Washington State Health Care Authority

Health Technology Assessment

Stereotactic Radiosurgery and Stereotactic Body Radiation Therapy

Appendix E. Summary of Findings Table by Malignancy

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Appendix E. Summary of Findings Table by Tumor Type and Location

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About the Center for Evidence-based Policy

The Center for Evidence-based Policy (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 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.

Nature and Purpose of Technology Assessments

This technology assessment report is based on research conducted by a contracted technology assessment center, with updates as contracted by the Washington State Health Care Authority. 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 investigators and authors who are responsible for the content. These findings and conclusions may not necessarily represent the views of the HCA/Agency and thus, no statement in this report shall be construed as an official position or policy of the HCA/Agency.

The information in this assessment is intended to assist health care decision makers, clinicians, patients and policy makers in making sound 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.

Appendix E. Summary of Findings Table by Tumor Type and Location

Introduction

This summary of findings provides an overview of the strength of evidence for the use of SRS and SBRT compared to EBRT. This summary of findings is intended to *supplement* the Washington Health Technology Assessment Program's *Stereotactic Radiosurgery and Stereotactic Body Radiation Therapy* report. The findings presented in this document are in aggregate. For specific details and findings per tumor type and location, please refer to the full report on the WA HTA website.

Strength of Evidence

⊕⊕⊕⊕	**High**: Further research is *very unlikely* to change the estimate of effect and our confidence in that estimate. Typical sets of studies would be large RCTs without serious limitations.
⊕⊕⊕◯	**Moderate**: Further research *may* change the estimate of effect and will *likely* have an important impact on our confidence in the estimate of effect.
⊕⊕◯◯	**Low**: Further research is *likely* to change the estimate and *very likely* to have an important impact on our confidence in the estimate.
⊕◯◯◯	**Very Low**: Any estimate of effect is *very uncertain.*

Outcomes

↔	No Difference
↕	Inconsistent Evidence
↑	Increased
↓	Decreased

Overview

The summary tables provide a detailed summary of the strength and direction of evidence per tumor type and location, comparator, and outcomes. Strength and direction of evidence is only provided for tumor types and locations where there is comparative data (Table 1). For non-comparative data, outcomes are listed without strength or direction of the evidence (Table 2).

Table 1. Tumor Types and Locations with Comparative Evidence

Procedure		Strength of Evidence[1]		
Malignancy Comparator	**# of SRs (# included studies in SRs), # of subsequently published studies**	⊕⊕⊕◯ **Moderate**	⊕⊕◯◯ **Low**	⊕◯◯◯ **Very Low**
CNS – Brain Metastases	7 SRs[2], 12 cohorts, 25 case series			
SRS+WBRT vs WBRT				
KQ # 1 Efficacy	3 SRs (3 RCTs), 1 cohort			
		↔ OS ↑ Local tumor control		
KQ # 2 Harms				
		↔ Acute and late toxicities		
KQ # 3 Subpopulations: *Single brain metastases and RPA Class 1*				
			↑ Median survival ↑ Local tumor control ↓Worsened performance status(at 6 months)	
KQ # 4 Cost and Cost-Effectiveness				
No studies on cost or cost-effectiveness identified.				
SRS+WBRT vs SRS				
KQ # 1 Efficacy	2 SRs (3 RCTs), 4 cohorts			
		↔ OS	↔ QoL	

[1] No procedure had a high strength of evidence, thus this column is not displayed in this table.
[2] Many overlapping individual between SRs, thus total number of individual studies across all SRs is not provided
Outcomes: ↔ No Difference; ↕ Inconsistent Evidence; ↑ Increased; ↓ Decreased
Abbreviations: OS – overall survival; PFS – progression free survival; QoL – quality of life; EBRT – external beam radiation therapy; WBRT – whole brain radiation therapy; GI – gastrointestinal; GU – gastrourinary

