical Device Recall Database

Device Name and Description	Manufacturer	Recall Class	Classification Date dd/mm/yyyy	Reason for Recall
REGARD Stereotactic Tray	ROi CPS LLC	2	18/11/2021	Povidone-Iodine swabstick manufactured by PDI, Inc. recalled due to Out of Specifications was used as a component in some of ROI CPS, LLC products.
ExacTrac Dynamic software, Model 20910-01B ETD Positioning and Monitoring Installer 1.0.2 - Product Usage: intended to position patients at an accurately defined point within treatment beam of a medical accelerator for stereotactic radiosurgery or radiotherapy procedures, to monitor patient position, and to provide a beam hold signal in case of a deviations to treat lesions, tumors, and conditions anywhere in body when radiation treatment is indicated.	Brainlab AG	2	10/06/2021	Display of potential patient movement might be delayed to user for high-dose treatments.
ViewRay MRIdian Linac System: Model No. 20000-01 software, CE 0086 - Product Usage: intended to be used for planning external beam irradiation with photon beams and delivering stereotactic radiosurgery and precision radiotherapy for lesions, tumors, and conditions anywhere in body when radiation treatment is indicated, in conjunction with ViewRay System, an MRI image-guided radiation therapy system.	Viewray, Inc.	2	09/06/2021	Software anomalies affecting French, German, and Italian versions of treatment delivery system (TDS) software.
CyberKnife Treatment Delivery System - Product Usage: indicated for image-guided stereotactic radiosurgery and precision radiotherapy for	Accuray Incorporated	2	17/03/2021	The set screws that connect Standard Treatment Couch linkage arm to roll

lesions, tumors, and conditions anywhere in body when radiation treatment is indicated.				motor can loosen over time allowing couch to roll.
TomoTherapy Treatment System - Product Usage: used as an integrated system for planning and precise delivery of radiation therapy, stereotactic radiotherapy, or stereotactic radiosurgery to tumors or other targeted tissues while minimizing delivery of radiation to vital healthy tissue.	Accuray Incorporated	2	07/01/2021	"MLC tickle error" may result in delivered dose to effectively rotate from planned dose.
TomoTherapy Treatment Delivery System with iDMS - Product Usage: used as an integrated system for planning and precise delivery of radiation therapy, stereotactic radiotherapy, or stereotactic radiosurgery to tumors or other targeted tissues while minimizing delivery of radiation to vital healthy tissue.	Accuray Incorporated	2	07/01/2021	"MLC tickle error" may result in delivered dose to effectively rotate from planned dose.
ViewRay MRIdian System: Model No. 10000, CE, Rated Supply Voltage - 380/480 VAC, 3 - Frequency Range (Hertz) - 50/60 Hz, Rated Input in Amperes - 210 A, UDI. The MRIdian system and MRIdian Linac system, with magnetic resonance imaging capabilities, is intended to provide stereotactic radiosurgery and precision radiotherapy for lesions, tumors, and conditions anywhere in body where radiation treatment is indicated.	Viewray, Inc.	2	20/11/2020	There is a potential that components of receive coil can reach elevated temperatures, which has potential to cause a burn injury to patient or user.
ViewRay MRIdian Linac System: Model No. 20000, CE, Rated Supply Voltage - 380/480 VAC, 3 - Frequency Range (Hertz) - 50/60 Hz, Rated Input in Amperes - 210 A, UDI. The MRIdian system and MRIdian Linac system, with magnetic resonance imaging capabilities, is intended to provide stereotactic radiosurgery and precision radiotherapy for lesions, tumors, and conditions anywhere in body where radiation treatment is indicated.	Viewray, Inc.	2	20/11/2020	There is a potential that components of receive coil can reach elevated temperatures, which has potential to cause a burn injury to patient or user.
Leksell Vantage Stereotactic System, UDI/GTIN 7340048304887	Elekta Instrument AB	2	26/06/2020	The locking mechanism at interface of Instrument Carrier and Leksell Vantage Arc may not function properly.

Elekta Unity, UDI 05060191071321, Image-guided radiation therapy system - Product Usage: is indicated for radiation therapy treatments and stereotactic radiation treatments of malignant and benign diseases anywhere in body as determined by a licensed medical practitioner in accordance with a defined treatment plan.	Elekta, Inc.	2	05/06/2020	There is potential risk that Legionella may be present in Unity machine room, specifically heat exchanger condensation collection tray.
Medtronic Nexframe Stereotactic System and StealthStation Cranial software version 3.0 or newer with StealthStation DBS License or StealthStation S8 Software with Stealth DBS License and O-arm Imaging System utilizing auto-registration (fiducial- less) workflow used in combination during a DBS (deep brain stimulation) procedure. Neurological stereotaxic instrument	Medtronic Navigation, Inc.	1	18/05/2020	Entry point and lead placement inaccuracies during deep brain stimulation lead implantation procedures may occur when using a specific combination of firm's Steriotactic System and auto-registration feature with a specific imaging system (also known as a fiducial-less procedure). Minor patient movement may not be initially detected by user or software during auto-registration scan process potentially resulting in inaccuracies and risks for patient including: inaccurate lead placement, delay of surgery, aborted surgery, or additional intervention (including revision of lead placement and subsequent imaging).
Leksell Vantage Stereotactic System. Instrument Carrier, Part of Leksell Vantage Arc (1053958). Neurological stereotaxic instrument	Elekta Inc	2	29/04/2020	A faulty locking piece of Instrument Carrier that does not fulfil requirement of locking force to Arc has been found during an internal check of a Leksell Vantage Stereotactic Arc System.
Bard Biopsy EnCor Probe, Stereotactic/Ultrasound 7G, REF number ECP017G, packaged individually in sterile pouches, 5 pouches/carton, Single Use, Rx, Sterile.	Bard Peripheral Vascular Inc	2	03/03/2020	Lot numbers and products inadvertently not included in scope of previous recall. Original recall was conducted due to an increase in probe failures for leaks, suction issues, and failure to obtain samples.
GammaPod Stereotactic Radiotherapy System Model A, REF XMSGP030A00-0.02 Product Usage:	Xcision Medical Systems, LLC	2	25/07/2019	One bolt on V motor was not fully tightened, which caused a drift of .13

GammaPod is a teletherapy device intended for use in noninvasive stereotactic delivery of a radiation dose to a partial volume of breast in conjunction with breast conserving treatment.				degrees in alignment resulting in reduced dose output.
Elekta Unity, Image-Guided Radiation Therapy System Elekta Unity using Magnetic Resonance Imaging is indicated for radiation therapy treatments and stereotactic radiation treatments of malignant and benign diseases anywhere in body as determined by a licensed medical practitioner in accordance with a defined treatment plan.	Elekta, Inc.	2	16/07/2019	The QA software solution to perform MR to MV alignment check, does not display stored MR to MV offset values. The user is unable to independently inspect values during their QA.
Elekta Unity systems Product Usage: Elekta Unity using Magnetic Resonance Imaging is indicated for radiation therapy treatments and stereotactic radiation treatments of malignant and benign diseases anywhere in body as determined by a licensed medical practitioner in accordance with a defined treatment plan. Elekta Unity is intended for use with compatible Treatment Planning and Oncology Information Systems.	Elekta Limited	2	08/05/2019	There is no warning in Elekta Unity manual for administration of gadolinium-based or other contrast agents for imaging or image guidance purposes has not been validated.
RT Elements Software revisions of RT Elements applications have a specific software version number. Specifically, the following RT Elements applications/versions are affected: - Cranial SRS 1.0.0 and 1.5.0 - Spine SRS 1.0.0 and 1.5.0 - Multiple Brain Mets SRS 1.5.0 - RT QA 1.0.0 and 1.5.0 Product Usage: The RT Elements are applications for radiation treatment planning for use in stereotactic, conformal, computer planned, Linac based radiation treatment of cranial, head and neck, and extracranial lesions.	Brainlab AG	2	20/04/2019	There is a potential for an incorrect dose distribution calculation by Brainlab RT Elements software (for affected versions) under specific circumstances when using Pencil Beam algorithm on GPU (graphics card), as is default system setting.

Elekta Unity, Image-Guided Radiation Therapy System Product Usage: Elekta Unity using Magnetic Resonance Imaging is indicated for radiation therapy treatments and stereotactic radiation treatments of malignant and benign diseases anywhere in body as determined by a licensed medical practitioner in accordance with a defined treatment plan. Elekta Unity is intended for use with compatible Treatment Planning and Oncology Information Systems.	Elekta Limited	2	08/04/2019	Users need to be aware when using these protocols for daily online plan adaptation that: 1) The images acquired using these protocols do not represent average position of anatomy during respiratory motion cycle. The images are based on data acquired around full expiration. 2) The display of images in Elekta Unity Application software does not provide information about protocol used to acquire image (eg., with or without respiratory triggering). 3) Users must select an appropriate scan protocol representative of respiratory phase used in reference plan.
St. Jude Medical InfinityTM DBS System 8CH Directional Lead, 30 cm, 0.5 REF 6170 - STERILE EO Rx ONLY CE 0086 0123 St. Jude Medical Plano, TX St. Jude Medical InfinityTM DBS System 8CH Directional Lead, 40 cm, 0.5 REF 6172 STERILE EO Rx ONLY St. Jude Medical Plano, TX Instructions For Use: Lead and Extension Kits for Deep Brain Stimulation Systems Clinician's Manual ST. JUDE MEDICAL - Product Usage: St. Jude Medical Deep Brain Stimulation (DBS)leads are intended to deliver stimulation to target areas in brain. DBS extensions are intended to connect leads to implantable pulse generators (IPGs). St. Jude Medical DBS leads are designed for introduction into brain using standard stereotactic neurosurgical techniques. DBS system delivers electrical stimulation to a precisely targeted area	St. Jude Medical, Inc.	2	10/12/2018	The most proximal unsegmented electrode of Deep Brain Stimulation leads may be constructed with MP35N instead of required 90/10 platinum-iridium.

in brain. Leads are implanted in brain and are connected to extensions, which are passed under skin and are connected to neurostimulator. Leads for St. Jude Medical Infinity DBS System feature electrodes on a stiff distal end with an inactive lead tip. The proximal end of lead contains contact bands that correspond with each of distal electrodes and an inactive band that functions as a contact for a setscrew when connecting to a compatible extension. The 8-channel leads contain cylindrical and segmented electrodes. The segmented electrodes can be activated independently to focus stimulation in one direction to help target desired neurological structures. As stated in Clinician manual (ARTEN600008305 Rev A), leads materials which are intended to come into contact with tissue are Platinum-iridium and polycarbonate urethane. In addition, drawing for Stim Tip, 1-3-3-1 Directional DBS lead requires that electrode material shall be 90/10 Platinum Iridium.				
CyberKnife M6, Part Number 054000-004 The CyberKnife M6 Systems are indicated for treatment planning and image guided stereotactic radiosurgery and precision radiotherapy for lesions, tumors, and conditions anywhere in body when radiation treatment is indicated.	Accuray Incorporated	2	08/11/2018	A robotics supplier notified Accuray of 2 manufacturing variations in fastening of in-line wrist and casting of wrist for robot. The variation may result in premature failure of component.
VitalBeam Radiotherapy Delivery System Version 2.5 Product Usage: The VitalBeam delivery systems are intended to provide precision radiotherapy and stereotactic radiosurgery for lesions, tumors, and conditions anywhere in body where radiation treatment is indicated.	Varian Medical Systems	2	01/10/2018	Reports have been received of an anomaly that can result in a treatment without intended gating (respiratory tracking/monitoring). This issue occurs when a patient planned with gating is treated on more than one system.
TrueBeam Radiotherapy Delivery System version 2.0 and 2.5 EDGE Radiotherapy Delivery System version 2.0 and 2.5	Varian Medical Systems	2	01/10/2018	Reports have been received of an anomaly that can result in a treatment without intended gating (respiratory tracking/monitoring). This issue occurs

Product Usage: The TrueBeam delivery systems are intended to provide radiotherapy and stereotactic radiosurgery for lesions, tumors, and conditions anywhere in body where radiation treatment is indicated.				when a patient planned with gating is treated on more than one system.
Makoplasty RIO Standard System; Ethernet to Fiber Optic Converter Catalog # 200933 Product Usage: The Partial Knee Application (PKA), for use with Mako System, is indicated for use in surgical knee procedures, in which use of stereotactic surgery may be appropriate, and where reference to rigid anatomical bony structures can be identified relative to a CT based model of anatomy. These procedures include Unicondylar knee replacement and/or patellofemoral knee replacement.	Mako Surgical Corporation	2	14/09/2018	Communication-connection error
Rio System Irrigation Clip - Catalog # 111690 Product Usage: The RESTORIS Partial Knee Application (PKA) for use with Robotic Arm Interactive Orthopedic System (RIO) is intended to assist surgeon in providing software defined spatial boundaries for orientation and reference information to anatomical structures during orthopedic procedures. The RESTORIS Partial Knee Application (PKA) for use with Robotic Arm Interactive Orthopedic System (RIO) is indicated for use in surgical knee procedures, in which use of stereotactic surgery may be appropriate, and where reference to rigid anatomical bony structures can be identified relative to a CT based model of anatomy. These procedures include unicondylar knee replacement and/or patellofemoral knee replacement.	Mako Surgical Corporation	2	13/08/2018	Out of tolerance
ROSA(TM) Robotized Stereotactic Assistant, Version 2.5 ROSA Surgical Device is a computer-controlled electromechanical arm. It is intended to be used in	MEDTECH SAS	2	07/06/2018	Replacement of units lacking an updated device approval

operating room for spatial positioning and orientation of an instrument holder or tool guide. Guidance is based on a pre-operative plan developed with 3-dimensional imaging software, and uses fiducial markers or optical registration. The system is intended for use by neurosurgeons to guide standard neurosurgical instruments. It is indicated for any neurosurgical condition in which use of stereotactic surgery may be appropriate.				
Disposable Drill Kit which includes 2 drill bits, 2 drill stops, and 2 adjustment wrenches, sterile. The drill bits are 30cm long and made of stainless steel. The drill kits are supplied in a sterile state and are single-use only. Used to drill cranial holes using a stereotactic frame.	Ad-Tech Medical Instrument Corporation	2	25/05/2018	There is a possibility that DDK2-2.4-30X Disposable Drill Kits, Lot Number 111664 208140649 contained 2.8mm drill bits from DDK2-2.8-30X Disposable Drill Kits, Lot Number 111745 208140649 and vice versa.
ExacTrac versions 6.5 through 6.5 intended to be used to place patients at an accurately defined point within treatment beam of a medical accelerator for stereotactic radiosurgery or radiotherapy procedures to treat lesions, tumors and conditions anywhere in body when radiation treatment is indicated. ExacTrac may also be used to monitor patient position during treatment.	Brainlab AG	2	14/03/2018	The usage of workflows that deviate from recommended specifications in User manual for ExacTrac Patient Positioning System (versions 6.0, 6.1, 6.2, 6.5) with Auxiliary Device Interface (ADI) and Varian Clinac or Varian TrueBeam, which may result in misinterpretation of beam authorization via ADI.
Hi-Art(R) System, Model Number H-000-0003 Product Usage: The TomoTherapy treatment system is intended to be used as an integrated system for the planning and precise delivery of radiation therapy, stereotactic radiotherapy, or stereotactic radiosurgery to tumors or other targeted tissues while minimizing delivery of radiation to vital healthy tissues. The megavoltage x-ray radiation is delivered in a rotational, nonrotational, modulated (IMRT), or nonmodulated (non-IMRT/3 dimensional conformal) format in accordance with physicians prescribed and approved plan.	Accuray Incorporated	2	26/12/2017	Uncontrolled couch Z-axis movement (descent)

TomoHDA(R) System, Model Number 1018286 Product Usage: The TomoTherapy treatment system is intended to be used as an integrated system for the planning and precise delivery of radiation therapy, stereotactic radiotherapy, or stereotactic radiosurgery to tumors or other targeted tissues while minimizing delivery of radiation to vital healthy tissues. The megavoltage x-ray radiation is delivered in a rotational, nonrotational, modulated (IMRT), or nonmodulated (non-IMRT/3 dimensional conformal) format in accordance with physicians prescribed and approved plan.	Accuray Incorporated	2	26/12/2017	Uncontrolled couch Z-axis movement (descent)
TomoHD(R) System, Model Number 1018283 Product Usage: The TomoTherapy treatment system is intended to be used as an integrated system for the planning and precise delivery of radiation therapy, stereotactic radiotherapy, or stereotactic radiosurgery to tumors or other targeted tissues while minimizing delivery of radiation to vital healthy tissues. The megavoltage x-ray radiation is delivered in a rotational, nonrotational, modulated (IMRT), or nonmodulated (non-IMRT/3 dimensional conformal) format in accordance with physicians prescribed and approved plan.	Accuray Incorporated	2	26/12/2017	Uncontrolled couch Z-axis movement (descent)
TomoH(R) System, Model Number 1018284 Product Usage: The TomoTherapy treatment system is intended to be used as an integrated system for the planning and precise delivery of radiation therapy, stereotactic radiotherapy, or stereotactic radiosurgery to tumors or other targeted tissues while minimizing delivery of radiation to vital healthy tissues. The megavoltage x-ray radiation is delivered in a rotational, nonrotational, modulated (IMRT), or nonmodulated (non-IMRT/3	Accuray Incorporated	2	26/12/2017	Uncontrolled couch Z-axis movement (descent)

dimensional conformal) format in accordance with physicians prescribed and approved plan.				
Elekta ERGO++ Product Usage: ERGO is often used for stereotactic treatments.	Elekta Inc	2	12/12/2017	Incorrect DICOM mapping of exported collimator or couch angles from ERGO, which would lead to incorrect rotation of collimator or couch when using an MLC device for planning.
ROSA Surgical Device 2.5.8 ROSA Surgical Device is a computer-controlled electromechanical arm. It is intended to be used in operating room for spatial positioning and orientation of an instrument holder or tool guide. Guidance is based on a preoperative plan developed with 3-dimensional imaging software, and uses fiducial markers or optical registration. The system is intended for use by neurosurgeons to guide standard neurosurgical instruments. It is indicated for any neurosurgical condition in which use of stereotactic surgery may be appropriate.	Zimmer Biomet, Inc.	2	28/11/2017	The software issue described was corrected in modification to MXTTOUT controller parameter settings.
ROSA Brain 3.0.0 Usage: The device is intended for spatial positioning and orientation of instrument holders or tool guides to be used by neurosurgeons to guide standard neurosurgical instruments (biopsy needle, stimulation or recording electrode, endoscope). The device is indicated for any neurosurgical procedure in which use of stereotactic surgery may be appropriate.	Zimmer Biomet, Inc.	2	21/11/2017	Communication errors between ROSANNA BRAIN software, MARIO software and St¿ubli CS8C controller.
ROSA Surgical Device 2.5.8 It is intended to be used in operating room for spatial positioning and orientation of an instrument holder or tool guide. Guidance is based on a preoperative plan developed with 3-dimensional imaging software, and uses fiducial markers or optical registration. The system is intended for use by neurosurgeons to guide standard neurosurgical instruments. It is indicated	Zimmer Biomet, Inc.	2	21/11/2017	Software corrections reactivating cooperative endoscopy mode.

for any neurosurgical condition in which use of stereotactic surgery may be appropriate.				
ROSA Brain 3.0 Intended for spatial positioning and orientation of instrument holders or tool guides to be used by neurosurgeons to guide standard neurosurgical instruments. The device is indicated for any neurosurgical procedure in which use of stereotactic surgery may be inappropriate.	Zimmer Biomet, Inc.	2	17/11/2017	Insufficient amount of washers in Telescopic Arm, allowing some movement of device.
ROSA Surgical Device 2.5.8 ROSA Surgical Device is a computer-controlled electromechanical arm. It is intended to be used in operating room for spatial positioning and orientation of an instrument holder or tool guide. Guidance is based on a preoperative plan developed with 3-dimensional imaging software, and uses fiducial markers or optical registration. The system is intended for use by neurosurgeons to guide standard neurosurgical instruments. It is indicated for any neurosurgical condition in which use of stereotactic surgery may be appropriate.	Zimmer Biomet, Inc.	2	16/11/2017	Potential failure of optical distance sensor due to cable disconnection.
ROSA Surgical Device 2.5.8 ROSA Surgical Device is a computer-controlled electromechanical arm. It is intended to be used in operating room for spatial positioning and orientation of an instrument holder or tool guide. Guidance is based on a preoperative plan developed with 3-dimensional imaging software, and uses fiducial markers or optical registration. The system is intended for use by neurosurgeons to guide standard neurosurgical instruments. It is indicated for any neurosurgical condition in which use of stereotactic surgery may be appropriate.	Zimmer Biomet, Inc.	2	16/11/2017	Observed instability of device.
ROSA Surgical Device 2.5.8 ROSA Surgical Device is a computer-controlled electromechanical arm. It is intended to be used in operating room for spatial positioning and orientation of an instrument holder or tool guide.	Zimmer Biomet, Inc.	2	16/11/2017	Possible break in connector of Force Sensor.

