Washington State Health Care Authority

Use of Stereotactic Body Radiation Therapy

Draft Key Questions: Public Comment and Response

September 9, 2022

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Use of Stereotactic Body Radiation Therapy

Draft Key Questions

Public Comment and Response

Provided by:

Center for Evidence-based Policy
Oregon Health & Science University

September 9, 2022

Responses to Public Comment on Draft Key Questions

The Center for Evidence-based Policy is an independent vendor contracted to produce evidence assessment reports for the Washington Health Technology Assessment (HTA) program. For transparency, all comments received during the public comment periods are included in this response document. Comments related to program decisions, process, or other matters not pertaining to the evidence report are acknowledged through inclusion only.

Draft key question document comments received:

- David Kantorowitz, MD, PhD
- Mack Roach III, MD

Specific responses pertaining to submitted comments are shown in Table 1.

Table 1. Responses to Comments on Draft Key Questions for Stereotactic Body Radiation Therapy

Comments		Response
Commenter: David Kantorowitz, MD, PhD		
General Comments:		
Dear Sir or Madame, I am employed by Regence doing determinations regarding medical necessity for Radiation Oncology Cases. As Regence manages HTCC insurance cases, I have had the opportunity to make such determinations regarding 3 HTCC policies. Such policies differ substantially from the Regence policies. It always strikes me as wrong that what care is permitted to patients differs based upon what insurance they have. In that vein I offer for your consideration the following suggestions for changes in the 3 HTCC Rad Onc policies. *[See specific comments below]* Many thanks for listening.		Thank you for your comments. Please see detailed responses to specific points below.
Specific Comments:		
Scope	1. HTCC 20121116A Stereotactic Radiation Surgery (SRS) and Stereotactic Body Radiation Therapy (SBRT) - As you know SRS refers to radiosurgery given in 1 treatment or "fraction." SBRT, by convention, is the exact same process but treatment is given in 2-5 fractions. Otherwise there is no difference. As regards CNS tumors, HTCC only covers CNS tumors if treated via SRS but not via SBRT. Perhaps this was the 2012 standard, but today many such tumors are treated not via SRS but via SBRT, which appears to be then safer. This is especially true for larger target volumes or overlap/proximity to previously irradiated regions. My suggestion is that you edit the policy so that all subsections make no differentiation between SRS and SBRT. If it is appropriate to use radiosurgery, then it is appropriate to either treat in 1 fraction (SRS) or 2-5 (SBRT). Leave the decision up to providers.	Thank you for your comment. In this Key Questions document and the coverage criteria, SRS is used to describe radiosurgery delivered in fewer than 10 fractions to CNS tumors. The number of fractions is not used as a factor for coverage decisions.
Cost-Effectiveness Information: Subgroups	I suggest you cover low and intermediate (both favorable and unfavorable subgroups) risk prostate cancer (as NCCN recommends and Regence covers) or, if you wish to be more conservative, cover low and favorable	Thank you for your comment. The role of the committee will be to review the evidence, including cost and cost-effectiveness data, presented to

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	intermediate risk subgroups (as the Blues of CA now does). SBRT will save money compared to 45 IMRT treatments and data for it is excellent. High risk and very high risk subgroups needs more supportive data.	them when drafting the coverage decision. The committee will also consider any evidence identified on the differential effects (benefits or harms) on subgroups of patients, including cancer stage or severity of disease.
Clinical Information: Subgroups	SRS and especially SBRT is widely used to treat lung metastasis if < 5 in number and KPS > 60. Suggest you cover.	Thank you for your comment. The role of the committee will be to review the evidence presented to them when drafting the coverage decision. The committee's prior decision recommends coverage for nonoperable NSCLC stage 1, and for this new review the committee will also consider any evidence identified on the differential effects (benefits or harms) on subgroups of patients, including cancer site and severity of disease, including lung metastases.
Clinical Information: Subgroups	SRS and SBRT is widely and increasingly being used to chase oligometastasis and oligoprogression ... one can reasonably argue that a zeitgeist change has occurred as these formally conceived hopeless situations are now viewed as "treatable" and perhaps, in 10-20% of cases "curable". Supportive data suggests improvement in PFS and OS if all oligo sites can be so ablated. I suggest coverage if a. 1-3 or 1-5 oligo mets, b. primary is controlled or expectation of same, KPS > 60.	Thank you for your comment. The role of the committee will be to review the evidence presented to them when drafting the coverage decision. The committee will also consider any evidence identified on the differential effects (benefits or harms) on subgroups of patients, including cancer site and severity of disease.
Clinical Information: Subgroups	There are other smaller volume subgroups that are commonly treated today with SBRT or SRS and please consider coverage. These include a.AV malformations, b. pancreatic adenocarcinoma, c. craniopharyngiomas, d. treatment resistant epilepsy, e. treatment resistant essential tremor and parkinsons, f. retreatment of head and neck for local recurrence, g. trigeminal neuralgia, h. uveal melanoma,	Thank you for your comment. The focus of this review is on evidence for SBRT in cancers, including pancreatic adenocarcinoma, if evidence meets the eligibility criteria. Currently, retreatment for cancer of the central nervous system is a covered indication.