Procedure		Strength of Evidence[1]		
Malignancy Comparator	**# of SRs (# included studies in SRs), # of subsequently published studies**	⊕⊕⊕◯ **Moderate**	⊕⊕◯◯ **Low**	⊕◯◯◯ **Very Low**
		↑ Local tumor control ↑ Distant tumor control	↔ Functional independence ↔ Time to worsened performance status	
KQ # 2 Harms				
			↔ Acute and late toxicities	
KQ # 3 Subpopulations				
No studies on subpopulations identified.				
KQ # 4 Cost and Cost-Effectiveness				
No studies on cost or cost-effectiveness identified.				
SRS vs WBRT				
KQ # 1 Efficacy	1 SR (6 cohorts), 1 cohort			
				↑ OS
KQ # 2 Harms				
			↔ Toxicities	
KQ # 3 Subpopulations				
No studies on subpopulations identified.				
KQ # 4 Cost and Cost-Effectiveness				
WBRT alone				SRS is more cost-effective than WBRT alone or combined with SRS

Outcomes: ↔ No Difference; ↕ Inconsistent Evidence; ↑ Increased; ↓ Decreased
Abbreviations: OS – overall survival; PFS – progression free survival; QoL – quality of life; EBRT – external beam radiation therapy; WBRT – whole brain radiation therapy; GI – gastrointestinal; GU – gastrourinary

Procedure		Strength of Evidence[1]		
Malignancy Comparator	**# of SRs (# included studies in SRs), # of subsequently published studies**	⊕⊕⊕◯ **Moderate**	⊕⊕◯◯ **Low**	⊕◯◯◯ **Very Low**
SRS for recurrent or progressive brain metastases				
KQ # 1 Efficacy	1 SR (12 case series)			
			↕ OS ↕ Local tumor control	
KQ # 2 Harms				
			↕ Harms	
KQ # 3 Subpopulations				
No studies on subpopulations identified.				
KQ # 4 Cost and Cost-Effectiveness				
No studies on cost or cost-effectiveness identified.				
CNS – Glioblastoma multiforme	1 RCT, 2 cohorts, 3 case series			
KQ # 1 Efficacy	1 RCT, 2 cohorts, 1 case series			
EBRT			↔ Survival	
KQ #2 Harms	1 RCT, 1 cohort, 3 case series			
EBRT			↑ Symptomatic radionecrosis	
KQ #3 Subgroups				
No studies on subpopulations identified.				
KQ #4 Cost and Cost-Effectiveness				
No studies on costs or cost-effectiveness identified.				
CNS – Glioma	1 cohort, 8 case series			
KQ # 1 Efficacy	1 cohort			
EBRT				↕ Median survival

Outcomes: ↔ No Difference; ↕ Inconsistent Evidence; ↑ Increased; ↓ Decreased

Abbreviations: OS – overall survival; PFS – progression free survival; QoL – quality of life; EBRT – external beam radiation therapy; WBRT – whole brain radiation therapy; GI – gastrointestinal; GU – gastrourinary

Procedure		Strength of Evidence[1]		
Malignancy Comparator	**# of SRs (# included studies in SRs), # of subsequently published studies**	⊕⊕⊕◯ **Moderate**	⊕⊕◯◯ **Low**	⊕◯◯◯ **Very Low**
KQ #2 Harms	1 cohort, 8 case series			
No comparator				Radiation necrosis
KQ #3 Subgroups: *Pediatric patients*				
No comparator				OS, PFS, Moya Moya syndrome
KQ #4 Cost and Cost-Effectiveness				
No studies on costs or cost-effectiveness identified.				
CNS – Pituitary Adenoma	2 cohort studies, 13 case series			
KQ # 1 Efficacy	2 cohort studies			
EBRT			↔ OS ↔ Local tumor control	
KQ #2 Harms	2 cohort studies, 13 case series			
EBRT				↓ New hypopituitarism
No comparator				Headache, nausea, fatigue, edema, visual deficits, cranial nerve palsies
KQ #3 Subgroups				
No studies on subpopulations identified.				
KQ #4 Cost and Cost-Effectiveness				
No studies on costs or cost-effectiveness identified.				
Head and Neck Cancers	1 cohort, 6 case series			
KQ # 1 Efficacy	1 cohort			
EBRT				↔ Patient survival ↔ Local tumor control