Guidance is based on a preoperative plan developed with 3-dimensional imaging software, and uses fiducial markers or optical registration. The system is intended for use by neurosurgeons to guide standard neurosurgical instruments. It is indicated for any neurosurgical condition in which use of stereotactic surgery may be appropriate.				
Herga foot switch, model 6289-WS, a component of ROSA Robotized Stereotactic Assistant Surgical Device, Model 2.5.8. The firm name on foot switch label is Herga Electric Limited, Bury, St. Edmunds, Suffolk IP32 6NN. ROSA Surgical Device is a computer-controlled electromechanical arm. It is intended to be used in operating room for spatial positioning and orientation of an instrument holder or tool guide. Guidance is based on a preoperative plan developed with 3-dimensional imaging software and uses fiducial markers or optical registration. The system is intended for use by neurosurgeons to guide standard neurosurgical instruments. It is indicated for any neurosurgical condition in which use of stereotactic surgery may be appropriate.	Zimmer Biomet, Inc.	2	12/09/2017	Complaints were received reporting system would freeze/shut down while in Fulgurate mode.
DBS Lead Depth Stop contained in Medtronic Deep Brain Stimulation (DBS) lead kits, models 3387/3387S, 3389/3389S, and 3391/3391S, The lead kit contains one DBS lead in addition to multiple accessories used in DBS lead implant procedures. Among these accessories is DBS lead holder, also referred to as lead depth stop. The lead holder affixes to DBS lead during lead implant procedure, marking distance to lead tip and providing control of DBS lead depth during implant by interfacing with stereotactic system.	Medtronic Neuromodulation	2	23/08/2017	Medtronic received reports that DBS depth stop did not adequately secure to lead, which can result in DBS lead placement beyond intended target.
ROSA Brain, 3.0.0 The device is intended for spatial positioning and orientation of instrument holders or tool guides to be used by neurosurgeons to guide standard	Zimmer Biomet, Inc.	2	03/08/2017	Complaint of head holder connector locking up mechanically when tightened.

neurosurgical instruments (biopsy needle, stimulation or recording electrode, endoscope). The device is indicated for any neurosurgical procedure in which use of stereotactic surgery may be appropriate.				
Leksell Gamma Knife Icon is a teletherapy device intended for stereotactic irradiation of head structures ranging from very small target sizes of a few millimeters to several centimeters e.g., metastatic tumors, recurrent glioblastomas, trigeminal neuralgia, medically refractory essential tremor, orbital tumors, ocular tumors, optic nerve tumors, benign diseases (such as meningiomas, vestibular schwannomas, post-surgical pituitary adenomas, craniopharyngioma, hemangioblastomas, schwannomas, arteriovenous malformations, cavernous malformations, chordomas, glomus tumors, hemangiomas), skull base tumors, head and neck tumors (such as unknown primary of head and neck, oral cavity, hypopharynx, oropharynx, nasopharynx, sinonasal, salivary gland), and pediatric tumors (such as glioma, ependymoma, pituitary tumors, hemangioblastoma, craniopharyngioma, meningioma, metastasis, medulloblastoma, nasopharyngeal tumors, arteriovenous malformations, cavernous malformations, skull base tumors).	Elekta, Inc.	2	07/07/2017	If gantry module is replaced after original installation configuration settings may be missing. The identified risk for this issue is electrical safety for technicians doing maintenance on X-ray generator.
MEDTECH ROSA Brain 3.0 The device is intended for spatial positioning and orientation of instrument holders or tool guides to be used by neurosurgeons to guide standard neurosurgical instruments (biopsy needle, stimulation or recording electrode, endoscope). The device is indicated for any neurological procedure in which use of stereotactic surgery may be appropriate.	Zimmer Biomet, Inc.	2	07/04/2017	Unapproved change made by supplier.

Mammomat Inspiration full, field digital system, x-ray, mammographic Product Usage: The Mammomat Inspiration system is intended for mammography exams, screening, diagnosis, and stereotactic biopsies under supervision of medical professionals. Mammographic images can be interpreted by either hard copy film or soft copy workstation.	Siemens Medical Solutions USA, Inc	2	31/01/2017	Software error
CyberKnife Robotic Radiosurgery Systems, models: G3, G4, VSI. Radiology: The CyberKnife Robotic Radiosurgery System is indicated for treatment planning and image guided stereotactic Radiosurgery and precision radiotherapy for lesions, tumors, and conditions anywhere in body when radiation treatment is indicated.	Accuray Incorporated	2	21/12/2016	Accuray has become aware of a potential safety issue involving possibility of electric shock during maintenance activities from Ion Pump HV Power Supply at back of modulator cabinet. This issue is limited to certain G3, G4, and VSI models of CyberKnife Robotic Radiosurgery System.
CyberKnife Robotic Radiosurgery System using software version 10.6; Catalog/Part Number: 54000 UDI: M658053301 0 Radiology: The CyberKnife Robotic Radiosurgery System is indicated for treatment planning and image guided stereotactic Radiosurgery and precision radiotherapy for lesions, tumors, and conditions anywhere in body when radiation treatment is indicated.	Accuray Incorporated	2	12/12/2016	Accuray has become aware of a potential safety issue involving unexpected treatment robot motion when removing an accessory. This issue is limited to certain CyberKnife Systems with software version 1 0.6.
Varian Head Frame - Model number HHF -ALL Head Frame Posts (PN1008016) and Post Kits (PN1008016). The Varian Head Frame System is for use with a computed tomography scanner to perform imaging for treatment planning and a charged particle accelerator to perform immobilization of treatment target for stereotactic radiosurgery or radiotherapy treatments on cranial lesions, tumors, and conditions where radiation treatment is indicated.	Varian Medical Systems, Inc.	2	13/10/2016	Varian Medical Systems has received a report that a user was able to easily rotate head frame posts when attached to mounting cam on metal head ring. There was no report of serious injury due to this issue

TrueBeam¿ Radiotherapy Delivery System and EDGE" Radiotherapy Delivery System, K140528. The TrueBeam and Edge Systems are intended to provide stereotactic radiosurgery and precision radiotherapy for lesions, tumors, and conditions anywhere in body where radiation therapy is indicated for adults and pediatric patients.	Vision RT Ltd	2	25/08/2016	Vision RT Ltd received three (3) reports from different sites that discovered following issue, unintended changes were made to planned couch parameters, specifically couch rotation parameter, during patient set-up for Optical Surface Monitoring System [OSMS]. 1. CRM 3194, No Serious Injury, No MDR, Aware date: Dec 11, 2015 2. CRM 3321, No Patient Involved, No MDR, Aware date: Jan 19, 2016 3. CRM 4570, No Serious Injury, No MDR, Aware date: March 15, 2016 No patient harm was reported in any of these cases.
FrameLink. The software application is sent in CD format with an IFU, wrapped in plastic with a label for shipping purposes. Product Usage: The StealthStation System is intended as an aid for precisely locating anatomical structures in either open or percutaneous procedures. The StealthStation System is indicated for any medical condition in which use of stereotactic surgery may be appropriate, and where reference to a rigid anatomical structure such as skull, a long bod, or vertebra can be identified relative to a CT or MR based model, fluoroscopy images, or digitized landmarks of anatomy.	Medtronic Navigation, Inc.	2	02/08/2016	Medtronic Navigation, Inc. announces a voluntary field action for Medtronic Navigation StealthStation Software applications affected by Neurologica BodyTom/CereTom floor-based scanners.
MACH Cranial Treon. The software application is sent in CD format with an IFU, wrapped in plastic with a label for shipping purposes. Product Usage: The StealthStation System is intended as an aid for precisely locating anatomical structures in either open or percutaneous procedures. The StealthStation System is indicated for any medical condition in which use of stereotactic surgery may	Medtronic Navigation, Inc.	2	02/08/2016	Medtronic Navigation, Inc. announces a voluntary field action for Medtronic Navigation StealthStation Software applications affected by Neurologica BodyTom/CereTom floor-based scanners.

be appropriate, and where reference to a rigid anatomical structure such as skull, a long bod, or vertebra can be identified relative to a CT or MR based model, fluoroscopy images, or digitized landmarks of anatomy.				
S7 MACH FrameLink. The software application is sent in CD format with an IFU, wrapped in plastic with a label for shipping purposes. Product Usage: The StealthStation System is intended as an aid for precisely locating anatomical structures in either open or percutaneous procedures. The StealthStation System is indicated for any medical condition in which use of stereotactic surgery may be appropriate, and where reference to a rigid anatomical structure such as skull, a long bod, or vertebra can be identified relative to a CT or MR based model, fluoroscopy images, or digitized landmarks of anatomy.	Medtronic Navigation, Inc.	2	02/08/2016	Medtronic Navigation, Inc. announces a voluntary field action for Medtronic Navigation StealthStation Software applications affected by Neurologica BodyTom/CereTom floor-based scanners.
Fusion ENT Application. The software application is sent in CD format with an IFU, wrapped in plastic with a label for shipping purposes. Product Usage: The StealthStation System is intended as an aid for precisely locating anatomical structures in either open or percutaneous procedures. The StealthStation System is indicated for any medical condition in which use of stereotactic surgery may be appropriate, and where reference to a rigid anatomical structure such as skull, a long bod, or vertebra can be identified relative to a CT or MR based model, fluoroscopy images, or digitized landmarks of anatomy.	Medtronic Navigation, Inc.	2	02/08/2016	Medtronic Navigation, Inc. announces a voluntary field action for Medtronic Navigation StealthStation Software applications affected by Neurologica BodyTom/CereTom floor-based scanners.
MACH AxiEM Cranial Treon. The software application is sent in CD format with an IFU, wrapped in plastic with a label for shipping purposes. Product Usage:	Medtronic Navigation, Inc.	2	02/08/2016	Medtronic Navigation, Inc. announces a voluntary field action for Medtronic Navigation StealthStation Software applications affected by Neurologica

The StealthStation System is intended as an aid for precisely locating anatomical structures in either open or percutaneous procedures. The StealthStation System is indicated for any medical condition in which use of stereotactic surgery may be appropriate, and where reference to a rigid anatomical structure such as skull, a long bod, or vertebra can be identified relative to a CT or MR based model, fluoroscopy images, or digitized landmarks of anatomy.				BodyTom/CereTom floor-based scanners.
Synergy Spine. The software application is sent in CD format with an IFU, wrapped in plastic with a label for shipping purposes. Product Usage: The StealthStation System is intended as an aid for precisely locating anatomical structures in either open or percutaneous procedures. The StealthStation System is indicated for any medical condition in which use of stereotactic surgery may be appropriate, and where reference to a rigid anatomical structure such as skull, a long bod, or vertebra can be identified relative to a CT or MR based model, fluoroscopy images, or digitized landmarks of anatomy.	Medtronic Navigation, Inc.	2	02/08/2016	Medtronic Navigation, Inc. announces a voluntary field action for Medtronic Navigation StealthStation Software applications affected by Neurologica BodyTom/CereTom floor-based scanners.
Synergy Cranial S7. The software application is sent in CD format with an IFU, wrapped in plastic with a label for shipping purposes. Product Usage: The StealthStation System is intended as an aid for precisely locating anatomical structures in either open or percutaneous procedures. The StealthStation System is indicated for any medical condition in which use of stereotactic surgery may be appropriate, and where reference to a rigid anatomical structure such as skull, a long bod, or vertebra can be identified relative to a CT or MR based model, fluoroscopy images, or digitized landmarks of anatomy.	Medtronic Navigation, Inc.	2	02/08/2016	Medtronic Navigation, Inc. announces a voluntary field action for Medtronic Navigation StealthStation Software applications affected by Neurologica BodyTom/CereTom floor-based scanners.

Radionuclide Radiation Therapy System Product The product is a teletherapy device intended for stereotactic irradiation of head structures ranging from very small target sizes of a few millimeters to several centimeters.	Elekta, Inc.	2	22/04/2016	The latches of frame adapter can be locked even if locating pins of frame adapter is not inserted into corresponding holes in coordinate frame.
MRIdian ViewRay Radiation Therapy System, ViewRay Treatment Planning and Delivery System (also known as MRIdian System) is indicated for stereotactic radiosurgery and precision radiotherapy for lesions, tumors, and conditions anywhere in body when radiation treatment is indicated	Viewray Incorporated	2	31/03/2016	When editing isocenter or couch position of plan while in treatment workflow (in Points screen) and re-optimizing, software will not prompt user to shift couch to new isocenter. As a result there is potential to deliver dose to initial isocenter rather than new location.
BioTex Reusable Adapter Kit, Part Number 401-021-1010, packaged nonsterile in a dedicated case for steam sterilization. The Adapter Kit is used during surgical procedures as an instrument guide holder that maintains position of an instrument after these have been aligned by physician via stereotactic guidance during planning and operation of neurological procedures performed in conjunction with use of Medtronic StealthStation Image Guided Workstation System.	Medtronic Navigation, Inc.	2	23/03/2016	Medtronic Navigation is recalling Biotex Adapter Kit because it was commercially distributed by BioTex without a cleared premarket [510(k)] from FDA.
CyberKnife Robotic; Catalog/part number 032000 and 033000 Cosmetic cover package. Product Usage: The CyberKnife Robotic Radiosurgery System is indicated for treatment planning and image guided stereotactic Radiosurgery and precision radiotherapy for lesions, tumors, and conditions anywhere in body when radiation treatment is indicated.	Accuray Incorporated	2	08/02/2016	The gun box mounting bracket may fail to support weight of gun box when in vertical (inverted) position. If this failure occurs gun box may become loose and could come into contact with a patient.
Brainlab Cranial Navigation System: An Image Guided Surgery System / Stereotactic. Radiology Departments. The BrainLAB Cranial IGS System is intended to be an intra-operative image guided localization system to enable minimally invasive surgery.	Brainlab AG	1	19/01/2016	Software Error: The effect of setup on overall navigation accuracy could potentially intensify small inaccuracies arising from individual steps of a complex navigation procedure that may cause an inaccurate display of instruments by

				navigation system compared with actual patient anatomy.
RT Elements are applications for radiation treatment planning for use in stereotactic, conformal, computer planned, Linac based radiation treatment of cranial, head and neck, and extracranial lesions. The simulated plan is intended for treatment evaluation for example in tumor board meetings or operating rooms.	Brainlab AG	2	14/01/2016	Large objects with fine resolution are potentially displayed cropped when imported into Adaptive Hybrid Surgery Analysis version 1.0.0.
RT Elements are applications for radiation treatment planning for use in stereotactic, conformal, computer planned, Linac based radiation treatment of cranial, head and neck, and extracranial lesions. The simulated plan is intended for treatment evaluation for example in tumor board meetings or operating rooms.	Brainlab AG	2	14/01/2016	Large objects with fine resolution are potentially displayed cropped when imported into Brainlab Brain Metastases 1.0.0.
MRIdian ViewRay Radiation Therapy System, ViewRay Is indicated for stereotactic radiosurgery and precision radiotherapy for lesions, tumors, and conditions anywhere in body when radiation treatment is indicated.	Viewray Incorporated	2	09/10/2015	ViewRay discovered that in event an encoder breaks or fails on Patient Handling System (PHS, or couch), when attempting to restart system, couch could move unexpectedly.
Universal Compact Head Ring Adapter Plate (UCHRAP), a component of Universal Compact Head Ring Adapter, UCHRA. The UCHRA is a component of Integra CRW Precision Arc Stereotactic System.	Integra LifeSciences Corp.	2	06/10/2015	Integra identified that UCHRAP component (Arc Adapter Plate) would not assemble properly to UCHRAR component (ARC Adapter Ring) of Compact Head Ring Adapter due to an error in manufacturing drawing.
ExacTrac 6.0.x Patient Positioning System, Radiation therapy. Intended to be used to place patients at an accurately defined point within treatment beam of a medical accelerator for stereotactic radiosurgery or radiotherapy procedures.	Brainlab AG	2	21/08/2015	ExacTrac 6.0 Patient Positioning System: Display of potentially incorrect Digitally Reconstructed Radiograph (DRR) for x-ray correction and verification.
Patient Handling System (Motion Control Software) Product Usage:	Viewray Incorporated	2	16/07/2015	ViewRay received a report that couch moved unexpectedly into bore after performing a RTCS reboot.

Indicated for stereotactic radiosurgery and precision radiotherapy for lesions, tumors, and conditions anywhere in body when radiation treatment is indicated.				
MOSAIQ Oncology Information System MOSAIQ is an oncology information system used to manage workflows for treatment planning and delivery. It supports information flow among healthcare facility personnel and can be used wherever radiotherapy and/or chemotherapy are prescribed.	Elekta, Inc.	2	14/07/2015	A problem exists in MOSAIQ resulting in incorrect field size being sent to treatment machine for stereotactic plans using cones.
Treatment Planning and Delivery System Software version 3.6. ViewRay. Indicated for stereotactic radiosurgery and precision radiotherapy for lesions, tumors, and conditions anywhere in body when radiation treatment is indicated.	Viewray Incorporated	2	02/07/2015	The software was failing to determine new patient locations if imaging is not enabled during treatment.
ExacTrac 6.x. is software used to place patients at an accurately defined point within treatment beam of a medical accelerator for stereotactic radiosurgery or radiotherapy procedures.	Brainlab AG	2	06/05/2015	ExacTrac 6.x Patient Positioning System: Potentially incorrect patient positioning when using ExacTrac Cone Beam CT (CBCT) with a CBCT acquired at a couch angle other than 0.0 degrees.
Restoris Partial Knee Application (PKA) RIO (TGS 2.0). For use with Robotic Arm Interactive Orthopedic System (RIO), is indicated for use in surgical knee procedures.	Mako Surgical Corporation	2	19/02/2015	When using MAKOplasty partial knee Arthroplasty application, burr continues spinning outside of stereotactic boundary and after control switches (foot pedal and trigger) cease to be activated
iPlan RT Dose is a stereotactic radiation treatment planning system that is intended for use in stereotactic, conformal, computer planned, Linac based radiation treatment of cranial, head and neck, and extracranial lesions.	Brainlab AG	2	13/01/2015	iPlan RT Radiation Treatment Planning Software: Potentially incorrect patient positioning when using multiple localized CT image data sets.
iPlan RT is a radiation treatment planning system that is intended for use in stereotactic, conformal, computer planned, Linac based radiation treatment of cranial, head and neck, and extracranial lesions.	Brainlab AG	2	13/01/2015	iPlan RT Radiation Treatment Planning Software: Potentially incorrect patient positioning when using multiple localized CT image data sets.
Mammomat Inspiration system:	Siemens Medical	2	05/12/2014	It was determined if Mammomat Inspiration system is not secured to floor