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Terminology	SRS criteria mandate "evaluation includes multidisciplinary team analysis (e.g. tumor board), including surgical input. This wording creates confusion. Has a patient had above team analysis if first he/she has been seen by a neurosurgeon and then referred to a radiation oncologist who recommends SRS? What if the neurosurgeon says that the tumor is non resectable? Does this satisfy the criteria? What if the neurosurgeon offers both surgery and radiation treatment as viable options and the patient chooses the latter; does this satisfy the criteria? What if the patient has ONLY seen a neurosurgeon and radiation oncologist, in seperate consultations, as is usually the case, but never presented formally to tumor board, and opts for radiation; does this satisfy? These are real life contexts I deal with all the time. Please clarify. If you insist on a tumor board ... fine. Eliminate the e.g. wording as e.g. which means " for example." as this implies that alternative contexts as above satisfy. Clarify what you mean!!	Thank you for your comment. The committee will draft a determination that will be available for public review and comment.
Other Coverage Decisions	HTCC 20190517A Protons: In contrast to the SRS/SBRT policy, which seems to restrictive, the Proton policy seems to me to lax. Esophageal: to my knowledge so far only 1 randomized small phase 2 clinical study has been published i.e. Kim et al. which showed marked decrease in side effects with proton vs IMRT photon treatment. Sounds convincing. Yet when one looks at the details of same, presented in table 2, it seems that the advantage of Protons is limited to very mild side effects i.e. asymptomatic pleural/pericardial effusions and grade 1 pneumonitis. I would suggest that these are modest side effects noticed in academic studies, such as this from MD Anderson, but in clinical daily practice would not even be noticed. There was apparently no difference in serious, high grade, side effects risk between Protons vs IMRT photons; the ones that impair people's lives and kill people. This reality is also suggested by equal survival at 3 years. if	Thank you for your comment.

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	IMRT photons were so much more toxic then, since doses of the two arms were adjusted to result in equal efficacy, one should see better survival with Protons reflecting that Protons kill less folks then IMRT photons. That this was not the case again suggests that the side effect advantage for Protons was the kind that looks good on paper but does not injure/kill patients. I suggest wait till the current phase 3 study data is available.	
Other Coverage Decisions	I suggest you consider coverage in contexts a. intraocular/uveal melanoma I suggest you consider coverage in context of recurrent head and neck but not denovo until phase 3 data is supportive versus IMRT photons	Thank you for your comment.
Other Coverage Decisions	I think frankly the final criteria " other primary cancers where all other treatment options are contraindicated after review by a multidisciplinary tumor board" is an open invitation to abuse. Such tumor boards, by definition, will be tumor boards assembled at institutions/clinics that offer Protons. Such tumor boards, knowing the immense cost of Proton facility operation and how Protons clearly look better dosimetrically on paper than IMRT photons in so many, if not nearly all, clinical contexts will be "inclined" may we say to have a low threshold for advocating Protons in the total or near total absence of supportive clinical outcome studies thus pleasing their Proton colleagues and administrators. This would not be such an issue if abuse of such advocacy was not present and if the cost differential of Protons vs IMRT Photons was not so stark....in a time of limited medical resources for poor people who need basic services. We need to remove this clause and review the clinical outcome literature and limit Proton availability to sites where it has demonstrated clinical value....and not just dosimetric advantage noted by the Proton clinic's tumor boards.	Thank you for your comment.
Other Coverage Decisions	Balancing this commentary, one might consider covering Protons for sites in which multi institutional randomized comparison studies are being done vis a vis IMRT photons	Thank you for your comment.