Outcomes: ↔ No Difference; ↕ Inconsistent Evidence; ↑ Increased; ↓ Decreased
Abbreviations: OS – overall survival; PFS – progression free survival; QoL – quality of life; EBRT – external beam radiation therapy; WBRT – whole brain radiation therapy; GI – gastrointestinal; GU – gastrourinary

Procedure		Strength of Evidence[1]		
Malignancy Comparator	**# of SRs (# included studies in SRs), # of subsequently published studies**	⊕⊕⊕◯ **Moderate**	⊕⊕◯◯ **Low**	⊕◯◯◯ **Very Low**
KQ #2 Harms	1 cohort, 6 case series			
EBRT				↓ Harms (nasopharyngeal carcinoma, head and neck squamous cell carcinoma) cranial neuropathy, carotid blow-out, brain necrosis, mortality, leucopenia, anemia, thrombocytopenia, mucositis, nausea, vomiting, weight loss, skin reactions, massive nasal bleeding, transient facial numbness, retinopathy, carotid aneurysm, xerostomia, pain, dysgeusia, dysphagia, fibrosis, trimus
KQ #3 Subgroups				
No studies on subpopulations identified.				
KQ #4 Cost and Cost-Effectiveness				
No studies on cost or cost-effectiveness identified.				
Lung Cancer	1 SR (35 case series), 33 case series, 3 economic analyses			
KQ # 1 Efficacy	1 SR (35 case series), 33 case series			
No comparator				3-yr OS, local control
KQ #2 Harms	1 SR (35 case series), 33 case series			
No comparator				Fatigue, general malaise,

Outcomes: ↔ No Difference; ↕ Inconsistent Evidence; ↑ Increased; ↓ Decreased
Abbreviations: OS – overall survival; PFS – progression free survival; QoL – quality of life; EBRT – external beam radiation therapy; WBRT – whole brain radiation therapy; GI – gastrointestinal; GU – gastrourinary

Procedure		Strength of Evidence[1]		
Malignancy Comparator	**# of SRs (# included studies in SRs), # of subsequently published studies**	⊕⊕⊕◯ **Moderate**	⊕⊕◯◯ **Low**	⊕◯◯◯ **Very Low**
				pneumonitis, esophagitis, dermatitis, chest wall pain
KQ #3 Subgroups				
No studies on subpopulations identified.				
KQ #4 Cost and Cost-Effectiveness	3 economic analyses			
EBRT				↕ cost, cost-effectiveness

Outcomes: ↔ No Difference; ↕ Inconsistent Evidence; ↑ Increased; ↓ Decreased
Abbreviations: OS – overall survival; PFS – progression free survival; QoL – quality of life; EBRT – external beam radiation therapy; WBRT – whole brain radiation therapy; GI – gastrointestinal; GU – gastrourinary

Table 2. Tumor Types and Locations with Non-Comparative Evidence

Procedure		Strength of Evidence[3]		
Malignancy Comparator	**# of SRs (# included studies in SRs), # of subsequently published studies**	⊕⊕⊕◯ **Moderate**	⊕⊕◯◯ **Low**	⊕◯◯◯ **Very Low**
Abdomen – Adrenal Metastases	2 case series			
KQ # 1 Efficacy	2 case series			
No comparator[4]				1-yr actuarial survival, 2-yr actuarial survival, local control
KQ # 2 Harms	2 case series			
No comparator				Fatigue, nausea, adrenal insufficiency
KQ # 3 Subpopulations				
No studies on subpopulations identified.				
KQ # 4 Cost and Cost-Effectiveness				
No studies on costs or cost-effectiveness identified.				
Abdomen – Colorectal Cancer	2 case series			
KQ # 1 Efficacy				
No studies on efficacy identified.				
KQ # 2 Harms	2 case series			
No comparator				hepaticfailure, duodenal ulceration, colonic ulceration, pain , nausea, diarrhea, skin effects