Product Usage: mammography exams, screening, diagnosis, and stereotactic biopsies under supervision of medical professionals. Mammographic images can be interpreted by either hard copy film or soft copy workstation.	Solutions USA, Inc			(per customer request) and monitors are positioned too far from table top, there is a potential risk the Acquisition Workstation (AWS) table may become unstable and fall over. This may result in a serious injury to operator.
AlignRT- Intended for prescription use. The system is indicated for use during simulation, setup and stereotactic radiosurgery and precision radiotherapy for lesions, tumors, and conditions anywhere in body where radiation is indicated.	Vision Rt Inc	2	25/11/2014	Potential failure of AlignRT to assert interlock.
CyberKnife Robotic Radiosurgery System with first generation IRIS Variable Aperture Collimator. The CyberKnife is indicated for treatment planning and image guided stereotactic Radiosurgery and precision radiotherapy for lesions, tumors, and conditions anywhere in body when radiation treatment is indicated.	Accuray Incorporated	2	14/11/2014	Software upgrade to correct potential safety issue related to CyberKnife System that occurs when upgrading Treatment Delivery Software for first generation Iris Variable Aperture Collimator.
Siemens Mammomat Inspiration mammography systems The Mammomat Inspiration system is intended for mammography exams, screening, diagnosis, and stereotactic biopsies under supervision of medical professionals. Mammographic images can be interpreted by either hard copy film or soft copy workstation.	Siemens Medical Solutions USA, Inc	2	17/10/2014	The stereo biopsy devices for Mammomat Inspiration mammography systems might have integrated a safety switch which causes a failure of functionality. The pin implemented in safety switch may not put enough pressure on safety circuit to prohibit movement. The needle positioning device may move even with safety switch being set sideward. If this occurs with needle being already i [...]
TomoTherapy Treatment System, Model: Hi-Art, Catalog/Part Number: H-0000-0003, software versions 2.0.0 and 2.0.1 (Hi-Art 5.0.0 and 5.0.1). The TomoTherapy treatment system is intended to be used as an integrated system for planning and precise delivery of radiation therapy, stereotactic radiotherapy, or stereotactic radiosurgery to tumors or other targeted tissues while minimizing delivery of radiation to vital	TomoTherapy Incorporated	2	15/08/2014	Accuray is voluntarily recalling TomoTherapy H Series software versions 2.0.0 and 2.0.1 (Hi-Art¿ 5.0.0 and 5.0.1). Accuray has identified potential safety issues (anomalies) with these software versions.

healthy tissues. The megavoltage x-ray radiation is delivered in a rotational, nonrotational, modulated (IMRT), or nonmodulated (non-IMRT/3 dimensional conformal) format in accordance with physicians prescribed and approved plan.				
Navigation Spine & Trauma 3D Version 2.0 and 2.1 Is intended as an intraoperative image-guided localization system to enable minimally invasive surgery. It links a freehand probe, tracked by a passive marker sensor system to virtual computer image space on a patient's preoperative or Intraoperative 2D or 3D image data. The system is indicated for any medical condition in which use of stereotactic surgery may be appropriate and where a reference to a rigid anatomical structure, such as skull, pelvis, a long bone or vertebra can be identified relative to acquired image (CT, MR, 2D fluoroscopic image or 3D fluoroscopic image reconstruction) and/or an image data-based model of anatomy.	Brainlab AG	2	13/08/2014	Brainlab Navigation Software Spine & Trauma 3D 2.0/2.1 offers automatic registration of intraoperatively acquired CT image data sets. To enable automatic registration, software requires gantry position of scanner. The gantry position can either be entered manually or submitted automatically from CT scanner. If automatic gantry communication is available, so-called &quot
ExacTrac is intended to be used to place patients at an accurately defined point within treatment beam of a medical accelerator for stereotactic radiosurgery or radiotherapy procedures, in order to treat lesions, tumors and conditions anywhere in body when radiation treatment is indicated. ExacTrac may also be used to monitor patient position during treatment.	Brainlab AG	2	04/08/2014	When using multiple isocenters (radiation treatment targets) within a single plan, in certain workflow conditions ExacTrac v.6.0.4 might move patient to an unintended isocenter position, despite displaying green "OK" icon. If this anomaly occurs and is not detected by user, radiation treatment dose at linear accelerator may be delivered to unintended target position.
Medtronic Nexdrive Micropositioning Drive. Models MI-1000 and MI-2000. For use in conjunction with Medtronic Nexframe Stereotactic System for precise positioning of microelectrodes and implantable leads. A stereotactic guidance system used in conjunction with Medtronic StealthStation Navigation	Medtronic Neuromodulation	2	25/07/2014	Potential for misalignment of Z-stage scale. Using one of these devices for a procedure could result in microelectrode being inserted to an incorrect target depth.

Systems-image-guided surgery (IGS) systems-for Deep Brain Stimulation (DBS) procedures.				
Siemens Linear Accelerator (LINAC) models. Product Usage: Deliver X-ray radiation for therapeutic treatment of cancer	Siemens Medical Solutions USA, Inc	2	23/05/2014	Siemens Radiation Oncology became aware that customers may be using Siemens Linear Accelerator in combination with stereotactic accessories which have not been validated as being compatible with Siemens LINAC models.
MAMMOMAT Inspiration. Intended for mammography exams, screening, diagnosis, and stereotactic biopsies under supervision of medical professionals.	Siemens Medical Solutions USA, Inc	2	20/05/2014	There is a potential and possible hazard to user when using MAMMOMAT Inspiration PC monitor at control desk, in that holder of PC monitor can break causing an unstable monitor to fall causing possible serious injury.
Accuray CyberKnife Robotic Radiosurgery System; Accuray Incorporated Sunnyvale, CA. Indicated for treatment planning and image guided stereotactic radiosurgery and precision radiotherapy.	Accuray Incorporated	2	27/01/2014	Potential Safety issue with Synchrony Boom Arm Mounting Assembly - one complaint of mounting assembly detaching.
C-Series: Clinac, Trilogy, Trilogy Tx., Novalis high energy linear accelerators and UNIQUE single energy linear accelerator; Versions 7, 8 and 9. The UNIQUE is not sold in US. Product Usage: The Varian High Energy Linear Accelerator is indicated for stereotactic radiosurgery and precision radiotherapy for lesions, tumors, and conditions anywhere in body when radiation treatment is indicated. The UNIQUE is a single energy medical linear accelerator. UNIQUE is indicated for precision radiotherapy for lesions, tumors, and conditions anywhere in body where radiation treatment is indicated.	Varian Medical Systems, Inc.	2	03/12/2013	This correction is to notify users that a solution to a previous correction has been developed and Varians reps will be contacting locations to schedule installation.
Stereotactic Circular Collimator - 3D Line stereotatic Hardware Accessories The device is part of class of medical devices that are used in radiotherapy for treatments of head tumors.	Elekta, Inc.	2	04/11/2013	Potential for clinical errors.

BRAINLAB; FRAMELESS SRS QA TARGET POINTER Robotics is a device used to compensate rotational patient misalignment (roll and pitch) in a linear accelerator environment for stereotactic radiosurgery or radiotherapy procedures. The Frameless Radiosurgery Components are a device used for fixation, localization and repositioning of patient's: head and neck; and head, neck, and shoulders, in a linear accelerator environment for stereotactic radiosurgery/radiotherapy procedures.	Brainlab AG	2	26/08/2013	The Frameless SRS QA Target Pointer - Pointer Cap with engraved cross hairs may become loose even when only a moderate force is applied to Pointer Cap.
Varian High Energy Clinacs, High Energy Accelerator, Radiation Treatment System, Model Numbers: H14, H27, H29, HCX. Product Usage: The Varian High Energy Accelerator is intended to provide stereotactic radiosurgery and precision radiotherapy for lesions, tumors, and conditions anywhere in body when radiation treatment is indicated.	Varian Medical Systems, Inc. Oncology Systems	2	14/05/2013	Under certain conditions, photon beams in High Energy Clinacs may experience a gradual change in beam symmetry, potentially reaching an asymmetry of up to about 7% before interlock occurs. At maximum asymmetry, this may result in no more than about 3.5% dose deviation from expected at any point in beam, and may result in minor injury to patient or slightly decreased local disease control.
Integra XKnife Stereotactic Radiosurgery and Radiotherapy Treatment Planning, Software Versions 5.0.1 and 5.0.2. Intended for use in stereotactic and non-stereotactic (frameless stereotactic), collimated beam, computer planned, linear accelerator (Linac) based treatment.	Integra LifeSciences Corp.	2	12/04/2013	Depending on system configuration, a software error message in versions 5.0.1 and 5.0.2. occurs if a beam plan is transmitted from XKnife using DICOM-RT.
The RIO (TGS 2.), Model # MAKO TGS 2.0 (Part No. 204000). The RIO is intended to assist surgeon in providing software defined spatial boundaries for orientation and reference information to anatomical structures during orthopedic procedures. The RIO is indicated for use in surgical knee and hip procedures, in which use of stereotactic surgery may be appropriate, and	Mako Surgical Corporation	2	19/11/2012	MAKO Surgical Group recalled their RIO System software, version 2.4 and is implementing software version 2.5 to address a software functional issue with existing version of system's software. Loss of tactile feedback constraining cutting burr has been reported.

where reference to rigid anatomical bony structures can be identified relative to a CT based model of anatomy. These procedures include: Unicondylar knee replacement (UKA) and/or Patellofemoral knee replacement (PKA) and Total Hip Arthroplasty (THA).				
Integra HRAIM Head Ring Assembly with Intubation Mounts The CRW stereotactic system is used in conjunction with HRAIM head ring is a target-centered system that can be configured to be CT-only or CT/MR compatible. The CRW stereotactic system is a multipurpose system used for localizing intercranial targets for precisely directing instruments such as: Biopsy forceps, RF lesioning electrodes, Deep brain electrodes, Recording and stimulating electrodes	Integra LifeSciences Corporation	2	20/09/2012	T-handle screw is used on a complementary product to CRW, Integra HRAIM, which is CT-compatible intubation Head Ring Assembly. When T-handle on HRAIM intubation hoop is tightened, T-handle could stop in a vertical position that prevents CRWPRECISE and certain models of CRW-ASL from seating properly on head ring although it appears to be fully seated.
Integra CRW Precision Arc (CRWPRECISE), CRW Arc System (CRWASL), HRAIM Head Ring Assembly with Intubation Mounts The CRW stereotactic system is used in conjunction with HRAIM head ring is a target-centered system that can be configured to be CT-only or CTIMR compatible. The CRW stereotactic system is a multipurpose system used for localizing intercranial targets for precisely directing instruments such as: Biopsy forceps, RF lesioning electrodes, Deep brain electrodes, Recording and stimulating electrodes	Integra LifeSciences Corporation	2	20/09/2012	T-handle screw is used on a complementary product to CRW, Integra HRAIM, which is CT-compatible intubation Head Ring Assembly. When T-handle on HRAIM intubation hoop is tightened, T-handle could stop in a vertical position that prevents CRWPRECISE and certain models of CRW-ASL from seating properly on head ring although it appears to be fully seated
Varian brand Clinac, Trilogy, Novalis Tx, Unique, linear accelerators; Model Number: H14, H18, H29, Reference/FSCA Identifier: CP-08881; Product is manufactured and distributed by Varian Medical Systems Inc., Palo Alto, CA. 1) The Varian Low Energy Linear Accelerator is indicated for precision radiotherapy for lesions, tumors, and conditions anywhere in body when radiation treatment is indicated. (2) The Varian	Varian Medical Systems, Inc. Oncology Systems	2	14/09/2012	Some X-jaw (lower collimator jaw) carriers were made using incorrect metal alloy, which can cause jaw carrier to crack. If both carriers on same X-jaw crack, jaw would be able to move freely in closed direction. The position readout interlock circuitry will not detect this jaw position deviation. This may lead to

High Energy Linear Accelerator is indicated for stereotactic radiosurgery and precision radiotherapy for lesions, tumors, and conditions anywhere in body when radiation treatment is indicated.				treatment with an under-dose of intended target volume.
OEC IT3000; IT2500 (EnTrak); IT2500 Plus (EnTrak Plus); IT3500 (InstaTrak); IT3500 Plus (InstaTrak Plus); ConneCTstat; and ConneCTstat Plus picture archiving and communications systems. The systems are an aid to locate anatomical structures during open or percutaneous surgical procedures. It is intended for use in medical conditions that may benefit from use of stereotactic surgical technique. The system provides a reference to rigid anatomical structures such as sinus, skull, long bone, or vertebra, which are visible on medical images such as CT, MRI, or X-ray.	GE OEC Medical Systems, Inc	1	28/08/2012	GE Healthcare Surgery had discovered that using Inverted Headset Placement is not a validated configuration with IT 3000, 2500, 2500 plus, 3500, 3500 plus, ConneCTstat, and ConneCTstat Plus Surgical Navigation equipment.
OEC InstaTrak 3500, picture archiving and communications system intended as an aid to locate anatomical structures during open percutaneous surgical procedures. It is indicated for use in medical conditions that may benefit from use of stereotactic surgical technique. The system provides a reference to rigid anatomical structures such as sinus, skull, long bone, or vertebra, which are visible on medical images such as CT, MRI, or X-ray.	GE OEC Medical Systems, Inc	2	21/08/2012	GE Healthcare had recalled certain OEC InstaTrak 3500 Carts due to potential for cart to tip over when arm of imaging device is extended during use.
Radiological Image Processing System The system is an aid to locate anatomical structures during open or percutaneous surgical procedures. It is indicated for use in medical conditions that may benefit from use of stereotactic surgical technique. The system provides a reference to rigid anatomical structures such as sinus, skull, long bone, or vertebra, which are visible on medical images such as CS, MR, or X-ray.	GE OEC Medical Systems, Inc	1	08/08/2012	The FluoroTrak Spinal Navigation Application on OEC 9900 EliteNAV could result in an incorrect position of navigated instrument(s) vs. displayed reference image.

OEC 9900 Elite, OEC 9900 Elite MD Motorized C-arm System, OEC 9900 Elite NAV used as an aid to locate anatomical structures during open or percutaneous surgical procedures. The system is an aid to locate anatomical structures during open or percutaneous surgical procedures. It is indicated for use in medical conditions that may benefit from use of stereotactic surgery technique. The system provides a reference to rigid anatomical structures such as sinus, skull, long bone, or vertebra, which are visible on medical images such as CT, MRI, or X-ray.	GE OEC Medical Systems, Inc	2	18/07/2012	Please be aware that this is not a new recall. The firm has acted; but, due to administrative issues this recall is now being classified by Agency. GE OEC recalled imaging devices OEC 9900, OEC 9800, and OEC 8800 as a result of an FDA inspection identifying that vertical lift column power supply in mainframe C-arm is defective and subject to early life failure.
InstaTrak with Multiple Dataset Navigation, 892.2050 System, Image Processing System, Model Number IT3500 Plus. Product Usage: Usage: The system is an aid to locate anatomical structures during open or percutaneous surgical procedures. It is indicated for use in medical conditions that may benefit from use of stereotactic surgical technique. The system provides a reference to rigid anatomical structures such as sinus, skull, long bone, or vertebra, which are visible on medical images such as CT, MR, or X-ray.	GE OEC Medical Systems, Inc	1	12/07/2012	Please be aware that this is not a new recall. The firm has acted; but, due to administrative issues this recall is now being classified by Agency. On October 11, 2006, GE Healthcare recalled GE OEC InstaTrak 3500 Plus System with Software version 5.2, surgical Navigation and Visualization Application due to software related issues.
TrueBeam and TrueBeam STx V1.0, 1.5, 1.6.95 and below. TrueBeam Radiotherapy Delivery System is intended to provide stereotactic radiosurgery and precision radiotherapy anywhere in body where radiation treatment is indicated. Varian Medical Systems, Palo Alto, CA.	Varian Medical Systems, Inc. Oncology Systems	2	16/05/2012	Varian received a report involving a Gantry collision and is sending a notification to remind users of collision protection tools available with TrueBeam and TrueBeam STx, including actions operator should be aware of.
TrueBeam and True Beam STx versions 1.0 through 1.5, Model number H19; Varian Medical Systems, Palo, Alto, CA 94304. TrueBeam Radiotherapy Delivery System is intended to provide stereotactic radiosurgery and precision radiotherapy for lesions, tumors, and conditions	Varian Medical Systems, Inc. Oncology Systems	2	06/03/2012	An anomaly has been identified with respiratory gating software of TrueBeam. When importing breath-hold gating protocols, gating thresholds can be reset to default values, rather than retaining thresholds established during planning.

anywhere in body where radiation treatment is indicated.				
CyberKnife Robotic Radiosurgery System with 4D Planning procedure option of MultiPlan Treatment Planning System, versions 3.0, 3.1, 3.5.1, 3.5.2 and 3.5.3 with Ray-Tracing dose calculation. Accuray Incorporated, Sunnyvale, CA. Treatment planning and image guided stereotactic radiosurgery and precision radiotherapy of lesions, tumors, and conditions anywhere in body when radiation treatment is indicated.	Accuray Incorporated	2	23/02/2012	An anomaly was discovered during internal regression testing, where dose information is displayed incorrectly during treatment planning during a specific workflow using optional 4D Ray Tracing dose calculation algorithm. As a result, it is possible that dose calculation will display a lower dose than intended dose prescribed for treatment delivery.
Varian Unique Single Energy Linear Accelerator, C-Series Clinac or Trilogy, versions 7.x and 8.x, Reference/FSCA Identifier: CP-0661; Model Numbers: H14, H18, H27, H29; Product is manufactured and distributed by Varian Medical Systems Inc., Palo Alto, CA Varian Unique Single Energy Linear Accelerator: The UNIQUE is a Single Energy Linear Accelerator intended to be used for conventional radiotherapy and includes modifications to previously cleared Varian Trilogy. The UNIQUE provides additional features, safety improvements, and usability improvements. The UNIQUE is intended to provide stereotactic radiosurgery and precision radiotherapy for lesions, tumors, and conditions anywhere in body when radiation treatment is indicated.	Varian Medical Systems, Inc. Oncology Systems	2	11/01/2012	An event has been reported to Varian which entails excessive connector resistance, which caused actual jaw positions to differ from intended jaw positions without warning operator.
Varian High Energy Linear Accelerator, C-Series Clinac, Reference/FSCA Identifier: CP-06611; Models Numbers: 600C, 600CD, 6EX, DBX, 2100C, 2100CD, 2300CD, 21EX, 23EX, DMX, DHX versions 2.x through 6.x; Product is manufactured and distributed by Varian Medical Systems Inc., Palo Alto, CA. The Varian High Energy Linear Accelerator is intended to provide stereotactic radiosurgery and precision radiotherapy for lesions, tumors, and	Varian Medical Systems, Inc. Oncology Systems	2	11/01/2012	An event has been reported to Varian which entails excessive connector resistance, which caused actual jaw positions to differ from intended jaw positions without warning operator.

conditions anywhere in body when radiation treatment is indicated.				
CyberKnife Robotic Radiosurgery System: Lung Optimized Treatment option. The CyberKnife treatment is indicated for treatment planning and image guided stereotactic radiosurgery and precision radiotherapy of lesions, tumors and conditions anywhere in body when radiation treatment is indicated.	Accuray Incorporated	2	06/12/2011	User Facility reported an anomaly where inhale and exhale CT pairs used for treatment planning did not represent same magnitude of respiration that was displayed during treatment delivery.
TrueBeam and TrueBeam STx, Model Number: H19, Ref/FSCA identifier: CP-06381 are intended to provide stereotactic radiosurgery and precision radiotherapy for lesions, tumors, and conditions anywhere in body where radiation treatment is indicated.	Varian Medical Systems, Inc. Oncology Systems	2	02/12/2011	An anomaly has been identified with TrueBeam and TrueBeam STx systems where, under certain tuning conditions, electron beam emerging from bend magnet may have an elongated spot shape.
Head Ring Posts with part number 970.280 - reusable components of Frame Array Module (of Optical Guidance Platform and Floorstand devices. Varian Medical Systems, Palo Alto, CA 94304. The Optical Guidance Platform is for use with a charged particle accelerator to perform precise positioning of treatment for stereotactic radiosurgery or radiotherapy treatments on cranial extracranial lesions.	Varian Medical Systems, Inc. Oncology Systems	2	01/12/2011	An anomaly has been identified with Head Ring posts used by both Optical Guidance Platform FrameArray module and Floorstand where head ring posts may be damaged due to excessive mechanical stress resulting in possible failure during usage.
Elekta Leksell Gamma Knife C 1.2, 4 and 4C Product Usage: Leksell Gamma Knife is a teletherapy device intended for stereotactic irradiation of head structures.	Elekta, Inc.	2	30/11/2011	Several of LMR03 actuators with bronze drive nut have failed unexpectedly, creating a potential safety hazard for operator and patient.
Stereotactic Circular Collimator Product Usage: This device is intended to hold a patient's head in a fixed position and to localize and center output of a linear accelerator (UNAC) to allow radiotherapy of brain tumors and other types of cerebral lesions.	Elekta, Inc.	2	30/11/2011	Recent newspaper articles outlined improper use of SRS Cone Collimator accessories that injured patients on Brainlab and Varian systems.
Varian Clinac, Trilogy, Trilogy Tx and Novalis linear accelerators. Manufactured by Varian Medical System, Palo Alto, CA.	Varian Medical Systems, Inc. Oncology Systems	2	09/11/2011	Varian has received reports in which a user has remotely rotated gantry into contact with couch or with patient, in both manual mode and automate mode.