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	or SRS/SBRT...cheaper forms of treatment and thus let Protons prove itself. The trick here is how do we encourage same, while avoiding Proton facilities setting up comparative studies for every tumor in the body, with little to no chance of actually successfully enacting such studies but solely as a vehicle to get WA state taxpayers to pay for Protons where there is inadequate data? Proton clinics have tried to use enrollment in registry trials as way to justify payment for Protons. This in my view is transparent abuse; we need randomized comparative trials that will lead to something meaningful.	
Other Coverage Decisions	The criteria " to spare critical structures to prevent toxicities within expected life span" need revision. How are providers to prove they meet this criteria ... by commentary in their consultations that this is the case? We need an objective way to operationalize this sentence. I suggest that providers who assert need for IMRT in tumor contexts not to include those in which clinical studies have made its need standard of care, such as Head and Neck and Prostate etc. by meeting two criteria a. they need to send in comparative 3D vs IMRT Color DVHs ovelain on the same graph (so reviewers can compare the lines) which suggest dosimetric advantage for IMRT and b. complete a simple table in which providers need to list any OAR at risk, such as lung, then list a Quantec or RTOG PUBLISHED dose constraint, then what they achieved with 3D planning, then what they achieved with IMRT planning and then answer yes or no.....is the constraint only met via IMRT? Such table is then our proxy measure for whether the dosimetric advantage for IMRT as seen in the DVHs of such magnitude as to really make a clinical difference and thus justified.	Thank you for your comment.
Other Coverage Decisions	I suggest for final criteria where you allow IMRT in the context of pursuing data that you eliminate "registry" and " observational" trials. They rarely lead to any improvements in treatment over time and are open invitations for abuse. It is so easy for any clinic to set up a registry trial for any and all tumors in the body and thus skirt the intention of the HTCC	Thank you for your comment.

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	committee to limit use of more expensive IMRT, versus 3D, to contexts in which supportive clinical data exists or is "at least operationally supported" by the need to submit the comparative DVHs and relate the DVH advantage to a published dose constraint to some OAR.	
Other Coverage Decisions	I suggest you defacto approve IMRT in the following contexts which represent modern standard of care: a. documented prior RT to same PTV, b. pediatric CNS, c. Hippocampal sparing CNS tumors where tumor is >5 mm from the hippocampus, d. anaplastic or locally recurrent thyroid, e. mesothelioma, f. thymic cancer, g. soft tissue sarcomas especially of retroperitoneum, h. pancreas cancer, i. APBI. These are clinical contexts where radiation oncologists in 2022 would be completely hesitant, even approaching violations of the standard of care, to treat with 2D or 3D planning and thus their defacto inclusion would parallel widespread current clinical practice.	Thank you for your comment.

Comments	Response
Commenter: Mack Roach III, MD	
General Comments:	
To whom it may concern: This letter was prepared to promote the formal recognition of SBRT as a highly cost-effective alternative option for men with localized prostate cancer. *[See specific comments below]* As a co-author for American College of Radiology (ACR) Guidelines for more than 15 years and a co-author of National Comprehensive Cancer Network (NCCN) Guidelines for >10 years, I am quite familiar with various prostate cancer guidelines and their limitations. Based on my more than 30 years of experience managing prostate cancer and having published hundreds of papers, book chapters, editorials, and letters, as well as having served on the Advanced Prostate Cancer Consensus Consortia (2017 and 2019), and as the Principal Investigator (PI) for two large phase III randomized trial including nearly 4000 patients and having performed >1500 brachytherapy procedures, I am clearly	Thank you for your comments. Please see detailed responses to specific points below.