[3] No procedure had a high strength of evidence, thus this column is not displayed in this table.
[4] Due to lack of comparative data, no directionality can be given for outcomes
Outcomes: ↔ No Difference; ↕ Inconsistent Evidence; ↑ Increased; ↓ Decreased
Abbreviations: OS – overall survival; PFS – progression free survival; QoL – quality of life; EBRT – external beam radiation therapy; WBRT – whole brain radiation therapy; GI – gastrointestinal; GU – gastrourinary

Procedure		Strength of Evidence[3]		
Malignancy Comparator	**# of SRs (# included studies in SRs), # of subsequently published studies**	⊕⊕⊕◯ **Moderate**	⊕⊕◯◯ **Low**	⊕◯◯◯ **Very Low**
KQ # 3 Subpopulations				
No studies on subpopulations identified.				
KQ # 4 Cost and Cost-Effectiveness				
No studies on costs or cost-effectiveness identified.				
Abdomen – Liver Cancer	2 SRs (17 case series), 7 case series			
KQ # 1 Efficacy	2 SRs (17 case series), 7 case series			
No comparator				OS, local control, PFS, QoL
KQ # 2 Harms	2 SRs (17 case series), 7 case series			
No comparator				fatigue, nausea, gastritis, liver enzyme abnormalities, liver toxicity, colonic perforation, small bowel obstruction, death
KQ # 3 Subpopulations				
No studies on subpopulations identified.				
KQ # 4 Cost and Cost-Effectiveness				
No studies on costs or cost-effectiveness identified.				
Abdomen – Pancreatic Cancer	1 SR (6 trials[5]), 4 case series			
KQ # 1 Efficacy	1 SR (6 trials), 4 case series			
No comparator				OS, pain
KQ # 2 Harms	1 SR (6 trials), 4 case series			
No comparator				bowel perforation, mucositis, stomach and bowel ulcerations,

[5] Trials included two pilot trials, two Phase I trials, and two Phase II trials

Outcomes: ↔ No Difference; ↕ Inconsistent Evidence; ↑ Increased; ↓ Decreased

Abbreviations: OS – overall survival; PFS – progression free survival; QoL – quality of life; EBRT – external beam radiation therapy; WBRT – whole brain radiation therapy; GI – gastrointestinal; GU – gastrourinary

Procedure		Strength of Evidence[3]		
Malignancy Comparator	**# of SRs (# included studies in SRs), # of subsequently published studies**	⊕⊕⊕◯ **Moderate**	⊕⊕◯◯ **Low**	⊕◯◯◯ **Very Low**
				nausea, vomiting, ulcers, gastritis, duodenitis, diarrhea, fatigue
KQ # 3 Subpopulations				
No studies on subpopulations identified.				
KQ # 4 Cost and Cost-Effectiveness 1 cost-effectiveness study				
EBRT				SBRT + gemcitabine is more cost-effective than EBRT + gemcitabine
CNS – Astrocytoma	3 case series			
KQ # 1 Efficacy	3 case series			
No comparator				OS, 5-yr survival, median survival
KQ # 2 Harms				
No comparator				neurologic adverse events, hearing loss, tiredness
KQ # 3 Subpopulations				
No studies on subpopulations identified.				
KQ # 4 Cost and Cost-Effectiveness				
No studies on costs or cost-effectiveness identified.				
CNS – Ependymoma	2 case series			
KQ # 1 Efficacy	2 case series			
No comparator				OS
KQ # 2 Harms	2 case series			
No comparator				radiation toxicity, facial paresis

Outcomes: ↔ No Difference; ↕ Inconsistent Evidence; ↑ Increased; ↓ Decreased

Abbreviations: OS – overall survival; PFS – progression free survival; QoL – quality of life; EBRT – external beam radiation therapy; WBRT – whole brain radiation therapy; GI – gastrointestinal; GU – gastrourinary