Varian High Energy Linear Accelerator is indicated for stereotactic radiosurgery and precision radiotherapy for lesions, tumors, and conditions anywhere in body where radiation treatment is indicated.				
Labeling for RIO Robot Unit is comprised of three main components: 20399 RIO SURGICAL ARM, 201251 RIO GUIDANCE MODULE, 200294 RIO CAMERA STAND ASSEMBLY***PN 203999 SN ROB 125 2010-12 V 100/120/230 A 9.6/8.0/4.2 Hz 50/60 Class I Equipment. Conforms to IEC 60601-1/A2: 1995, EN 60601-1/A2: 1995 UL 60601-1: 2003, CAN/CSA-C22.2 No. 601.1-M90.***Manufactured in USA***MAKO SURGICAL CORP. 2555 DAVIE ROAD, FT. LAUDERDALE, FL 33317. RIO System - The Tactile Guidance System v2.0 is intended to assist surgeon in providing software defined spatial boundaries for orientation and reference information to anatomical structures during orthopedic procedures. The Tactile Guidance System v2.0 is indicated for use in surgical knee procedures, in which use of stereotactic surgery may be approriate, and where reference to rigid anatomical bony structures can be identified relative to a CT base model of anatomy. These procedures include unicondylar knee replacement and/or patellofemoral knee replacement.	Mako Surgical Corporation	2	01/11/2011	MAKO Surgical Corp. is recalling the RIO Robotic Arm Interactive Orthopedic System (RIO) due to software issue that exists that could potentially result in a bone resection. No adverse events reported.
TomoMobile, Hi-Art System, H-0000-0003, TomoTherapy 1240 Deming Way, Madison, WI 53717 The TomoTherapy HI-ART System is intended to be used as an integrated system for planning and precise delivery of radiation therapy, stereotactic radiotherapy, or stereotactic radiosurgery to tumors or other targeted tissues while minimizing delivery of radiation to vital healthy tissue. The	Accuray Incorporated	2	07/09/2011	TomoTherapy Inc. is sending this Field Safety Notice to make you aware of an anomaly which may affect performance of TomoMobile Hi-Art System. TomoTherapy has discovered that when attempting to open TomoMobile shielding doors, while door hinges are in locked position, hinges may fail allowing door to disengage from shielding.

megavoltage x-ray radiation is delivered in a rotational, nonrotational, modulated (IMRT), or nonmodulated (non-IMRT/3 dimensional conformal) format in accordance with physician approved plan.				
On-Board Imager (OBI) 1.3, 1.4, 1.5; and Trilogy Mx, TrueBeam 1.0, Offline Review 1.0 - 2.0; Product is manufactured and distributed by Varian Medical Systems Inc., Palo Alto, CA The On-Board Imager device is used for verification of correct patient position in relation to isocenter and verification of treatment fields relation to anatomical and/or fiducial landmarks. Trilogy Mx is intended to provide stereotactic radiosurgery and precision radiotherapy for lesions, tumors, and conditions anywhere in body where radiation treatment is indicated.	Varian Medical Systems, Inc. Oncology Systems	2	31/08/2011	Varian has identified a software anomaly in 3D Match environment, regarding a slight mismatch between CT image and Structures in On-Board Imager w/s.
HiArt versions 4.0.x, and HD versions 1.0.x, H-0000-0003. The TomoTherapy HI-ART System is intended to be used as an integrated system for planning and precise delivery of radiation therapy, stereotactic radiotherapy, or stereotactic radiosurgery to tumors or other targeted tissues while minimizing delivery of radiation to vital healthy tissue. The megavoltage x-ray radiation is delivered in a rotational, nonrotational, modulated (IMRT), or nonmodulated (non-IMRT/3 dimensional conformal) format in accordance with physician approved plan.	Accuray Incorporated	2	31/08/2011	As a result of an internal review, TomoTherapy has identified an issue with Hi¿¿Art versions 4.0.x, and HD versions 1.0.x that we would like to bring to your attention. During DICOM export of plan level images with a nonsquare exported Field of View (FOV), an anomaly in process of squaring plan level image may cause image to shift with respect to ROIs and dose. When anomaly occu
Clinac, Trilogy. Trilogy Tx and Novalis Tx Linear Accelerators. Varian Medical Systems, Inc. Oncology Systems Intended for stereotactic radiosurgery and precision radiotherapy for lesions, tumors, and conditions in body where radiation treatment is indicated.	Varian Medical Systems, Inc. Oncology Systems	2	10/08/2011	On Varian Linear Accelerators where customer may calibrate collimator angle position readout in reverse, switching 90-degree and 270-degree positions.

Clinac Linear Accelerators; Varian Medical Systems, Palo Alto, CA. Radiation Therapy intended to deliver megavoltage x-ray treatments for conventional radiotherapy and stereotactic radiosurgery and radiotherapy.	Varian Medical Systems, Inc. Oncology Systems	2	28/07/2011	The throat cover on High Energy Clinac may detach if not properly installed and possibly strike a patient.
Clinac Linear Accelerator; Model numbers H14, H27 and H29. Product Usage: Varian High Energy Linear Accelerator is indicated for stereotactic radiosurgery and precision radiotherapy for lesions, tumors, and conditions anywhere in body where radiation treatment is indicated.	Varian Medical Systems, Inc. Oncology Systems	2	08/07/2011	The Coolant System input water supply manifold may leak in some Clinac Linear Accelerators, posing a risk of electrical shock to any person working within protective housing.
TrueBeam Linear Accelerators (aka Trilogy Mx) Varian Medical Systems, Palo Alto, CA Product Usage: Intended to provide stereotactic radiosurgery and precision radiotherapy for lesions, tumors, and conditions anywhere in body where radiation treatment is indicated.	Varian Medical Systems, Inc. Oncology Systems	2	08/07/2011	Imaging arms of TrueBeam Accelerator may have loose encoder pulleys that could lead to inaccurate readout of arm geometry.
ERGO++ Stereotactic Radiation Treatment Planning System, ERGO++ Release 1.6.3 and 1.6.3.1 Product Usage: Used to create treatment plans for any cancer patient for who external beam radiation therapy has been prescribed. It is an accessory to linear accelerators used for radiation therapy. It is indicated for use in planning of 3-dimensional radiation therapy.	Computerized Medical Systems Inc	2	23/06/2011	ERGO Release 1.6.3 is overestimating MU values.
Varian brand Clinac and TrueBeam, High Energy Linear Accelerator, Model Numbers: H14, H19, H29; Product is manufactured and distributed by Varian Medical Systems Inc., Palo Alto, CA Indicated for stereotactic radiosurgery and precision radiotherapy for lesions, tumors, and conditions anywhere in body when radiation treatment is indicated.	Varian Medical Systems, Inc. Oncology Systems	2	19/05/2011	The coolant may leak. The resulting coolant leak presents a risk of electrical shock to any person working within protective housing.
Optical Guidance Platform, Version 2.6 and 2.6.1, Model Number: HZl, Manufactured and	Varian Medical Systems, Inc.	2	16/05/2011	A software anomaly has been identified with Optical Guidance Platform (OGP)

Distributed by: Varian Medical Systems Inc., Palo Alto, CA. For use with a charged particle accelerator to perform precise positioning of treatment target for stereotactic radiosurgery or radiotherapy treatments on cranial or extracranial lesions.	Oncology Systems			Software v2.6 and v2.6.1 where transfer of datasets from treatment planning systems other than FastPlan system result in a lateral offset error.
Varian brand Clinac, Medical Linear Accelerator, All Varian Clinac with Model Numbers: H14, H18, H26, H27, H28, H29, Hcx; Product is manufactured and distributed by Varian Medical Systems Inc., Palo Alto, CA The Trilogy Radiotherapy Delivery System is a radiation therapy accelerator intended to deliver megavoltage x-ray treatments for conventional radiotherapy (3-dimensional conformal radiotherapy and intensity modulated radiotherapy) and stereotactic radiosurgery and radiotherapy. Stereotactic treatments are intended for therapy of lesions, e.g., arteriovenous malformations, primary tumors, and metastases.	Varian Medical Systems, Inc. Oncology Systems	2	13/05/2011	Varian has identified an anomaly whereby, following prolonged use, screw fastener holding wedge body to tray may fail.
Optical Guidance Platform, version 2.6 and 2.6.1; Reference/FSCA Identifier: CP-03976; Model Number: HZ1; Product is manufactured and distributed by Varian Medical Systems Inc., Palo Alto, CA Optical Guidance Platform is for use with a charged particle accelerator to perform precise positioning of treatment target for stereotactic radiosurgery or radiotherapy treatments on cranial or extracranial lesions.	Varian Medical Systems, Inc. Oncology Systems	2	10/05/2011	The anomaly that has been identified with Optical Guidance Platform (OGP) software may not be always displaying correct transfer date on patient file.
Varian Medical System TrueBeam system for stereotactic radiosurgery and radiotherapy. Model number H19	Varian Medical Systems, Inc. Oncology Systems	2	10/05/2011	Position sensor failure mode may result in an inaccurate position calculation. 1. The video returned by 1 of 2 cameras inside Spectra is all white or all black, and Spectra stops tracking. Or 2. Certain video intensities are not available on 1 of 3 cameras. The image has abnormally

				abrupt transitions from dark to light portions, without normal shades of gray.
Optical Guidance Platform, version 2.6 and 2.6.1; Reference/FSCA Identifier: CP-03899; Product is manufactured and distributed by Varian Medical Systems Inc., Palo Alto, CA Optical Guidance Platform is for use with a charged particle accelerator to perform precise positioning of treatment target for stereotactic radiosurgery or radiotherapy treatments on cranial or extracranial lesions.	Varian Medical Systems, Inc. Oncology Systems	2	25/04/2011	The optical guidance platform may not be properly enforcing a 24-hour time limit between optical camera recalibrations.
Clinac High Energy Medical Linear Accelerator, a Trilogy Radiotherapy Delivery System; Model #s: H14, H18, H27, H29, HCX; Product is manufactured and distributed by Varian Medical Systems Inc., Palo Alto, CA The Trilogy Radiotherapy Delivery System is a radiation therapy accelerator intended to deliver megavoltage x-ray treatments for conventional radiotherapy (3-dimensional conformal radiotherapy and intensity modulated radiotherapy) and stereotactic radiosurgery and radiotherapy. Stereotactic treatments are intended for therapy of lesions, e.g., arteriovenous malformations, primary tumors, and metastases. Stereotactic treatments may be intracranial or extra cranial and consist of single-session or fractionated delivery.	Varian Medical Systems, Inc. Oncology Systems	2	20/04/2011	The wedge angle labeling on wedge tray may not correctly match wedge body. However, wedge body is labeled with correct wedge angle.
Receiver Sensor Cables, Part Numbers: 1001989, 1001990, 1004069, 1007907-NAV, GE Healthcare Surgery, Salt Lake City, UT 84116. Cables are used with InstraTrak Navigation Systems, Models IT3000, IT2500, IT2500+, IT3500, IT3500+. InstaTrak System is intended as an aid to surgeon for precisely locating anatomical structures anywhere on human body during either open or percutaneous procedures. It is indicated for any medical condition that may benefit from	GE OEC Medical Systems, Inc	2	11/04/2011	Sensor cables may suffer material degradation when exposed to certain sterilization procedures.

use of stereotactic surgery and which provides a reference to rigid anatomical structures such as sinus, skull, long bone, or vertebra, visible on medical images such as CT, MR, or X-ray.				
Transmitter Sensor Cables, Part Numbers: 1002008, 1004587, 1007914-NAV, GE Healthcare Surgery, Salt Lake City, UT 84116. Cables are used with InstraTrak Navigation Systems, Models IT3000, IT2500, IT2500+, IT3500, IT3500+. InstaTrak System is intended as an aid to surgeon for precisely locating anatomical structures anywhere on human body during either open or percutaneous procedures. It is indicated for any medical condition that may benefit from use of stereotactic surgery and which provides a reference to rigid anatomical structures such as sinus, skull, long bone, or vertebra, visible on medical images such as CT, MR, or X-ray.	GE OEC Medical Systems, Inc	2	11/04/2011	Sensor cables may suffer material degradation when exposed to certain sterilization procedures.
TomoTherapy Hi-ART System, Model # H-0000-0003 Intended to be used as an integrated system for planning and precise delivery of radiation therapy, stereotactic radiotherapy, or sterotactic radiosurgery to tumors or targeted tissues.	TomoTherapy Incorporated	2	14/03/2011	It was determined that Treatment Planning Station (TPS) can potentially under dose.
Integra Radionics HRAIM Intubation Head Ring Assembly Ref: HRAIM Head Rings serve as general stereotactic treatment platform. Head Rings are used to provide a reference frame for instrumentation used for precise spatial localization and treatment of physiologic targets for stereotactic neurosurgical procedures such as craniotomies, biopsies, functional neurosurgery, and radiation therapy. Head Rings are delivered to user nonsterile, and are reusable.	Integra LifeSciences Corp.	2	23/02/2011	Overall length of intubation hoop in the HRAIM Intubation Head Ring Assembly is too long and will not allow a device to to attach.
Elekta Leksell Stereotactic System, used for localization (spatial reference) for cranial surgery using X-ray or CT and MRI Image data.	Elekta, Inc.	2	15/02/2011	New protocols for MR sequences may result in higher RF energies deposited

				during MR scanning, generating heat in uninsulated fixation posts.
Leksell GammaPlan, Model 5.34. Intended to be used for planning dosimetry of treatments in stereotactic radiation therapy.	Elekta, Inc.	2	14/02/2011	Investigation found if a user accidentally selects wrong image/tube position images can be displayed flipped.
Varian High Energy Linear Accelerator: Varian Medical Systems, Palo Alto, CA 94304 Indicated for stereotactic radiosurgery and precision radiotherapy for lesions, tumors, and conditions anywhere in body when radiation treatment is indicated.	Varian Medical Systems, Inc. Oncology Systems	2	08/02/2011	An anomaly was identified whereby bolts used to fasten counterweight to gantry may not, in some cases, be fully tightened to required torque specification.
CyberKnife Treatment Planning System, a subsystem of CyberKnife Robotic Radiosurgery System, with MultiPlan Treatment Planning System Software version 3.5 Medical charged-particle radiation therapy system, intended for treatment planning and image-guided stereotactic radiosurgery and precision radiotherapy of lesions, tumors, and conditions anywhere in body when radiation treatment is indicated.	Accuray Inc	2	01/02/2011	If electron density values are left empty, calculation of radiation dose in a patient will be modeled as air-like density material rather than correct density. A plan may be created and saved, thus creating risk of mistreatment.
Varian brand C Series Clinic¿s (Includes Trilogy, and Novalis Tx), Model Numbers: H14, H26, H27, H29, Distributed by and/or Manufactured by: Varian Medical Systems Inc., Palo Alto, CA The system consists of 2 major components, a photon, electron, and diagnostic kV X-ray radiation beam-producing component that is installed in a radiation-shielded vault and a control console area located outside treatment room. Intended use: The Trilogy Mx System is indicated for stereotactic radiosurgery and precision radiotherapy for lesions, tumors, and conditions anywhere in body when radiation treatment is indicated. 7/9/2013 - UPDATE: Determined that correction only applied to C3 users, not C1 and C2 users.	Varian Medical Systems Oncology Systems	2	31/01/2011	A circuit design anomaly whereby a faulty balance potentiometer can lead to an undetected electron beam asymmetry.

C-Series Clinac, Trilogy and Novalis Tx used for SRS treatments, Model Numbers H14, H18, H27, H29, HCX, manufactured by Varian Medical Systems, Palo Alto, CA. Device is a radiation Therapy accelerator intended to deliver megavoltage x-ray treatments for conventional radiotherapy (3-dimensional conformal radiotherapy and intensity modulated radiotherapy) and stereotactic radiosurgery and radiotherapy. Stereotactic treatments are inteded for therapy of lesions such as arteriovenous malformations, primary tumors, and metastatses. Stereotactic treatments may be intracranial or extracranial and consist of single-session or fractionated delivery.	Varian Medical Systems Oncology Systems	2	18/01/2011	Product may deliver radiation treatment to areas larger than intended to healthy tissue.
CyberKnife Treatment Planning System, a subsystem of CyberKnife Robotic Radiosurgery System radiation therapy device, manufactured by Accuray Inc., Sunnyvale, CA. Device indicated for treatment planning and image guided stereotactic radiosurgery and precision radiotherapy of lesions, tumors, and conditions anywhere in body where radiation treatment is indicated.	Accuray Inc	2	10/01/2011	Latches responsible for securing cover to device may come lose if not properly secured and cover may unexpectedly drop off. A design change is planned.
Varian brand C-series Clinac, Trilogy and Novalis Tx, Software Versions 6.X and 7.X, Model Numbers: H14, H27, H29, HCX, Product is manufactured and distributed by Varian Medical Systems Inc., Palo Alto, CA The Trilogy Radiotherapy Delivery System is a radiation therapy accelerator intended to deliver megavoltage x-ray treatments for conventional radiotherapy (3-dimensional conformal radiotherapy and intensity modulated radiotherapy) and stereotactic radiosurgery and radiotherapy. Stereotactic treatments are intended for therapy of lesions, e.g., arteriovenous malformations, primary tumors, and metastases.	Varian Medical Systems Oncology Systems	2	07/01/2011	The Auto goto or Auto setup functions in C-Series version 7 software ignore couch angle and exceed motion zone (unless a tolerance is defined by user); it has potential for collision with patient on couch.