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qualified and I challenge anyone to offer a more evidence-based strategy for managing prostate cancer. Thank you for your prompt attention to this matter		
Specific Comments:		
Supporting Evidence	Many single institution, and prospective phase II trials that have shown that SBRT is at least as safe and effective for treating prostate cancer as other forms of radiation therapy. In addition, there are also several systematic reviews and/or meta-analysis and at least three prospective trials including RTOG 0938, HYPO-RT-PC and PACE-B demonstrating that SBRT is both safe and effective (1-3). For example, PACE-B (3) was a Randomized Phase III non-inferiority trial that included 874 men randomized to conventionally delivered external radiotherapy (RT) vs. SBRT. At med. follow-up of 12 weeks, there was no difference in > Grade 2 and higher GI or GU toxicity. At UCSF I use SBRT as an alternative to HDR for boost to the prostate (Chen ... and Roach et al., IJROBP 2021 (4). We performed a propensity-score matched analysis comparing SBRT boost and high-dose-rate (HDR) boost in men treated with pelvic external beam radiation therapy (EBRT). The SBRT boost (21 Gy and 19 Gy in 2 fractions) patients were compared to cohort treated here with HDR brachytherapy boost (19 Gy in 2 fractions). One hundred thirty-one men were treated with SBRT boost and 101 with HDR boost with median follow-up of 73.4 and 186.0 months, respectively. Five- and 10-year unadjusted BCRF was 88.8% and 85.3% for SBRT and 91.8% and 74.6% for HDR boost (log-rank P = .3), and 5- and 10-year unadjusted MF was 91.7% and 84.3% for SBRT and 95.8% and 82.0% for HDR (log-rank P = .8). After adjusting for covariates, there was no statistically significant difference in BCRF (hazard ratio [HR] 0.81; 95% confidence interval [CI], 0.37-1.79; P = .6) or MF (HR 1.07; 95% CI, 0.44-2.57; P = .9) between SBRT and HDR boost. Similarly, after PS matching, there was no statistically significant difference between SBRT and HDR (BCRF: HR 0.66, 0.27-1.62, P = .4; MF: HR 0.84, 0.31-2.26, P = .7). Grade 3+ genitourinary and gastrointestinal toxicity in the SBRT cohort were 4.6% and 1.5%, and 3.0% and 0.0% in the HDR cohorts (P = .4, Fisher exact test). We concluded that SBRT boost plus pelvic EBRT for prostate cancer resulted in similar BCRF and MF to HDR boost in this single institution, PS matched retrospective analysis. Toxicity was modest.	Thank you for your comment. The role of the committee will be to review the evidence presented to them to inform the coverage decision. This will include evidence that meets the prespecified eligibility criteria, including people with prostate cancer. Thank you for these references. We will check each reference included in this comment and summarized in the next comment row against our eligibility criteria.

Comments		Response
Commenter: Mack Roach III, MD		
References	• 1. Lukka HR, Pugh SL, Bruner DW, Bahary JP, Lawton CAF, Efstathiou JA, et al. Patient reported outcomes in NRG Oncology RTOG 0938, evaluating two ultrahypofractionated regimens for prostate cancer. International journal of radiation oncology, biology, physics. 2018. • 2. Widmark A, Gunnlaugsson A, Beckman L, Thellenberg-Karlsson C, Hoyer M, Lagerlund M, 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):385-95. • 3. Brand DH, Tree AC, Ostler P, van der Voet H, Loblaw A, Chu W, et al. Intensitymodulated fractionated radiotherapy versus stereotactic body radiotherapy for prostate cancer (PACE-B): acute toxicity findings from an international, randomised, open-label, phase 3, noninferiority trial. The lancet oncology. 2019;20(11):1531-43. • 4. Chen WC, Li Y, Lazar A, Altun A, Descovich M, Nano T, et al. Stereotactic Body Radiation Therapy and High-Dose-Rate Brachytherapy Boost in Combination With Intensity Modulated Radiation Therapy for Localized Prostate Cancer: A Single-Institution Propensity Score Matched Analysis. International journal of radiation oncology, biology, physics. 2021;110(2):429-37.	Thank you for these references. We will check each reference against our final eligibility criteria.