Procedure		Strength of Evidence[3]		
Malignancy Comparator	**# of SRs (# included studies in SRs), # of subsequently published studies**	⊕⊕⊕◯ **Moderate**	⊕⊕◯◯ **Low**	⊕◯◯◯ **Very Low**
KQ # 3 Subpopulations				
No studies on subpopulations identified.				
KQ # 4 Cost and Cost-Effectiveness				
No studies on costs or cost-effectiveness identified.				
CNS – Meningioma	28 case series, 1 cost analysis			
KQ # 1 Efficacy				
No studies on efficacy identified.				
KQ #2 Harms	28 case series			
No comparator				Erthema/radiodermatitis, alopecia, nausea, post-radiosurgery edema
KQ #3 Subgroups				
No studies on subpopulations identified.				
KQ #4 Cost and Cost-Effectiveness	1 cost analysis			
LINAC radiosurgery versus GammaKnife® Radiosurgery				Costs were slightly higher for LINAC radiosurgery than GKRS
CNS – Multiple CNS Tumors	14 case series			
KQ # 1 Efficacy	14 case series			
No comparator				*Unable to draw any conclusions due to study heterogeneity in tumors, dosing, and reported outcomes and harms.*

Outcomes: ↔ No Difference; ↕ Inconsistent Evidence; ↑ Increased; ↓ Decreased
Abbreviations: OS – overall survival; PFS – progression free survival; QoL – quality of life; EBRT – external beam radiation therapy; WBRT – whole brain radiation therapy; GI – gastrointestinal; GU – gastrourinary

Procedure		Strength of Evidence[3]		
Malignancy Comparator	**# of SRs (# included studies in SRs), # of subsequently published studies**	⊕⊕⊕◯ **Moderate**	⊕⊕◯◯ **Low**	⊕◯◯◯ **Very Low**
KQ #2 Harms	14 case series			
No comparator				*Unable to draw any conclusions due to study heterogeneity in tumors, dosing, and reported outcomes and harms.*
KQ #3 Subgroups				
No studies on subpopulations identified.				
KQ #4 Cost and Cost-Effectiveness				
No studies on costs or cost-effectiveness identified.				
CNS – Neurocytoma	1 SR (121 case reports/case series), 1 case series			
KQ # 1 Efficacy	1 SR (121 case reports/case series)			
No comparator				5-yr OS, 5-yr Local tumor control
KQ #2 Harms	1 SR (121 case reports/case series), 1 case series			
No comparator				*SR did not report harms.* *Case series reported no harms found.*
KQ #3 Subgroups				
No studies on subpopulations identified.				
KQ #4 Cost and Cost-Effectiveness				
No studies on costs or cost-effectiveness identified.				

Outcomes: ↔ No Difference; ↕ Inconsistent Evidence; ↑ Increased; ↓ Decreased
Abbreviations: OS – overall survival; PFS – progression free survival; QoL – quality of life; EBRT – external beam radiation therapy; WBRT – whole brain radiation therapy; GI – gastrointestinal; GU – gastrourinary

Procedure		Strength of Evidence[3]		
Malignancy Comparator	**# of SRs (# included studies in SRs), # of subsequently published studies**	⊕⊕⊕◯ **Moderate**	⊕⊕◯◯ **Low**	⊕◯◯◯ **Very Low**
CNS – Schwannoma	1 SR, 36 case series			
KQ # 1 Efficacy	2 case series			
No comparator				Local control, hearing preservation
KQ #2 Harms	1 SR, 36 case series			
No comparator				Hearing loss, hydrocephalus requiring a shunt, new malignancies, new cranial nerve neuropathies
KQ #3 Subgroups – Neurofibromatosis, Large Vestibular Schwannoma	3 case series			
No Comparator				Pts with neurofibromatosis may have worse outcomes than pts without neurofibromatosis
KQ #4 Cost and Cost-Effectiveness				
No studies on costs or cost-effectiveness identified.				
Head and Neck – Glomus Jugulare	1 SR (19 case series)			
KQ # 1 Efficacy				
No studies on efficacy identified.				
KQ #2 Harms	1 SR (19 case series)			
No comparator				Transient (e.g., dysphagia,nausea, imbalance) toxicities, servere toxicities

Outcomes: ↔ No Difference; ↕ Inconsistent Evidence; ↑ Increased; ↓ Decreased
Abbreviations: OS – overall survival; PFS – progression free survival; QoL – quality of life; EBRT – external beam radiation therapy; WBRT – whole brain radiation therapy; GI – gastrointestinal; GU – gastrourinary