Stereotactic treatments may be intracranial or extra cranial and consist of single-session or fractionated delivery.				
homoTherapy Hi-Art System Intended to be used as an integrated system for planning and precise delivery of radiation therapy, stereotactic radiotherapy, or stereotactic radiosurgery to tumors or other targeted tissues while minimizing delivery of radiation to vital healthy tissue.	TomoTherapy Incorporated	2	27/12/2010	TomoTherapy Inc. is sending this Field Safety Notice to make you aware of an anomaly which may affect performance of Hi-Art System and make it so user cannot generate a Completion Procedure.
CyberKnife Robotic Radiosurgery System, medical charged-particle radiation therapy system, manufactured by Accuray Inc., Sunnyvale, CA. Indicated for treatment planning and image-guided stereotactic radiosurgery and precision radiotherapy of lesions, tumors, and conditions anywhere in body when radiation treatment is indicated.	Accuray Inc	2	16/12/2010	If users modify dose calculation box to cover just contoured anatomy and not entire CT volume, dosage may not be properly calculated.
Elekta VBH Head FIX The VBH HeadFIX is intended for positioning and immobilization of head and neck, stereotactic diagnostic localization, and stereotactic radiotherapy of cranial targets.	Elekta, Inc.	2	03/12/2010	The HeadFIX Baseplate is not screwed down to adapter to allow to compensate for roll and pitch with HeadFIX leveling screws of HeadFIX Baseplate.
STar Drive System, Catalog numbers: ST-DS-MA, ST-DS-ME, 70-ZD-ME Product is FHC DBS Depth Stop Adapter, a component of microTargeting Drive and STar Drive. The Drives are intended to be used with commercially available stereotactic systems for neurosurgical procedures which require accurate positioning of microelectrodes, stimulating electrodes, or other instruments in brain or nervous system.	FHC, Inc.	2	03/11/2010	Fixation thumbscrew on DBS depth stop adapter may be overtightened and damage implantable lead.
microTargeting Drive DBS Lead Holder 66-CN-DB Product is FHC DBS Depth Stop Adapter, a component of microTargeting Drive and STar Drive. The Drives are intended to be used with	FHC, Inc.	2	03/11/2010	Fixation thumbscrew on DBS depth stop adapter may be overtightened and damage implantable lead.

commercially available stereotactic systems for neurosurgical procedures which require accurate positioning of microelectrodes, stimulating electrodes, or other instruments in brain or nervous system.				
Depth Stop Adapter 66-AC-DS(1.8), E6-01-.5 used with microTargeting and STar Drives Product is FHC DBS Depth Stop Adapter, a component of microTargeting Drive and STar Drive. The Drives are intended to be used with commercially available stereotactic systems for neurosurgical procedures which require accurate positioning of microelectrodes, stimulating electrodes, or other instruments in brain or nervous system.	FHC, Inc.	2	03/11/2010	Fixation thumbscrew on DBS depth stop adapter may be overtightened and damage implantable lead.
microTargeting Drive System with Mounted Accessories Catalog numbers: 66-ZD-MD-01, MT-DS-01, FC1006 (Medtronic) Product is FHC DBS Depth Stop Adapter, a component of microTargeting Drive and STar Drive. The Drives are intended to be used with commercially available stereotactic systems for neurosurgical procedures which require accurate positioning of microelectrodes, stimulating electrodes, or other instruments in brain or nervous system.	FHC, Inc.	2	03/11/2010	Fixation thumbscrew on DBS depth stop adapter may be overtightened and damage implantable lead.
Hi-Art System, H-0000-0003 Usage: The TomoTherapy Hi-Art System is intended to be used as an integrated system for planning and precise delivery of radiation therapy, stereotactic radiotherapy, or stereotactic radiosurgery to tumors or other targeted tissues while minimizing delivery of radiation to vital healthy tissue. The megavoltage x-ray radiation is delivered in a rotational, nonrotational, modulated (IMRT), or nonmodulated (non-IMRT/3	TomoTherapy Incorporated	2	12/08/2010	An issue was identified with the TomoTherapy HI-Art System. In event a patient or DQA plan has a moved image, roll adjustments applied during registration will be incorrect. The Planning Station Plan Settings and DQA Setup tabs allow for images to be moved during planning. During registration when roll is applied on moved images, Operator Station incorrectly rolls image about

dimensional conformal) format in accordance with physician approved plan				
TomoTherapy Hi-Art System¿, Version 4.0.0 & 4.0.1. TomoTherapy Incorporated 1240 Deming Way, Madison, WI 53717. Intended to be used as an integrated system for planning and precise delivery of radiation therapy, stereotactic radiotherapy, or stereotactic radiosurgery to tumors or other targeted tissues while minimizing delivery of radiation to vital healthy tissue.	TomoTherapy Incorporated	2	01/08/2010	In some cases, patient's diagnostic CT image is narrower than Hi-Art radiotherapy couch image.
Leksell Gamma Knife, radionuclide radiation therapy system. Model LGK. Elekta Inc. Norcross, GA 30092. Indicated for use in stereotactic irradiation of intracranial structures.	Elekta, Inc.	A	27/05/2010	It was discovered that y/z slide did not behave as expected.
Leksell GammaPlan 8.0 image fusion Leksell GammaPlan is designed for use with Leksell Gamma Knife manufactured by Elekta Instrument AB. Leksell GammaPlan is intended to be used for planning dosimetry of treatments in stereotactic radiosurgery and stereotactic radiation therapy. It processes inputs of health professions (Neurosurgeons, Radiation therapists, Radiation Physicists) such that desired radiation does is proved by Leksell Gamma Knife to a precisely defined target area within cranium.	Elekta, Inc.	2	14/05/2010	The precision of calculation used to create fused study in LGP 8.0 is too low and should not be used until system is upgraded to LGP 8.2.
Leksell GammaPlan. Leksell GammaPlan is designed for use with Leksell Gamma Knife manufactured by Elekta Instrument AB. The Leksell GammaPlan is intended to be used for planning dosimetry of treatments in stereotactic radiosurgery and stereotactic radiation therapy. It processes inputs of health care professional (Neurosurgeons, Radiation Therapists and Radiation Physicists) such that desired radiation dose is provided by	Elekta, Inc.	2	27/04/2010	Although co-registration looks good during verification step in co-registration dialog, obtain transformation may include an error that depends on voxel sizes and acquisition parameters of co-registered image studies.

Leksell Gamma Knife to a precisely defined target area within cranium.				
Elekta Stereotactic Body Frame. Model Number: MRT 4601. Designed for stereotactic diagnostic localization and stereotactic radiotherapy of extracranial targets.	Elekta, Inc.	A	23/04/2010	Notification of importance of ensuring that correct indicators are fitted for imaging modality in use.
Leksell Stereotactic System, Elekta Inc. Norcross, GA 30092. Intended for localization for cranial surgery using x-ray, or CT and MRI image data.	Elekta, Inc.	A	16/04/2010	There was a reported case of a fragment of a Quick Fixation Screw was left inside patient skull.
Leksell Gamma Knife. Leksell Gamma Knife is a teletherapy device indicated for use in stereotactic irradiation of intracranial structures.	Elekta, Inc.	2	13/04/2010	After updating LGK actuator in spare part 810361, old sleigh became obsolete due to causing insufficient locking of helmet in combination with new actuator.
Leksell Gamma Knife Perfexion. Radionuclide radiation therapy system. Elekta, Inc. Norcross, GA. Indicated for use in stereotactic irradiation of intracranial structures.	Elekta, Inc.	2	05/04/2010	There has been an issue with "Image Fushing" where low precision calculation caused images to become inaccurate.
Leksell Gamma Knife Perfexion, Radionuclide radiation therapy system. Article Number 715000, Elekta, Inc. Norcross, GA 30092. Teletherapy device intended for stereotactic irradiation of head structures ranging from very small target sized os a few millimeters to several centimeters.	Elekta, Inc.	2	05/04/2010	Radiation unit doors could close too fast on emergency exit.
Leksell Gamma Knife Perfexion, Product Number: 715000. Radionuclide radiation therapy system. Elekta, Inc. Norcross, GA. Intended for stereotactic irradiation of head structures ranging from very small target sizes of a few millimeters to several centimeters.	Elekta, Inc.	2	05/04/2010	There may be a situation where Frame Adapter might lock stereotactic Frame in wrong position.
Leksell Stereotactic System. The Leksell Stereotactic System is a system intended for localization and diagnosis of intracranial disorders and their surgical treatment,	Elekta, Inc.	A	01/04/2010	Painted numbers and number scale markings were reported by customer to be coming off of arc and arc supports.

including radiotherapy and stereotactic radiation therapy.				
Leksell Gamma Knife Perfexion, Article #715000. Teletherapy device intended for stereotactic irradiation of head structures ranging from very small target sizes of a few millimeters to several centimeters.	Elekta, Inc.	2	17/03/2010	Need to modify closing speed of shielding doors in event of an emergency exit
BrainLab Radiotherapy Treatment Planning Software; Catalog number 20610 - Radiosurgery 3.0 Catalog number 20620 - Radiosurgery 3.5 and Catalog number 20630 - Circular ARC SRS/SRT Planning. The software is intended for use in stereotactic, conformal, computer planned, LINAC based radiation treatment of cranial, head and neck, and extracranial lesions. It is intended to be used by experienced and trained health professionals.	Brainlab AG	2	20/09/2009	Failure to conduct important safety checks when using BrainLab radiotherapy treatment planning software in combination with BrainLab conical collimators could result in unintended radiation outside conical shaped field, which may lead to serious injury of patient.
CyberKnife Treatment Delivery System, a subsystem of CyberKnife Robotic Radiosurgery System, manufactured by Accuray Inc., Sunnyvale, CA. Indicated for treatment for planning and image-guided stereotactic radiosurgery and precision radiotherapy of lesions, tumors, and conditions anywhere in body when radiation treatment is indicated.	Accuray Inc	2	14/09/2009	Targeting accuracy out of specification, Error alert does not render system down, which may result in mistreatment in wrong area.
Clinac with Version 7.x Software, manufactured by Varian Medical Systems, Palo Alto, CA. Part of Trilogy Radiotherapy Delivery System for radiation therapy intended to delivery megavoltage x-ray treatments for conventional radiotherapy and stereotactic radiosurgery and radiotherapy.	Varian Medical Systems Oncology Systems	2	27/08/2009	Unexpected Movement: if stereotactic motion disable function is turned on, couch can be moved via float mode unexpectedly.
Mammo Test Model number 10144185, x-ray guided stereotactic biopsy system	Siemens Medical Solutions USA, Inc	2	01/06/2009	Table may unintentionally lift during procedure

TomoTherapy HI-ART Systems with versions 2.2.4, 3.1.2, 3.1.3 or 3.2.1 software. The affected applications include Planning Station, Planned Adaptive, Data Management System, and TomoPortal. TomoTherapy HI-ART Systems is intended to be used as an integrated system for planning and delivery of intensity modulated radiation therapy (IMRT). The HI-ART System provides precise delivery of radiation to tumors or other targeted tissues while minimizing delivery of radiation to vital health tissue. The HI-Art system's planning station or operator station is intended to be used by physician/oncologists to prescribe a radiation therapy plan for a particular patient. The HI-ART System then calculates treatment plan which physician reviews and approves. The HI-ART system's operator station and status console is then intended to be used by therapist to select and implement patient's treatment plan. The treatment process will begin by performing a TomoImage (MVCT) scan (a CT using on board linear accelerator as radiation source). This TomoImage (MVCT) will confirm that patient's position is correct for radiation therapy as well as assist in patient re-positioning when necessary. The TomoImage (MVCT) image is not for diagnostic use. When patient positioning is complete, HI-ART System i sthen intended to be used by therapist to treat patient using selected treatment plan. The HI-ART System delivers radiation therapy, stereotactic radiotherapy or stereotactic radiosurgery treatment in accordance with physician approved plan delivered in a helical tomographic pattern.	TomoTherapy Incorporated	2	22/01/2009	TomoTherapy Incorporated identified a potential issue with Hi-Art system during course of ongoing testing. The Operator Station Calibration panel provides access to view and modify machine specific configuration settings. Access to these settings has always been restricted to individuals with appropriate security rights, being limited to only "Superuser" and "Field Service engine.
Cyberknife Robotic Radiosurgery System. A radiation therapy device, MultiPlan (MP)	Accuray Inc	2	17/01/2009	System may use random incorrect data to calculate dose. Resulting dose calculation

Treatment Planning Software and Iris Variable Aperture Collimator, Software version 3.0. Product is indicated for treatment planning and image guided stereotactic radiosurgery and precision radiotherapy of lesions, tumors, and conditions anywhere in body when radiation treatment is indicated.				error can exceed 100% of correct dose which may lead to serious patient injury.
RoboCouch Patient Support System, a component of CyberKnife Robotic Radiosurgery System. Model number 025007, manufactured by Accuray Inc., Sunnyvale, CA The CyberKnife is indicated for treatment planning and imageguided stereotactic radiosurgery and precision radiotherapy of lesions, tumors, and conditions anywhere in body when radiation treatment is indicated. The RoboCouch Patient Support System is intended for use in support and positioning of a patient during radiosurgery and radiotherapy procedures and other medical procedures when precise positioning is required.	Accuray Inc	2	14/01/2009	Product may not be tensioned properly, potentially causing unexpected rotation or descent.
FHC microTargeting Platform DBS Measuring Fixture, a component of microtargeting Drive System (Catalog Number 66-FA-SF). The device is a stereotactic instrument used for placement of recording and stimulating electrodes in brain.	FHC, Inc.	2	22/12/2008	Measuring fixture is incorrectly graduated.
GE Stereotaxy Positioner, model 2405544-3, for use with Senographe DS Full Field Mammography system, models 2383168, 2383168-2, 2383168-3, 2383168-3-1, 2383168-4-1. The expected use of Senographe DS Stereotaxy is an optional accessory for Senographe system for mammography examinations.	GE Healthcare	2	26/09/2008	GE Healthcare has recently become aware of x-ray emission beyond edge of detector primary barrier. This issue occurs when an exam is performed in a specific angulated view associated with use of Stereotactic Positioner of your Senographe DS Acquisition system and could impact patient safety.
GE Stereotaxy Positioner, model 2405544-2, for use with Senographe DS Full Field Mammography system, models 2383168, 2383168-2, 2383168-3,	GE Healthcare	2	26/09/2008	GE Healthcare has recently become aware of x-ray emission beyond edge of detector primary barrier. This issue

2383168-3-1, 2383168-4-1. The expected use of Senographe DS Stereotaxy is an optional accessory for Senographe system for mammography examinations.				occurs when an exam is performed in a specific angulated view associated with use of Stereotactic Positioner of your Senographe DS Acquisition system and could impact patient safety.
VectorVision (VV) Sky Navigation Platform (19" Computer Rack); 19" computer rack is a component of VVsky Vario, BrainSUITE iMRI, BrainSUITE NET and BrainSUITE iCT systems; BrainLab AG, Kapellenstrasse 12, 85622 Feldkirchen, Germany Intended to be an intraoperative image guided localization system to enable minimally invasive surgery. Indicated for any medical condition in which use of stereotactic surgery may be appropriate and where a reference to a rigid anatomical structure can be identified to relative to a CT, CTA, X-ray, MR, MRA, and ultrasound-based model of anatomy.	Brainlab AG	2	17/09/2008	Diameter of cables used for installation are to small for applied current. If an internal short circuit is produced medical power supply will not shut down automatically and will continue to deliver current, which could result in overheating cables.
Accuracy Cyberknife Robotic Radiosurgery System, medical charged particle radiation therapy device. Model number 020700 (axum/standard treatment couch) and 021756 hand controller. The device is indicated for treatment planning and image-guided stereotactic radiosurgery and precision radiotherapy of lesions, tumors, and conditions anywhere in body when radiation treatment is indicated.	Accuray Inc	2	12/09/2008	Couch may move unexpectedly, which may result in patient impacting linear accelerator.
Varian brand Clinac, Accelerator, Linear, Medical charged-particle radiation therapy system; Model: Low Energy Clinacs with one or more of following options: -- BrainLAB micro MLC -- Stereotactic motion disable Product is manufactured and distributed by Varian Medical Systems, Palo Alto, CA	Varian Medical Systems Inc	2	13/02/2008	The collimator drive chain may break or slip off of its drive track, allowing collimator to rotate freely without motor control; if undetected resulting in a treatment with wrong collimator angle.
Varian brand Clinac, Accelerator, Linear, Medical charged-particle radiation therapy system: Model:	Varian Medical Systems Inc	2	13/02/2008	Treatment Error: The collimator drive chain may break or slip off of its drive

High Energy Clinacs with one or more of following options: -- BrainLAB micro MLC -- 6MV SRS photon beam -- Fine Beam Isocenter Accuracy -- Stereotactic motion disable ----Product is manufactured and distributed by Varian Medical Systems, Palo Alto, CA				track, allowing collimator to rotate freely without motor control; if undetected resulting in a treatment with wrong collimator angle.
Nexframe Stereotactic System Kits, Model Number(s): DB-1021-MR, DB-1031, DB-1040-BL, DB-1040-ST, DB-1041, DB-1041-BL, DB-1041-ST, DB-1042, DB-1042-BL, DB-1042-ST, DB-1043, DB-1043-BL, DB-1043-ST, DB-2031, DB-2040-BL, DB-2040-ST, DB-2041, DB-2041-BL, DB-2041-ST, DB-2042, DB-2042-BL, DB-2042-ST, DB-2043, DB-2043-BL, DB-2043-ST Medtronic, Inc, Minneapolis, Minnesota	Medtronic Image Guided Neurologics, Inc.	2	06/02/2008	Sterilty (package integrity) Compromised: Some failures were for damage to outer pouch, while another set of failures were for seals on this pouch. The seal between inner tray and lid has not been compromised and contents remain sterile, however, sterility of outer surfaces of inner tray and lid cannot be assured.
FramelessArray software, Version 1.0.; Medical Device firmware incorporated with RadioCamera Extracranial System, distributed by Varian Medical System, Palo Alto, CA.	Varian Medical Systems Oncology Systems	2	05/06/2007	Localization error; with planning data transferred to Optical Guidance Platform via DICOM RT; The software incorrectly computes center of CT volume, resulting in a potential axial error ranging from 0.3 mm to 1.5 mm, affecting both Fractionated and Stereotactic Radiosurgery (SRS) Treatments
GE Healthcare Navigation Pin Transmitter (GE P/N 1004070) -Medical Systems InstaTrak Pin Transmitter	GE OEC Medical Systems, Inc	3	06/04/2006	Small retaining pin may detach and fall into surgical field during stereotactic surgery.
FHC 66-ZD-MD microTargeting Drive System: System for Stereotactic Positioning Used with Power Assist (66-DA-ME) or Display Assembly (66-DA-EN)	FHC, Inc.	2	15/06/2005	Potential for non-sterile pin to contaminate sterile field

Notes. Class 1: A situation where there is a reasonable chance that a product will cause serious health problems or death; Class 2: A situation where a product may cause a temporary or reversible health problem or where there is a slight chance that it will cause serious health problems or death; Class 3: A situation where a product is not likely to cause any health problem or injury.
Abbreviations. FDA: US Food and Drug Administration;

Appendix G. Studies Registered at ClinicalTrials.gov

Table G1. Ongoing Randomized Controlled Trials

NCT Number	Acronym	Study Results	Cancer Site	Interventions	Outcome Measures	Sample Size	Primary Completion Date
NCT01730937	NR	No results available	Adults with HCC	• SBRT • Sorafenib	• OS • QoL • Toxicity	193	July 2022
NCT01792934	ORCHESTRA	No results available	Adults with multi-organ metastatic colorectal cancer	• SBRT and other treatment with chemotherapy • Chemotherapy	• OS • PFS • Response • Toxicity	478	December, 2022
NCT01965223	SAFRON II	No results available	Adults with metastases to lung	• SBRT • MFRT	• OS • Disease-free survival • QoL • Disease control • Toxicity • Resource use and costs	90	July 2020
NCT01968941	LUSTRE	No results available	Adults with NSCLC	• SBRT • cRT	• OS • Disease control • Disease-free survival • Event-free survival • QoL • Toxicity • Cost-utility	324	February 2022
NCT02089100	STEREO-SEIN	No results available	Adults with breast cancer	• SBRT • No treatment (palliation)	• OS • PFS • Local failure	280	February 2020
NCT02212860	SIGNAL 2	No results available	People aged 50 and older with early stage breast carcinoma	• SBRT previous to surgery • No SBRT	• OS • Disease-free survival	139	April 2021

					• Mastectomy-free survival • Toxicity		
NCT02339701		No results available	Men with prostate cancer	• SBRT • IMRT	• OS • Disease-free survival • Biochemical failure • QoL	68	December 2022
NCT02361515	RPAH2	No results available	Adults with prostatic adenocarcinoma	• SBRT • Moderate hypofractionated RT	• Relapse • Toxicity.	96	January 2020
NCT02417662	SARON	No results available	Adults with NSCLC	• SBRT and cRT • Systematic therapy	• OS • OFS • Local control • QoL • Toxicity	340	August 2022
NCT02685397	PCS IX	No results available	Adults with castration-resistant prostate cancer with oligometastases	• SBRT • No SBRT	• OS • PFS • QoL • Toxicity	130	April 2025
NCT02756793	NR	No results available	Adults with metastatic cancer	• SBRT • Standard of care	• OS • PF • Local control • QoL • Toxicity	90	July 2022
NCT02759783	CORE	No results available	Adults with oligometastatic disease	• SBRT • Standard care	• OS • PFS • Local control • QoL • Toxicity	245	October 2024
NCT02791503	CROSSFIRE	No results available	Adults with pancreatic neoplasm	• SBRT • Irreversible electroporation	• OS • PFS • QoL • Toxicity	74	September 2022

NCT02794337	TACE-SBRT	No results available	Adults with HCC	• SBRT • No SBRT	• PFS • Response • Toxicity	67	January 2024
NCT02921139	TASABR	No results available	Adults with HCC	• SBRT • Re-TACE	OS PFS Response Toxicity	120	November 2022
NCT02984761	VALOR	No results available	Adults with lung neoplasm	• SBRT • Surgery	• OS • QoL	670	September 2026
NCT03143322	STEREO-OS	No results available	Adults with bone metastases	• SBRT • Standard of care	• OS • PFS • Local control • QoL • Cost-utility	196	January 2026
NCT03256981	HALT	No results available	Adults aged 16 and older with NSCLC	• SBRT • No SBRT	• OS • PFS • QoL • Toxicity	110	November 2021
NCT03326375	STH	No results available	Adults with HCC	• SBRT • TACE	• OS • PFS • Local control • Toxicity	80	March 2020
NCT03338647	NR	No results available	Adults with HCC	• SBRT • TACE	• OS • Progression • Response • Local control • Toxicity • Cost-benefit	180	December 2023
NCT03367702	NR	No results available	Adults with stage II prostate adenocarcinoma	• SBRT • IMRT	• OS • Failure • QoL • Toxicity	698	December 2024

NCT03386045	NR	No results available	Men with prostate cancer	• SBRT (boost) • RT	• Local control • Failure	214	March 2026
NCT03597984	PREST	No results available	Adults with bone metastases	• SBRT (boost) • RT	• OS • PFS • Local control • QoL	330	July 2019
NCT03704662	NR	No results available	Adults with pancreatic cancer	• SBRT • Standard of care	• Disease-free survival • Control • Toxicity	102	December 2030
NCT03721341	SABR-COMET 10	No results available	Adults with metastatic tumors	• SBRT • Standard of care	• OS • PFS • Recurrence • QoL • Toxicity	204	January 2029
NCT03831243	ROBOMET	No results available	Adults with bone metastases	• SBRT • Conformal RT	• QoL • Toxicity	126	March 2022
NCT03862911	SABR-COMET-3	No results available	Adults with metastatic tumors	• SBRT • Palliative RT	• OS • PFS • QoL • Resource use • Toxicity	330	December 2028
NCT03867175	NR	No results available	Adults with stage IV NSCLC	• SBRT • No SBRT	• OS • PFS • Failure • Toxicity	112	July 2027
NCT03895359	TACE	No results available	Adults with HCC	• SBRT • TACE	• OS • Progression • Response • QoL • Toxicity • Cost-benefit	128	June 2027
NCT03960008	SBRTvsTACE	No results available	Adults with HCC	• SBRT as bridging therapy	• Control • Toxicity	196	December 2022

				• TACE as bridging therapy	• Transplant outcomes		
NCT04081168	COLLISION-XL	No results available	Adults with unresectable colorectal liver metastases	• SBRT • Microwave ablation	• OS • PFS	68	September 2024
NCT04115007	PRESTO	No results available	Adults with oligometastatic hormone sensitive prostate cancer	• SBRT • Standard of care	• OS • OFS • QoL • Toxicity • Cost-effectiveness	350	January 2023
NCT04498767	OligoRARE	No results available	Adults with rare oligometastatic cancers	• SBRT • Palliative RT	• OS • PFS • QoL • Toxicity	200	August 2028
NCT04610372	PROMPT	No results available	Adults with oligometastatic prostate cancer	• SBRT • Brachytherapy • cRT	• OS • Failure • QoL • Cost-effectiveness	168	January 23
NCT04861415	SHARP	No results available	Men with prostate cancer	• SBRT • cRT	• OS • Failure • QoL • Toxicity	55	December 2022
NCT04870567	NR	No results available	Adults with early-intermediate prostate cancer	• SBRT • Brachytherapy	• Biochemical relapse-free survival • Toxicity	350	April 2023
NCT04881487	ARCADE	No results available	Adults with recurrent pancreatic ductal adenocarcinoma	• SBRT • Standard of care	• OS • PFS • QoL • Toxicity	174	April 2026
NCT04883671	NR	No results available	Adults with oligometastatic adenoid cystic carcinoma	• SBRT • Standard of care	• OS • PFS • Local control • QoL	66	June 2028

NCT04983095	METRO	No results available	People (no age limit_ with metastatic prostate cancer	• SBRT • cRT	• OS • Failure • QoL • Toxicity	114	December, 2025
NCT05111197	TRAILOCLORI01	No results available	Adults with Palliative locally advanced or metastatic NSCLC	• SBRT • No SBRT	• OS • PFS • QoL	112	January 2025
NCT05181605	NR	No results available	Adults with resectable pancreatic cancer	• Chemotherapy and SBRT • Standard of care	• OS • Recurrence • Toxicity	116	April 2023
NCT05209243	START-MET	No results available	People (no age limit) with prostate cancer	• SBRT • Standard of care	• OS • PFS • QoL • Toxicity	266	March2025
NCT05265663	PANCOSAR	No results available	Adults with pancreatic cancer non-resectable	• SBRT • Supportive care	• OS • Progression • QoL • Toxicity	98	March 2024
NCT05377047	TAORMINA	No results available	Adults with oligometastatic breast cancer	• SABR • Systemic therapy	• OS • PFS • Local control • QoL • Toxicity	345	December 2025
NCT05433701	NR	No results available	Adults with small HCCs	• SBRT • RFA	• OS • PFS • Intrahepatic-free progression • Toxicity	162	December 2026
NCT05444270	SABR-ROC	No results available	Adults with recurrent epithelial ovarian cancer	• SBRT with salvage therapy • Salvage therapy	• OS	270	December 2026

Abbreviations. cRT: conventional radiation therapy; HCC: hepatocellular carcinoma; IMRT: intensity-modulated radiation therapy; NCT: US National Clinical Trial; NSCLC: non-small cell lung cancer; OS: overall survival; PFS: progression-free survival; QoL: quality of life; RT: radiation therapy; SBRT: stereotactic body radiation therapy.

Appendix H. Excluded Studies

See attachment for a list of excluded studies, with reasons for exclusion (pages H1-H82).

References

Note. Reference numbers are different to those in the full report.

1. Brand DH, Tree AC, Ostler P, et al. Intensity-modulated fractionated radiotherapy versus stereotactic body radiotherapy for prostate cancer (PACE-B): acute toxicity findings from an international, randomised, open-label, phase 3, non-inferiority trial. *Lancet Oncol.* 2019;20(11):1531-1543. doi: 10.1016/S1470-2045(19)30569-8.

2. Tree AC, Ostler P, van der Voet H, et al. Intensity-modulated radiotherapy versus stereotactic body radiotherapy for prostate cancer (PACE-B): 2-year toxicity results from an open-label, randomised, phase 3, non-inferiority trial. *Lancet Oncol.* 2022;23(10):1308-1320. doi: 10.1016/S1470-2045(22)00517-4.

3. Kwan W, Bahl G, Kim D, Ye A, Gagne I, Alexander A. Acute toxicity of ultrahypofractionation compared with moderate hypofractionation in prostate cancer treatment: a randomized trial. *Int J Radiat Oncol Biol Phys.* 2022;113(5):1036-1043. doi: 10.1016/j.ijrobp.2022.04.006.

4. Lukka HR, Pugh SL, Bruner DW, et al. Patient reported outcomes in NRG Oncology RTOG 0938, evaluating two ultrahypofractionated regimens for prostate cancer. *Int J Radiat Oncol Biol Phys.* 2018;102(2):287-295. doi: 10.1016/j.ijrobp.2018.06.008.

5. Widmark A, Gunnlaugsson A, Beckman L, et al. Ultra-hypofractionated versus conventionally fractionated radiotherapy for prostate cancer: 5-year outcomes of the HYPO-RT-PC randomised, non-inferiority, phase 3 trial. *Lancet.* 2019;394(10196):385-395. doi: 10.1016/S0140-6736(19)31131-6.

6. Fransson P, Nilsson P, Gunnlaugsson A, et al. Ultra-hypofractionated versus conventionally fractionated radiotherapy for prostate cancer (HYPO-RT-PC): patient-reported quality-of-life outcomes of a randomised, controlled, non-inferiority, phase 3 trial. *Lancet Oncol.* 2021;22(2):235-245. doi: 10.1016/S1470-2045(20)30581-7.

7. Altorki NK, McGraw TE, Borczuk AC, et al. Neoadjuvant durvalumab with or without stereotactic body radiotherapy in patients with early-stage non-small-cell lung cancer: a single-centre, randomised phase 2 trial. *Lancet Oncol.* 2021;22(6):824-835. doi: 10.1016/S1470-2045(21)00149-2.

8. Lee B, Mynard N, Nasar A, et al. Surgical resection after neoadjuvant durvalumab and radiation is feasible and safe in non-small cell lung cancer: Results from a randomized trial. *J Thorac Cardiovasc Surg.* 2023;165(1):327-334 e322. doi: 10.1016/j.jtcvs.2022.07.017.

9. Theelen W, Peulen HMU, Lalezari F, et al. Effect of pembrolizumab after stereotactic body radiotherapy vs pembrolizumab alone on tumor response in patients with advanced

non-small cell lung cancer: Results of the PEMBRO-RT phase 2 randomized clinical trial. *JAMA Oncol.* 2019;5(9):1276-1282. doi: 10.1001/jamaoncol.2019.1478.

10. Kim S, Wuthrick E, Blakaj D, et al. Combined nivolumab and ipilimumab with or without stereotactic body radiation therapy for advanced Merkel cell carcinoma: a randomised, open label, phase 2 trial. *Lancet.* 2022;400(10357):1008-1019. doi: 10.1016/S0140-6736(22)01659-2.

11. McBride S, Sherman E, Tsai CJ, et al. Randomized phase II trial of nivolumab with stereotactic body radiotherapy versus nivolumab alone in metastatic head and neck squamous cell carcinoma. *J Clin Oncol.* 2021;39(1):30-37. doi: 10.1200/JCO.20.00290.

12. Ost P, Reynders D, Decaestecker K, et al. Surveillance or metastasis-directed therapy for oligometastatic prostate cancer recurrence: a prospective, randomized, multicenter phase II trial. *J Clin Oncol.* 2018;36(5):446-453. doi: 10.1200/JCO.2017.75.4853 Accessed 2022/11/21.

13. Deek MP, Van der Eecken K, Sutera P, et al. Long-term outcomes and genetic predictors of response to metastasis-directed therapy versus observation in oligometastatic prostate cancer: analysis of STOMP and ORIOLE Trials. *J Clin Oncol.* 2022;40(29):3377-3382. doi: 10.1200/JCO.22.00644.

14. Palma DA, Olson R, Harrow S, et al. Stereotactic ablative radiotherapy versus standard of care palliative treatment in patients with oligometastatic cancers (SABR-COMET): a randomised, phase 2, open-label trial. *Lancet.* 2019;393(10185):2051-2058. doi: 10.1016/S0140-6736(18)32487-5.

15. Palma DA, Olson R, Harrow S, et al. Stereotactic ablative radiotherapy for the comprehensive treatment of oligometastatic cancers: long-term results of the SABR-COMET phase II randomized trial. *J Clin Oncol.* 2020;38(25):2830-2838. doi: 10.1200/JCO.20.00818 Accessed 20200602//.

16. Olson R, Senan S, Harrow S, et al. Quality of life outcomes after stereotactic ablative radiation therapy (SABR) versus standard of care treatments in the oligometastatic setting: a secondary analysis of the SABR-COMET Randomized Trial. *Int J Radiat Oncol Biol Phys.* 2019;105(5):943-947. doi: 10.1016/j.ijrobp.2019.08.041 Accessed 20190827//.

17. Palma DA, Haasbeek CJ, Rodrigues GB, et al. Stereotactic ablative radiotherapy for comprehensive treatment of oligometastatic tumors (SABR-COMET): study protocol for a randomized phase II trial. *BMC Cancer.* 2012;12:305. doi: 10.1186/1471-2407-12-305.

18. Van Oirschot M, Bergman A, Verbakel W, et al. Determining planning priorities for SABR for oligometastatic disease: a secondary analysis of the SABR-COMET phase II

randomized trial. *Int J Radiat Oncol Biol Phys*. 2022;114(5):1016-1021. doi: 10.1016/j.ijrobp.2022.01.002.

19. Phillips R, Shi WY, Deek M, et al. Outcomes of observation vs stereotactic ablative radiation for oligometastatic prostate cancer: the ORIOLE phase 2 randomized clinical trial. *JAMA Oncol*. 2020;6(5):650-659. doi: 10.1001/jamaoncol.2020.0147.

20. Radwan N, Phillips R, Ross A, et al. A phase II randomized trial of observation versus stereotactic ablative radiation for oligometastatic prostate cancer (ORIOLE). *BMC Cancer*. 2017;17(1):453. doi: 10.1186/s12885-017-3455-6.

21. Nguyen QN, Chun SG, Chow E, et al. Single-Fraction Stereotactic vs Conventional Multifraction Radiotherapy for Pain Relief in Patients With Predominantly Nonspine Bone Metastases: A Randomized Phase 2 Trial. *JAMA Oncol*. 2019;5(6):872-878. doi: 10.1001/jamaoncol.2019.0192.

22. Andruska N, Fischer-Valuck BW, Agabalogun T, et al. Propensity-weighted survival analysis of SBRT vs. conventional radiotherapy in unfavorable intermediate-risk prostate cancer. *Clin Genitourin Cancer*. 2022;20(2):123-131. doi: 10.1016/j.clgc.2021.11.012.

23. Bolzicco G, Favretto MS, Satariano N, Scremin E, Tambone C, Tasca A. A single-center study of 100 consecutive patients with localized prostate cancer treated with stereotactic body radiotherapy. *BMC Urol*. 2013;13:49. doi: 10.1186/1471-2490-13-49.

24. Davis J, Sharma S, Shumway R, et al. Stereotactic body radiotherapy for clinically localized prostate cancer: Toxicity and biochemical disease-free outcomes from a multi-institutional patient registry. *Cureus*. 2015;7(12):e395. doi: 10.7759/cureus.395.

25. Katz A. Stereotactic body radiotherapy for low-risk prostate cancer: a ten-year analysis. *Cureus*. 2017;9(9):e1668. doi: 10.7759/cureus.1668.

26. Katz AJ, Kang J. Quality of life and toxicity after SBRT for organ-confined prostate cancer, a 7-year study. *Front Oncol*. 2014;4:301. doi: 10.3389/fonc.2014.00301.

27. Katz AJ, Kang J. Stereotactic body radiotherapy as treatment for organ confined low- and intermediate-risk prostate carcinoma, a 7-year study. *Front Oncol*. 2014;4:240. doi: 10.3389/fonc.2014.00240.

28. Katz AJ, Santoro M, Diblasio F, Ashley R. Stereotactic body radiotherapy for localized prostate cancer: disease control and quality of life at 6 years. *Radiation oncology*. 2013;8(1):1-8.

29. Katz AJ, Santoro M, Ashley R, Diblasio F, Witten M. Stereotactic body radiotherapy for organ-confined prostate cancer. *BMC urology*. 2010;10(1):1-10.

30. Freeman D, Dickerson G, Perman M. Multi-institutional registry for prostate cancer radiosurgery: a prospective observational clinical trial. *Front Oncol.* 2014;4:369. doi: 10.3389/fonc.2014.00369.

31. Fuller DB, Falchook AD, Crabtree T, et al. Phase 2 multicenter trial of heterogeneous-dosing stereotactic body radiotherapy for low- and intermediate-risk prostate cancer: 5-year outcomes. *Eur Urol Oncol.* 2018;1(6):540-547. doi: 10.1016/j.euo.2018.06.013.

32. Fuller DB, Crabtree T, Kane BL, et al. High dose "HDR-Like" prostate SBRT: PSA 10-year results from a mature, multi-institutional clinical trial. *Front Oncol.* 2022;12:935310. doi: 10.3389/fonc.2022.935310.

33. Chen LN, Suy S, Uhm S, et al. Stereotactic body radiation therapy (SBRT) for clinically localized prostate cancer: the Georgetown University experience. *Radiat Oncol.* 2013;8(1):58. doi: 10.1186/1748-717X-8-58.

34. Gurka MK, Chen LN, Bhagat A, et al. Hematuria following stereotactic body radiation therapy (SBRT) for clinically localized prostate cancer. *Radiat Oncol.* 2015;10:44. doi: 10.1186/s13014-015-0351-6.

35. Joh DY, Chen LN, Porter G, et al. Proctitis following stereotactic body radiation therapy for prostate cancer. *Radiat Oncol.* 2014;9(1):277. doi: 10.1186/s13014-014-0277-4.

36. Woo JA, Chen LN, Bhagat A, et al. Clinical characteristics and management of late urinary symptom flare following stereotactic body radiation therapy for prostate cancer. *Front Oncol.* 2014;4:122. doi: 10.3389/fonc.2014.00122.

37. Glowacki G, Majewski W, Wojcieszek P, et al. Acute toxicity of robotic ultrahypofractionated radiotherapy CyberKnifeTM in prostate cancer patients. *Neoplasma.* 2015;62(4):674-682. doi: 10.4149/neo_2015_081.

38. Glowacki G, Majewski W, Wojcieszek P, Grabinska K, Wozniak G, Miszczyk L. Ultrahypofractionated CyberKnife based stereotactic radiotherapy versus conventional radiotherapy in patients with prostate cancer - acute toxicity evaluation in two phase II prospective studies. *Neoplasma.* 2017;64(4):599-604. doi: 10.4149/neo_2017_421.

39. Halpern JA, Sedrakyan A, Hsu WC, et al. Use, complications, and costs of stereotactic body radiotherapy for localized prostate cancer. *Cancer.* 2016;122(16):2496-2504. doi: 10.1002/cncr.30101.

40. Johansson S, Isacsson U, Sandin F, Turesson I. High efficacy of hypofractionated proton therapy with 4 fractions of 5 Gy as a boost to 50 Gy photon therapy for localized prostate cancer. *Radiat Oncol.* 2019;141:164-173.

41. Katz A, Ferrer M, Suarez JF, Multicentric Spanish Group of Clinically Localized Prostate C. Comparison of quality of life after stereotactic body radiotherapy and surgery for early-stage prostate cancer. *Radiat Oncol.* 2012;7:194. doi: 10.1186/1748-717X-7-194.

42. Koskela K, Palmgren JE, Heikkila J, et al. Hypofractionated stereotactic body radiotherapy for localized prostate cancer - first Nordic clinical experience. *Acta Oncol.* 2017;56(7):978-983. doi: 10.1080/0284186X.2017.1288923.

43. Lee SH, Kim HJ, Kim WC. Prostate-specific antigen kinetics following hypofractionated stereotactic body radiotherapy versus conventionally fractionated external beam radiotherapy for low- and intermediate-risk prostate cancer. *Asia Pac J Clin Oncol.* 2016;12(4):388-395. doi: 10.1111/ajco.12566.

44. Loblaw A, Pickles T, Crook J, et al. Stereotactic ablative radiotherapy versus low dose rate brachytherapy or external beam radiotherapy: propensity score matched analyses of Canadian data. *Clin Oncol (R Coll Radiol).* 2017;29(3):161-170. doi: 10.1016/j.clon.2016.10.001.

45. Ma TM, Ballas LK, Wilhalme H, et al. Quality-of-life outcomes and toxicity profile among patients with localized prostate cancer after radical prostatectomy treated with stereotactic body radiation: the SCIMITAR multicenter phase 2 trial. *Int J Radiat Oncol Biol Phys.* 2023;115(1):142-152. doi: 10.1016/j.ijrobp.2022.08.041.

46. Mantz C. A phase II trial of stereotactic ablative body radiotherapy for low-risk prostate cancer using a non-robotic linear accelerator and real-time target tracking: report of toxicity, quality of life, and disease control outcomes with 5-year minimum follow-up. *Front Oncol.* 2014;4:279. doi: 10.3389/fonc.2014.00279.

47. Meier RM, Bloch DA, Cotrutz C, et al. Multicenter trial of stereotactic body radiation therapy for low- and intermediate-risk prostate cancer: survival and toxicity endpoints. *Int J Radiat Oncol Biol Phys.* 2018;102(2):296-303. doi: 10.1016/j.ijrobp.2018.05.040.

48. Miszczyk L, Namysl Kaletka A, Napieralska A, et al. Cyberknife radioablation of prostate cancer - preliminary results for 400 patients. *Asian Pac J Cancer Prev.* 2017;18(4):1007-1013. doi: 10.22034/APJCP.2017.18.4.1007.

49. Miszczyk L, Napieralska A, Namysł-Kaletka A, et al. CyberKnife-based prostate cancer patient radioablation–early results of irradiation in 200 patients. *Cent European J Urol.* 2015;68(3):289. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4643703/pdf/CEJU-68-00582.pdf.

50. Monaco A, Sommer J, Akerman M, et al. Four-year quality-of-life outcomes in low- to intermediate-risk prostate cancer patients following definitive stereotactic body radiotherapy versus management with active surveillance. *World J Urol.* 2022;40(9):2213-2219. doi: 10.1007/s00345-022-04084-2.