Procedure		Strength of Evidence[3]		
Malignancy Comparator	**# of SRs (# included studies in SRs), # of subsequently published studies**	⊕⊕⊕◯ **Moderate**	⊕⊕◯◯ **Low**	⊕◯◯◯ **Very Low**
				(hearing loss, vertigo, facial palsy)
KQ #3 Subgroups				
No studies on subpopulations identified.				
KQ #4 Cost and Cost-Effectiveness				
No studies on cost or cost-effectiveness identified.				
Head and Neck – Ocular Cancer	7 case series			
KQ # 1 Efficacy				
No studies on efficacy identified.				
KQ #2 Harms	7 case series			
No comparator				Dry eye syndrome, retinopathy, optic neuropathy, neovascular glaucoma, cataracts
KQ #3 Subgroups				
No studies on subpopulations identified.				
KQ #4 Cost and Cost-Effectiveness				
No studies on costs or cost-effectiveness identified.				
Prostate Cancer	4 case series			
KQ # 1 Efficacy				
No studies on efficacy identified.				
KQ #2 Harms	4 case series			
No comparator				QoL, sexual QoL, GU toxicities, GI toxicities
KQ #3 Subgroups				
No studies on subpopulations identified.				

Outcomes: ↔ No Difference; ↕ Inconsistent Evidence; ↑ Increased; ↓ Decreased

Abbreviations: OS – overall survival; PFS – progression free survival; QoL – quality of life; EBRT – external beam radiation therapy; WBRT – whole brain radiation therapy; GI – gastrointestinal; GU – gastrourinary

Procedure		Strength of Evidence[3]		
Malignancy Comparator	**# of SRs (# included studies in SRs), # of subsequently published studies**	⊕⊕⊕◯ **Moderate**	⊕⊕◯◯ **Low**	⊕◯◯◯ **Very Low**
KQ #4 Cost and Cost-Effectiveness				
No studies on cost or cost-effectiveness identified.				
Spine	1 SR (29 case series), 13 case series, 1 economic study			
KQ # 1 Efficacy	1 SR (29 case series), 11 case series			
No comparator				Local tumor control, median survival, pain control, QoL
KQ #2 Harms	1 SR (29 case series), 13 case series			
No comparator				Fatigue, nausea, esophagitis, mucositis, dysphagia, spinal fractures, lumbar plexopathy, paraparesis, myelopathy
KQ #3 Subgroups				
No studies on subpopulations identified.				
KQ #4 Cost and Cost Effectiveness	1 economic study			
EBRT				SBRT costs > EBRT costs
Multiple Tumor Sites	4 case series			
KQ # 1 Efficacy	4 case series			
No comparator				Local control
KQ #2 Harms	4 case series			
No comparator				Nausea, fatigue, skin irritation, pleural and pericardial effusion, gastric bleeding, vertebral

Outcomes: ↔ No Difference; ↕ Inconsistent Evidence; ↑ Increased; ↓ Decreased
Abbreviations: OS – overall survival; PFS – progression free survival; QoL – quality of life; EBRT – external beam radiation therapy; WBRT – whole brain radiation therapy; GI – gastrointestinal; GU – gastrourinary

Procedure		Strength of Evidence[3]		
Malignancy Comparator	**# of SRs (# included studies in SRs), # of subsequently published studies**	⊕⊕⊕◯ **Moderate**	⊕⊕◯◯ **Low**	⊕◯◯◯ **Very Low**
				fractures
KQ #3 Subgroups				
No studies on subpopulations identified.				
KQ #4 Cost and Cost Effectiveness				
No studies on costs or cost-effectiveness identified.				

Outcomes: ↔ No Difference; ↕ Inconsistent Evidence; ↑ Increased; ↓ Decreased
Abbreviations: OS – overall survival; PFS – progression free survival; QoL – quality of life; EBRT – external beam radiation therapy; WBRT – whole brain radiation therapy; GI – gastrointestinal; GU – gastrourinary