51. Oliai C, Bernetich M, Brady L, et al. Propensity score matched comparison of SBRT versus IMRT for the treatment of localized prostate cancer. *J Radiat Oncol.* 2016;5:187-195. doi: 10.1007/s13566-015-0237-0.

52. Bernetich M, Oliai C, Lanciano R, et al. SBRT for the primary treatment of localized prostate cancer: The effect of gleason score, dose and heterogeneity of intermediate risk on outcome utilizing 2.2014 NCCN risk stratification guidelines. *Front Oncol.* 2014;4:312. doi: 10.3389/fonc.2014.00312.

53. Ricco A, Manahan G, Lanciano R, et al. The comparison of stereotactic body radiation therapy and intensity-modulated radiation therapy for prostate cancer by NCCN risk groups. *Front Oncol.* 2016;6:184. doi: 10.3389/fonc.2016.00184.

54. Pan HY, Jiang J, Hoffman KE, et al. Comparative toxicities and cost of intensity-modulated radiotherapy, proton radiation, and stereotactic body radiotherapy among younger men with prostate cancer. *J Clin Oncol.* 2018;36(18):1823. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6008105/pdf/JCO.2017.75.5371.pdf.

55. Pasquier D, Martinage G, Janoray G, et al. Salvage stereotactic body radiation therapy for local prostate cancer recurrence after radiation therapy: a retrospective multicenter study of the GETUG. *Int J Radiat Oncol Biol Phys.* 2019;105(4):727-734. doi: 10.1016/j.ijrobp.2019.07.012.

56. Patel SA, Switchenko JM, Fischer-Valuck B, et al. Stereotactic body radiotherapy versus conventional/moderate fractionated radiation therapy with androgen deprivation therapy for unfavorable risk prostate cancer. *Radiat Oncol.* 2020;15(1):217. doi: 10.1186/s13014-020-01658-5.

57. Paydar I, Cyr RA, Yung TM, et al. Proctitis 1 week after stereotactic body radiation therapy for prostate cancer: implications for clinical trial design. *Front Oncol.* 2016;6:167. doi: 10.3389/fonc.2016.00167.

58. Pryor D, Sidhom M, Arumugam S, et al. Phase 2 multicenter study of gantry-based stereotactic radiotherapy boost for intermediate and high risk prostate cancer (PROMETHEUS). *Front Oncol.* 2019;9:217. doi: 10.3389/fonc.2019.00217.

59. Rana Z, Hong RL, Abugideiri M, et al. Sexual, irritative, and voiding outcomes, following stereotactic body radiation therapy for prostate cancer. *Radiat Oncol.* 2015;10(1):182. doi: 10.1186/s13014-015-0488-3.

60. Ricco A, Hanlon A, Lanciano R. Propensity score matched comparison of intensity modulated radiation therapy vs stereotactic body radiation therapy for localized prostate cancer: a survival analysis from the National Cancer Database. *Front Oncol.* 2017;7:185. doi: 10.3389/fonc.2017.00185.

61. Tsang YM, Tharmalingam H, Belessiotis-Richards K, et al. Ultra-hypofractionated radiotherapy for low- and intermediate risk prostate cancer: High-dose-rate brachytherapy vs stereotactic ablative radiotherapy. *Radiother Oncol.* 2021;158:184-190. doi: 10.1016/j.radonc.2021.02.028.

62. Werneburg GT, Kongnyuy M, Halpern DM, et al. Patient-reported quality of life progression in men with prostate cancer following primary cryotherapy, cyberknife, or active holistic surveillance. *Prostate Cancer Prostatic Dis.* 2018;21(3):355-363. doi: 10.1038/s41391-017-0004-y.

63. Yu JB, Cramer LD, Herrin J, Soulos PR, Potosky AL, Gross CP. Stereotactic body radiation therapy versus intensity-modulated radiation therapy for prostate cancer: comparison of toxicity. *J Clin Oncol.* 2014;32(12):1195-1201. doi: 10.1200/JCO.2013.53.8652.

64. Berkovic P, Gulyban A, Defraene G, et al. Stereotactic robotic body radiotherapy for patients with oligorecurrent pulmonary metastases. *BMC Cancer.* 2020;20(1):402. doi: 10.1186/s12885-020-06906-1 Accessed 20200508//.

65. Davis JN, Medbery C, Sharma S, et al. Stereotactic body radiotherapy for centrally located early-stage non-small cell lung cancer or lung metastases from the RSSearch patient registry. *Radiat Oncol.* 2015;10:113. doi: 10.1186/s13014-015-0417-5.

66. Duijm M, Tekatli H, Oomen-de Hoop E, et al. Esophagus toxicity after stereotactic and hypofractionated radiotherapy for central lung tumors: normal tissue complication probability modeling. *Radiother Oncol.* 2018;127(2):233-238. doi: 10.1016/j.radonc.2018.02.004.

67. Filippi AR, Guerrera F, Badellino S, et al. Exploratory analysis on overall survival after either surgery or stereotactic radiotherapy for lung oligometastases from colorectal cancer. *Clin Oncol (R Coll Radiol).* 2016;28(8):505-512. doi: 10.1016/j.clon.2016.02.001.

68. Fleming C, Rimner A, Foster A, Woo KM, Zhang Z, Wu AJ. Palliative efficacy and local control of conventional radiotherapy for lung metastases. *Ann Palliat Med.* 2017;6(Suppl 1):S21-S27. doi: 10.21037/apm.2017.03.08.

69. Guckenberger M, Wulf J, Mueller G, et al. Dose-response relationship for image-guided stereotactic body radiotherapy of pulmonary tumors: relevance of 4D dose calculation. *Int J Radiat Oncol Biol Phys.* 2009;74(1):47-54. doi: 10.1016/j.ijrobp.2008.06.1939.

70. Helou J, Thibault I, Poon I, et al. Stereotactic ablative radiation therapy for pulmonary metastases: histology, dose, and indication matter. *Int J Radiat Oncol Biol Phys.* 2017;98(2):419-427. doi: 10.1016/j.ijrobp.2017.02.093.

71. Jacobs CD, Gao J, Wang X, et al. Definitive radiotherapy for inoperable stage IIb non-small-cell lung cancer: patterns of care and comparative effectiveness. *Clin Lung Cancer.* 2020;21(3):238-246. doi: 10.1016/j.cllc.2019.10.005.

72. Kanzaki R, Suzuki O, Kanou T, et al. The short-term outcomes of pulmonary metastasectomy or stereotactic body radiation therapy for pulmonary metastasis from epithelial tumors. *J Cardiothorac Surg.* 2020;15(1):43. doi: 10.1186/s13019-020-1079-4 Accessed 20200227//.

73. Lagerwaard FJ, Verstegen NE, Haasbeek CJ, et al. Outcomes of stereotactic ablative radiotherapy in patients with potentially operable stage I non-small cell lung cancer. *Int J Radiat Oncol Biol Phys.* 2012;83(1):348-353. doi: 10.1016/j.ijrobp.2011.06.2003.

74. Lee YH, Kang KM, Choi HS, et al. Comparison of stereotactic body radiotherapy versus metastasectomy outcomes in patients with pulmonary metastases. *Thorac Cancer.* 2018;9(12):1671-1679. doi: 10.1111/1759-7714.12880.

75. Lee TH, Kim DY, Wu HG, Lee JH, Kim HJ. Treatment outcomes of re-irradiation using stereotactic ablative radiotherapy to lung: a propensity score matching analysis. *Radiat Oncol.* 2021;16(1):222. doi: 10.1186/s13014-021-01948-6.

76. Littau MJ, Freeman R, Vigneswaran WT, et al. Comparative effectiveness of stereotactic body radiation therapy versus surgery for stage I lung cancer in otherwise healthy patients: an instrumental variable analysis. *JTCVS Open.* 2022;9:249-261. doi: 10.1016/j.xjon.2021.09.052.

77. Lo H, Abel S, Finley G, Weksler B, Colonias A, Wegner RE. Surgical resection versus stereotactic body radiation therapy in early stage bronchopulmonary large cell neuroendocrine carcinoma. *Thorac Cancer.* 2020;11(2):305-310. doi: 10.1111/1759-7714.13260 Accessed 20191220//.

78. Nelson DB, Tayob N, Nguyen QN, et al. Local failure after stereotactic body radiation therapy or wedge resection for colorectal pulmonary metastases. *J Thorac Cardiovasc Surg.* 2019;158(4):1234-1241 e1216. doi: 10.1016/j.jtcvs.2019.02.133 Accessed 20190511//.

79. Osti MF, Agolli L, Valeriani M, et al. 30 Gy single dose stereotactic body radiation therapy (SBRT): report on outcome in a large series of patients with lung oligometastatic disease. *Lung Cancer.* 2018;122:165-170. doi: 10.1016/j.lungcan.2018.06.018.

80. Rosen JE, Salazar MC, Wang Z, et al. Lobectomy versus stereotactic body radiotherapy in healthy patients with stage I lung cancer. *J Thorac Cardiovasc Surg.* 2016;152(1):44-54 e49. doi: 10.1016/j.jtcvs.2016.03.060.

81. Scotti V, Bruni A, Francolini G, et al. Stereotactic ablative radiotherapy as an alternative to lobectomy in patients with medically operable stage I NSCLC: a retrospective, multicenter analysis. *Clin Lung Cancer*. 2019;20(1):e53-e61. doi: 10.1016/j.cllc.2018.09.003.

82. Sharma A, Duijm M, Oomen-de Hoop E, et al. Factors affecting local control of pulmonary oligometastases treated with stereotactic body radiotherapy. *Acta Oncol*. 2018;57(8):1031-1037. doi: 10.1080/0284186X.2018.1445285.

83. Sharma A, Duijm M, Oomen-de Hoop E, et al. Survival and prognostic factors of pulmonary oligometastases treated with stereotactic body radiotherapy. *Acta oncologica (Stockholm, Sweden)*. 2019;58(1):74-80. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med16&NEWS=N&AN=30280633 Accessed 20181003//.

84. Takeda A, Ohashi T, Kunieda E, et al. Early graphical appearance of radiation pneumonitis correlates with the severity of radiation pneumonitis after stereotactic body radiotherapy (SBRT) in patients with lung tumors. *Int J Radiat Oncol Biol Phys*. 2010;77(3):685-690. doi: 10.1016/j.ijrobp.2009.06.001.

85. Wegner RE, Abel S, Colonias A. Stereotactic ablative body radiotherapy versus conventionally fractionated radiotherapy for early stage large cell neuroendocrine carcinoma of the lung. *Lung Cancer Manag*. 2020;9(3):LMT32. doi: 10.2217/lmt-2020-0004 Accessed 20200421//.

86. Yamamoto T, Niibe Y, Aoki M, et al. Analyses of the local control of pulmonary oligometastases after stereotactic body radiotherapy and the impact of local control on survival. *BMC Cancer*. 2020;20(1):997. doi: 10.1186/s12885-020-07514-9 Accessed 20201014//.

87. Siva S, Ali M, Correa RJM, et al. 5-year outcomes after stereotactic ablative body radiotherapy for primary renal cell carcinoma: an individual patient data meta-analysis from IROCK (the International Radiosurgery Consortium of the Kidney). *Lancet Oncol*. 2022;23(12):1508-1516. doi: 10.1016/S1470-2045(22)00656-8.

88. Uhlig A, Uhlig J, Trojan L, Kim HS. Stereotactic body radiotherapy for stage I renal cell carcinoma: national treatment trends and outcomes compared to partial nephrectomy and thermal ablation. *J Vasc Interv Radiol*. 2020;31(4):564-571. doi: 10.1016/j.jvir.2019.11.009 Accessed 20200229//.

89. de Geus SWL, Eskander MF, Kasumova GG, et al. Stereotactic body radiotherapy for unresected pancreatic cancer: a nationwide review. *Cancer*. 2017;123(21):4158-4167. doi: 10.1002/cncr.30856.

90. Moningi S, Lei X, Fang P, et al. Contemporary use and outcomes of radiation and chemotherapy for unresectable pancreatic cancer. *Clin Transl Radiat Oncol.* 2022;35:9-16. doi: 10.1016/j.ctro.2022.04.007.

91. Zhong J, Patel K, Switchenko J, et al. Outcomes for patients with locally advanced pancreatic adenocarcinoma treated with stereotactic body radiation therapy versus conventionally fractionated radiation. *Cancer.* 2017;123(18):3486-3493. doi: 10.1002/cncr.30706.

92. Al-Mamgani A, Van Rooij P, Sewnaik A, et al. Brachytherapy or stereotactic body radiotherapy boost for early-stage oropharyngeal cancer: comparable outcomes of two different approaches. *Oral Oncol.* 2013;49(10):1018-1024. doi: 10.1016/j.oraloncology.2013.07.007.

93. Ozyigit G, Cengiz M, Yazici G, et al. A retrospective comparison of robotic stereotactic body radiotherapy and three-dimensional conformal radiotherapy for the reirradiation of locally recurrent nasopharyngeal carcinoma. *Int J Radiat Oncol Biol Phys.* 2011;81(4):e263-268. doi: 10.1016/j.ijrobp.2011.02.054.

94. Vargo JA, Ward MC, Caudell JJ, et al. A multi-institutional comparison of SBRT and IMRT for definitive reirradiation of recurrent or second primary head and neck cancer. *Int J Radiat Oncol Biol Phys.* 2018;100(3):595-605. doi: 10.1016/j.ijrobp.2017.04.017.

95. Yamazaki H, Demizu Y, Okimoto T, et al. Reirradiation for recurrent head and neck cancers using charged particle or photon radiotherapy. *Strahlenther Onkol.* 2017;193(7):525-533. doi: 10.1007/s00066-017-1129-6.

96. Yamazaki H, Demizu Y, Okimoto T, et al. Comparison of re-irradiation outcomes for charged particle radiotherapy and robotic stereotactic radiotherapy using cyberknife for recurrent head and neck cancers: a multi-institutional matched-cohort analysis. *Anticancer Res.* 2016;36(10):5507-5514. doi: 10.21873/anticanres.11132.

97. Andratschke N, Alheid H, Allgauer M, et al. The SBRT database initiative of the German Society for Radiation Oncology (DEGRO): patterns of care and outcome analysis of stereotactic body radiotherapy (SBRT) for liver oligometastases in 474 patients with 623 metastases. *BMC Cancer.* 2018;18(1):283. doi: 10.1186/s12885-018-4191-2.

98. Berber B, Ibarra R, Snyder L, et al. Multicentre results of stereotactic body radiotherapy for secondary liver tumours. *HPB (Oxford).* 2013;15(11):851-857. doi: 10.1111/hpb.12044.

99. Bettinger D, Pinato DJ, Schultheiss M, et al. Stereotactic body radiation therapy as an alternative treatment for patients with hepatocellular carcinoma compared to sorafenib: a propensity score analysis. *Liver Cancer.* 2019;8(4):281-294. doi: 10.1159/000490260.

100. Bujold A, Massey CA, Kim JJ, et al. Sequential phase I and II trials of stereotactic body radiotherapy for locally advanced hepatocellular carcinoma. *J Clin Oncol.* 2013;31(13):1631-1639. doi: 10.1200/JCO.2012.44.1659.

101. Mathew AS, Atenafu EG, Owen D, et al. Long term outcomes of stereotactic body radiation therapy for hepatocellular carcinoma without macrovascular invasion. *Eur J Cancer.* 2020;134:41-51. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med17&NEWS=N&AN=32460180 Accessed 20200524//.

102. Murray LJ, Sykes J, Brierley J, et al. Baseline albumin-bilirubin (albi) score in Western patients with hepatocellular carcinoma treated with stereotactic body radiation therapy (SBRT). *Int J Radiat Oncol Biol Phys.* 2018;101(4):900-909. doi: 10.1016/j.ijrobp.2018.04.011.

103. Hara K, Takeda A, Tsurugai Y, et al. Radiotherapy for hepatocellular carcinoma results in comparable survival to radiofrequency ablation: a propensity score analysis. *Hepatology.* 2019;69(6):2533-2545. doi: 10.1002/hep.30591.

104. Honda Y, Kimura T, Aikata H, et al. Stereotactic body radiation therapy combined with transcatheter arterial chemoembolization for small hepatocellular carcinoma. *J Gastroenterol Hepatol.* 2013;28(3):530-536. doi: 10.1111/jgh.12087.

105. Jacob R, Turley F, Redden DT, et al. Adjuvant stereotactic body radiotherapy following transarterial chemoembolization in patients with non-resectable hepatocellular carcinoma tumours of >/= 3 cm. *HPB (Oxford).* 2015;17(2):140-149. doi: 10.1111/hpb.12331.

106. Jeong Y, Lee KJ, Lee SJ, et al. Radiofrequency ablation versus stereotactic body radiation therapy for small (</= 3 cm) hepatocellular carcinoma: a retrospective comparison analysis. *J Gastroenterol Hepatol.* 2021;36(7):1962-1970. doi: 10.1111/jgh.15442 Accessed 20210305//.

107. Park S, Jung J, Cho B, et al. Clinical outcomes of stereotactic body radiation therapy for small hepatocellular carcinoma. *J Gastroenterol Hepatol.* 2020;35(11):1953-1959. doi: 10.1111/jgh.15011 Accessed 20200220//.

108. Ji R, Ng KK, Chen W, et al. Comparison of clinical outcome between stereotactic body radiotherapy and radiofrequency ablation for unresectable hepatocellular carcinoma. *Medicine (Baltimore).* 2022;101(4):e28545. doi: 10.1097/MD.0000000000028545.

109. Jun BG, Kim SG, Kim YD, et al. Combined therapy of transarterial chemoembolization and stereotactic body radiation therapy versus transarterial chemoembolization for </=5cm hepatocellular carcinoma: propensity score matching analysis. *PLoS One.* 2018;13(10):e0206381. doi: 10.1371/journal.pone.0206381 Accessed 20181031//.

110. Kibe Y, Takeda A, Tsurugai Y, et al. Feasibility of marker-less stereotactic body radiotherapy for hepatocellular carcinoma. *Acta Oncol.* 2022;61(1):104-110. doi: 10.1080/0284186X.2021.2001566 Accessed 20211117//.

111. Kim N, Cheng J, Jung I, et al. Stereotactic body radiation therapy vs. radiofrequency ablation in Asian patients with hepatocellular carcinoma. *J Hepatol.* 2020;73(1):121-129. doi: 10.1016/j.jhep.2020.03.005.

112. Kimura T, Aikata H, Doi Y, et al. Comparison of stereotactic body radiation therapy combined with or without transcatheter arterial chemoembolization for patients with small hepatocellular carcinoma ineligible for resection or ablation therapies. *Technol Cancer Res Treat.* 2018;17:1533033818783450. doi: 10.1177/1533033818783450.

113. Lock M, Chow R, Jayatilaka A, et al. Does stereotactic body radiation improve outcomes compared to conventional radiation for liver cancer patients? *Clin Transl Radiat Oncol.* 2022;35:17-20. doi: 10.1016/j.ctro.2022.04.002.

114. Loi M, Comito T, Franzese C, et al. Stereotactic body radiotherapy in hepatocellular carcinoma: patient selection and predictors of outcome and toxicity. *J Cancer Res Clin Oncol.* 2021;147(3):927-936. doi: 10.1007/s00432-020-03389-2 Accessed 20200918//.

115. Mahadevan A, Blanck O, Lanciano R, et al. Stereotactic body radiotherapy (SBRT) for liver metastasis - clinical outcomes from the international multi-institutional RSSearch patient registry. *Radiat Oncol.* 2018;13(1):26. doi: 10.1186/s13014-018-0969-2.

116. Mendez Romero A, Schillemans W, van Os R, et al. The Dutch-Belgian registry of stereotactic body radiation therapy for liver metastases: clinical outcomes of 515 patients and 668 metastases. *Int J Radiat Oncol Biol Phys.* 2021;109(5):1377-1386. doi: 10.1016/j.ijrobp.2020.11.045.

117. Munoz-Schuffenegger P, Barry A, Atenafu EG, et al. Stereotactic body radiation therapy for hepatocellular carcinoma with macrovascular invasion. *Radiother Oncol.* 2021;156:120-126. doi: 10.1016/j.radonc.2020.11.033.

118. Nabavizadeh N, Jahangiri Y, Rahmani R, et al. Thermal ablation versus stereotactic body radiotherapy after transarterial chemoembolization for inoperable hepatocellular carcinoma: a propensity score-weighted analysis. *AJR Am J Roentgenol.* 2021;217(3):691-698. doi: 10.2214/AJR.20.24117 Accessed 20200930//.

119. Nieuwenhuizen S, Dijkstra M, Puijk RS, et al. Thermal ablation versus stereotactic ablative body radiotherapy to treat unresectable colorectal liver metastases: a comparative analysis from the prospective Amsterdam CORE registry. *Cancers (Basel).* 2021;13(17):26. doi: 10.3390/cancers13174303.

120. Oladeru OT, Miccio JA, Yang J, Xue Y, Ryu S, Stessin AM. Conformal external beam radiation or selective internal radiation therapy-a comparison of treatment outcomes for hepatocellular carcinoma. *J Gastrointest Oncol.* 2016;7(3):433-440. doi: 10.21037/jgo.2015.10.04.

121. Parikh ND, Marshall VD, Green M, et al. Effectiveness and cost of radiofrequency ablation and stereotactic body radiotherapy for treatment of early-stage hepatocellular carcinoma: An analysis of SEER-medicare. *J Med Imaging Radiat Oncol.* 2018;62(5):673-681. doi: 10.1111/1754-9485.12754.

122. Rajyaguru DJ, Borgert AJ, Smith AL, et al. Radiofrequency ablation versus stereotactic body radiotherapy for localized hepatocellular carcinoma in nonsurgically managed patients: analysis of the National Cancer Database. *J Clin Oncol.* 2018;36(6):600-608. doi: 10.1200/JCO.2017.75.3228.

123. Sapisochin G, Barry A, Doherty M, et al. Stereotactic body radiotherapy vs. TACE or RFA as a bridge to transplant in patients with hepatocellular carcinoma. an intention-to-treat analysis. *J Hepatol.* 2017;67(1):92-99. doi: 10.1016/j.jhep.2017.02.022.

124. Sebastian NT, Tan Y, Miller ED, Williams TM, Alexandra Diaz D. Stereotactic body radiation therapy is associated with improved overall survival compared to chemoradiation or radioembolization in the treatment of unresectable intrahepatic cholangiocarcinoma. *Clin Transl Radiat Oncol.* 2019;19:66-71. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=pmnm4&NEWS=N&AN=31517072 Accessed 20190726//.

125. Stintzing S, Einem JV, Fueweger C, Haidenberger A, Fedorov M, Muavcevic A. Long-term survival in patients treated with a robotic radiosurgical device for liver metastases. *Cancer Res Treat.* 2019;51(1):187-193. doi: 10.4143/crt.2017.594.

126. Voglhuber T, Eitz KA, Oechsner M, Vogel MME, Combs SE. Analysis of using high-precision radiotherapy in the treatment of liver metastases regarding toxicity and survival. *BMC cancer.* 2021;21(1):780. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=medl&NEWS=N&AN=34229642 Accessed 20210706//.

127. Wahl DR, Stenmark MH, Tao Y, et al. Outcomes after stereotactic body radiotherapy or radiofrequency ablation for hepatocellular carcinoma. *J Clin Oncol.* 2016;34(5):452-459. doi: 10.1200/JCO.2015.61.4925.

128. Wang F, Numata K, Takeda A, et al. Safety and efficacy study: short-term application of radiofrequency ablation and stereotactic body radiotherapy for Barcelona Clinical Liver Cancer stage 0-B1 hepatocellular carcinoma. *PLoS One.* 2021;16(1):e0245076. doi: 10.1371/journal.pone.0245076 Accessed 20210105//.

129. Wong TC, Chiang CL, Lee AS, et al. Better survival after stereotactic body radiation therapy following transarterial chemoembolization in nonresectable hepatocellular carcinoma: a propensity score matched analysis. *Surg Oncol*. 2019;28:228-235. doi: 10.1016/j.suronc.2019.01.006 Accessed 20190129//.

130. Wong TC, Lee VH, Law AL, et al. Prospective study of stereotactic body radiation therapy for hepatocellular carcinoma on waitlist for liver transplant. *Hepatology*. 2021;74(5):2580-2594. doi: 10.1002/hep.31992 Accessed 20210930//.

131. Bouman-Wammes EW, van Dodewaard-De Jong JM, Dahele M, et al. Benefits of using stereotactic body radiotherapy in patients with metachronous oligometastases of hormone-sensitive prostate cancer detected by [18F]fluoromethylcholine PET/CT. *Clin Genitourin Cancer*. 2017;15(5):e773-e782. doi: 10.1016/j.clgc.2017.03.009.

132. Bowden P, See AW, Frydenberg M, et al. Fractionated stereotactic body radiotherapy for up to five prostate cancer oligometastases: interim outcomes of a prospective clinical trial. *Int J Cancer*. 2020;146(1):161-168. doi: 10.1002/ijc.32509.

133. Chalkidou A, Macmillan T, Grzeda MT, et al. Stereotactic ablative body radiotherapy in patients with oligometastatic cancers: a prospective, registry-based, single-arm, observational, evaluation study. *Lancet Oncol*. 2021;22(1):98-106. doi: 10.1016/S1470-2045(20)30537-4.

134. De Bleser E, Jereczek-Fossa BA, Pasquier D, et al. Metastasis-directed therapy in treating nodal oligorecurrent prostate cancer: a multi-institutional analysis comparing the outcome and toxicity of stereotactic body radiotherapy and elective nodal radiotherapy. *Eur Urol*. 2019. https://www.cochranelibrary.com/central/doi/10.1002/central/CN-01964903/full.

135. Franzese C, Marvaso G, Francolini G, et al. The role of stereotactic body radiation therapy and its integration with systemic therapies in metastatic kidney cancer: a multicenter study on behalf of the AIRO (Italian Association of Radiotherapy and Clinical Oncology) genitourinary study group. *Clin Exp Metastasis*. 2021;38(6):527-537. doi: 10.1007/s10585-021-10131-w Accessed 20211108//.

136. Hurmuz P, Onal C, Ozyigit G, et al. Treatment outcomes of metastasis-directed treatment using (68)Ga-PSMA-PET/CT for oligometastatic or oligorecurrent prostate cancer: Turkish Society for Radiation Oncology group study (TROD 09-002). *Strahlenther Onkol*. 2020;196(11):1034-1043. doi: 10.1007/s00066-020-01660-6.

137. Macchia G, Lazzari R, Colombo N, et al. A large, multicenter, retrospective study on efficacy and safety of stereotactic body radiotherapy (SBRT) in oligometastatic ovarian cancer (MITO RT1 Study): a collaboration of MITO, AIRO GYN, and MaNGO groups. *Oncologist*. 2020;25(2):e311-e320. doi: 10.1634/theoncologist.2019-0309.

138. Milano MT, Katz AW, Muhs AG, et al. A prospective pilot study of curative-intent stereotactic body radiation therapy in patients with 5 or fewer oligometastatic lesions. *Cancer.* 2008;112(3):650-658. doi: 10.1002/cncr.23209.

139. Milano MT, Katz AW, Zhang H, Okunieff P. Oligometastases treated with stereotactic body radiotherapy: long-term follow-up of prospective study. *Int J Radiat Oncol Biol Phys.* 2012;83(3):878-886. doi: 10.1016/j.ijrobp.2011.08.036.

140. Nicosia L, Franzese C, Mazzola R, et al. Recurrence pattern of stereotactic body radiotherapy in oligometastatic prostate cancer: a multi-institutional analysis. *Strahlenther Onkol.* 2020;196(3):213-221. doi: 10.1007/s00066-019-01523-9.

141. Olson R, Jiang W, Liu M, et al. Treatment with stereotactic ablative radiotherapy for up to 5 oligometastases in patients with cancer: primary toxic effect results of the nonrandomized phase 2 SABR-5 clinical trial. *JAMA Oncol.* 2022;8(11):1644-1650. doi: 10.1001/jamaoncol.2022.4394.

142. Ost P, Jereczek-Fossa BA, As NV, et al. Progression-free survival following stereotactic body radiotherapy for oligometastatic prostate cancer treatment-naive recurrence: a multi-institutional analysis. *Eur Urol.* 2016;69(1):9-12. doi: 10.1016/j.eururo.2015.07.004.

143. Poon I, Erler D, Dagan R, et al. Evaluation of definitive stereotactic body radiotherapy and outcomes in adults with extracranial oligometastasis. *JAMA Netw Open.* 2020;3(11):e2026312. doi: 10.1001/jamanetworkopen.2020.26312.

144. Sogono P, Bressel M, David S, et al. Safety, efficacy, and patterns of failure after single-fraction stereotactic body radiation therapy (SBRT) for oligometastases. *Int J Radiat Oncol Biol Phys.* 2021;109(3):756-763. doi: 10.1016/j.ijrobp.2020.10.011 Accessed 20201015//.

145. Sutera P, Clump DA, Kalash R, et al. Initial results of a multicenter phase 2 trial of stereotactic ablative radiation therapy for oligometastatic cancer. *Int J Radiat Oncol Biol Phys.* 2019;103(1):116-122. doi: 10.1016/j.ijrobp.2018.08.027 Accessed 20180825//.

146. Triggiani L, Alongi F, Buglione M, et al. Efficacy of stereotactic body radiotherapy in oligorecurrent and in oligoprogressive prostate cancer: new evidence from a multicentric study. *Br J Cancer.* 2017;116(12):1520-1525. doi: 10.1038/bjc.2017.103.

147. Franzese C, Nicosia L, Facondo G, et al. Stereotactic body radiation therapy for adrenal gland metastases: outcome and predictive factors from a multicenter analysis. *Clin Exp Metastasis.* 2021;38(6):511-518. doi: 10.1007/s10585-021-10124-9.

148. Grozman V, Onjukka E, Wersall P, et al. Extending hypofractionated stereotactic body radiotherapy to tumours larger than 70cc - effects and side effects. *Acta oncologica (Stockholm, Sweden).* 2021;60(3):305-311.

http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=medl&NEWS=N&AN=33448899 Accessed 20210115//.

149. McCammon R, Schefter TE, Gaspar LE, Zaemisch R, Gravdahl D, Kavanagh B. Observation of a dose-control relationship for lung and liver tumors after stereotactic body radiation therapy. *Int J Radiat Oncol Biol Phys.* 2009;73(1):112-118. doi: 10.1016/j.ijrobp.2008.03.062.

150. Yoon SM, Luterstein E, Chu FI, et al. Clinical outcomes of stereotactic magnetic resonance image-guided adaptive radiotherapy for primary and metastatic tumors in the abdomen and pelvis. *Cancer Med.* 2021;10(17):5897-5906. doi: 10.1002/cam4.4139.

151. Parikh NR, Chang EM, Nickols NG, et al. Cost-Effectiveness of Metastasis-Directed Therapy in Oligorecurrent Hormone-Sensitive Prostate Cancer. *Int J Radiat Oncol Biol Phys.* 2020;108(4):917-926. doi: 10.1016/j.ijrobp.2020.06.009.

152. Kim H, Vargo JA, Ling DC, Beriwal S, Smith KJ. Cost-effectiveness analysis of upfront SBRT for oligometastatic stage IV non-small cell lung cancer based on mutational status. *Am J Clin Oncol.* 2019;42(11):837-844. doi: 10.1097/COC.0000000000000608.

153. Kim H, Vargo JA, Beriwal S, et al. Cost-effectiveness analysis of salvage therapies in locoregional previously irradiated head and neck cancer. *Head Neck.* 2018;40(8):1743-1751. doi: 10.1002/hed.25142.

154. Kumar A, Straka C, Courtney PT, Vitzthum L, Riviere P, Murphy JD. Cost-effectiveness analysis of stereotactic ablative radiation therapy in patients with oligometastatic cancer. *Int J Radiat Oncol Biol Phys.* 2021;109(5):1185-1194. doi: 10.1016/j.ijrobp.2020.09.045.

155. Mehrens D, Unterrainer M, Corradini S, et al. Cost-effectiveness analysis of local treatment in oligometastatic disease. *Front Oncol.* 2021;11:667993. doi: 10.3389/fonc.2021.667993 Accessed 20210615//.

156. Santos PMG, Lapen K, Zhang Z, et al. Trends in radiation therapy for bone metastases, 2015 to 2017: Choosing Wisely in the era of complex radiation. *Int J Radiat Oncol Biol Phys.* 2021;109(4):923-931. doi: 10.1016/j.ijrobp.2020.11.016.

157. Eastham JA, Auffenberg GB, Barocas DA, et al. Clinically localized prostate cancer: AUA/ASTRO guideline, part I: introduction, risk assessment, staging, and risk-based management. *J Urol.* 2022;208(1):10-18. doi: 10.1097/JU.0000000000002757.

158. Eastham JA, Auffenberg GB, Barocas DA, et al. Clinically Localized Prostate Cancer: AUA/ASTRO guideline, part II: principles of active surveillance, principles of surgery, and follow-up. *J Urol.* 2022;208(1):19-25. doi: 10.1097/JU.0000000000002758.

159. Eastham JA, Auffenberg GB, Barocas DA, et al. Clinically Localized Prostate Cancer: AUA/ASTRO guideline. part III: principles of radiation and future directions. *J Urol.* 2022;208(1):26-33. doi: 10.1097/JU.0000000000002759.

160. European Association of Urology Prostate Cancer Guidelines Panel. EAU - EANM - ESTRO - ESUR - ISUP - SIOG guidelines on prostate cancer. 2022; https://uroweb.org/guidelines/prostate-cancer. Accessed December 29, 2022.

161. Lieng H, Hayden AJ, Christie DRH, et al. Radiotherapy for recurrent prostate cancer: 2018 recommendations of the Australian and New Zealand radiation oncology genito-urinary group. *Radiother Oncol.* 2018;129(2):377-386. doi: 10.1016/j.radonc.2018.06.027.

162. Daly ME, Ismaila N, Decker RH, et al. Radiation therapy for small-cell lung cancer: ASCO guideline endorsement of an ASTRO guideline. *J Clin Oncol.* 2021;39(8):931-939. doi: 10.1200/JCO.20.03364 Accessed 2022/12/29.

163. Genshaft SJ, Suh RD, Abtin F, et al. Society of Interventional Radiology multidisciplinary position statement on percutaneous ablation of non-small cell lung cancer and metastatic disease to the lungs: endorsed by the Canadian Association for Interventional Radiology, the Cardiovascular and Interventional Radiological Society of Europe, and the Society of Interventional Oncology. *J Vasc Interv Radiol.* 2021;32(8):1241 e1241-1241 e1212. doi: 10.1016/j.jvir.2021.04.024 Accessed 2022/12/29.

164. Planchard D, Popat S, Kerr K, et al. Metastatic non-small cell lung cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Ann Oncol.* 2018;29(Suppl 4):iv192-iv237. doi: 10.1093/annonc/mdy275.

165. European Society for Medical Oncology. Metastatic non-small-cell lung cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up 2020 update. 2020; https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer. Accessed December 29, 2020.

166. National Institute for Health and Care Excellence. Lung cancer: diagnosis and management [NG122]. *NICE guideline [NG122]* 2018; https://www.nice.org.uk/guidance/ng122/resources/lung-cancer-diagnosis-and-management-pdf-66141655525573. Accessed December 29, 2022.

167. Morris VK, Kennedy EB, Baxter NN, et al. Treatment of metastatic colorectal cancer: ASCO guideline. *J Clin Oncol.* 2023;41(3):678-700. doi: 10.1200/JCO.22.01690 Accessed 2022/12/29.

168. Cervantes A, Adam R, Rosello S, et al. Metastatic colorectal cancer: ESMO clinical practice guideline for diagnosis, treatment and follow-up. *Ann Oncol.* 2023;34(1):10-32. doi: 10.1016/j.annonc.2022.10.003 Accessed 2022/12/29.

169. National Institute for Health and Care Excellence. Colorectal cancer [NG151]. *NICE Guideline [NG151]* 2021; https://www.nice.org.uk/guidance/ng151/resources/colorectal-cancer-pdf-66141835244485. Accessed December 29, 2022.

170. Cibula D, Potter R, Planchamp F, et al. The European Society of Gynaecological Oncology/European Society for Radiotherapy and Oncology/European Society of Pathology guidelines for the management of patients with cervical cancer. *Virchows Arch.* 2018;472(6):919-936. doi: 10.1007/s00428-018-2362-9.

171. Concin N, Matias-Guiu X, Vergote I, et al. ESGO/ESTRO/ESP guidelines for the management of patients with endometrial carcinoma. *Int J Gynecol Cancer.* 2021;31(1):12-39. doi: 10.1136/ijgc-2020-002230.

172. Michielin O, van Akkooi ACJ, Ascierto PA, Dummer R, Keilholz U, Esmo Guidelines Committee. Cutaneous melanoma: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Ann Oncol.* 2019;30(12):1884-1901. doi: 10.1093/annonc/mdz411.

173. Motzer RJ, Jonasch E, Agarwal N, et al. Kidney cancer, version 3.2022, NCCN clinical practice guidelines in oncology. *J Natl Compr Canc Netw.* 2022;20(1):71-90. doi: 10.6004/jnccn.2022.0001.

174. European Association of Urology Renal Cell Cancer Guidelines Panel. EAU guidelines on renal cell carcinoma. 2022; https://uroweb.org/guidelines/renal-cell-carcinoma. Accessed December 29, 2022.

175. Campbell SC, Clark PE, Chang SS, Karam JA, Souter L, Uzzo RG. Renal mass and localized renal cancer: evaluation, management, and follow-up: AUA guideline: part I. *J Urol.* 2021;206(2):199-208. doi: 10.1097/JU.0000000000001911.

176. Campbell SC, Uzzo RG, Karam JA, Chang SS, Clark PE, Souter L. Renal mass and localized renal cancer: evaluation, management, and follow-up: AUA guideline: part II. *J Urol.* 2021;206(2):209-218. doi: 10.1097/JU.0000000000001912.

177. Escudier B, Porta C, Schmidinger M, et al. Renal cell carcinoma: ESMO clinical practice guidelines for diagnosis, treatment and follow-updagger. *Ann Oncol.* 2019;30(5):706-720. doi: 10.1093/annonc/mdz056.

178. Palta M, Godfrey D, Goodman KA, et al. Radiation therapy for pancreatic cancer: executive summary of an ASTRO clinical practice guideline. *Pract Radiat Oncol.* 2019;9(5):322-332. doi: 10.1016/j.prro.2019.06.016.

179. American College of Radiology. American College of Radiology ACR appropriateness criteria management of liver cancer. 2022; https://acsearch.acr.org/docs/69379/Narrative/. Accessed December 29, 2022.

180. Apisarnthanarax S, Barry A, Cao M, et al. External beam radiation therapy for primary liver cancers: an ASTRO clinical practice guideline. *Pract Radiat Oncol.* 2022;12(1):28-51. doi: 10.1016/j.prro.2021.09.004 Accessed 2022/10/10.

181. Vogel A, Bridgewater J, Edeline J, et al. Biliary tract cancer: ESMO clinical practice guideline for diagnosis, treatment and follow-up. *Ann Oncol.* 2022. doi: 10.1016/j.annonc.2022.10.506 Accessed 2022/12/29.

182. Vogel A, Cervantes A, Chau I, et al. Hepatocellular carcinoma: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Ann Oncol.* 2018;29(Suppl 4):iv238-iv255. doi: 10.1093/annonc/mdy308.

183. Strauss SJ, Frezza AM, Abecassis N, et al. Bone sarcomas: ESMO-EURACAN-GENTURIS-ERN PaedCan clinical practice guideline for diagnosis, treatment and follow-up. *Ann Oncol.* 2021;32(12):1520-1536. doi: 10.1016/j.annonc.2021.08.1995.

184. Lopez-Campos F, Cacicedo J, Counago F, et al. SEOR SBRT-SG stereotactic body radiation therapy consensus guidelines for non-spine bone metastasis. *Clin Transl Oncol.* 2022;24(2):215-226. doi: 10.1007/s12094-021-02695-6.

185. Oldenburg J, Berney DM, Bokemeyer C, et al. Testicular seminoma and non-seminoma: ESMO-EURACAN clinical practice guideline for diagnosis, treatment and follow-up. *Ann Oncol.* 2022;33(4):362-375. doi: 10.1016/j.annonc.2022.01.002 Accessed 2022/12/29.