Washington State Health Care Authority

Health Technology Assessment

Proton Beam Therapy

Draft Report Public Comment & Response

March 31, 2014

Health Technology Assessment Program (HTA)
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Proton Beam Therapy

Draft Report

Public Comment and Response

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Response to Public Comments

The Institute for Clinical and Economic Review (ICER) is an independent vendor contracted to produce evidence assessment reports for the Washington HTA program. For transparency, all comments received during the public comment period are included in this response document. Comments related to program decisions, process, or other matters not pertaining specifically to the draft key questions, project scope, or evidence assessment are acknowledged through inclusion only.

This document responds to comments from the following parties:

Draft Report

- Ramesh Rengan, MD, PhD, Medical Director, Seattle Cancer Care Alliance Proton Therapy, and Nina Mayr, MD, Chair, Department of Radiation Oncology, University of Washington School of Medicine
- Laura I. Thevenot, Chief Executive Officer, American Society for Radiation Oncology (ASTRO)

	Comment	Response
Ramesh Rengan, MD, PhD, Medical Director, Seattle Cancer Care Alliance Proton Therapy, and Nina Mayr, MD, Chair, Department of Radiation Oncology, University of Washington School of Medicine		
1	The report mentions the utter lack of strong clinical data upon which their conclusions are based- and we completely agree on this point. Therefore, we would want to emphasize that this report should truly be a clarion call to gather additional clinical data and that this cannot be achieved without payer partnership. In their position of authority, the HTA should highlight the critical need for payers to develop coverage agreements fro proton beam radiotherapy so that we may obtain the clinical data required to evaluate proton beam radiotherapy.	*Thank you for your comments. This point speaks to a need for ongoing discussions between the HCA and the clinical community rather than a structural or methodological change to the evidence review.*
2	From the standpoint of clinical data, it should also be noted that not all disease sites are candidates for investigation by clinical trial or RCTs. This underscores the importance of data registries that should serve as a complement to (and not a replacement of) clinical trials for disease indications not covered by the clinical trial paradigm.	*We highlight the potential for increased use of registries and other electronic health record-based studies in Section 9 of the report.*
3	From a methodological standpoint, we respectfully disagree with the exclusion of dosimetric comparisons, particularly in the setting of a paucity of clinical data. In the absence of clinical data, the first tool that radiation oncologists have at their disposal to guide clinical practice are dosimetric comparisons. We perform these on a daily basis in order to guide our daily practice (one set of critical organ constraints vs. another, IMRT vs. 3D-CRT, etc.). Although we agree that there are many weaknesses to dosimetric comparisons, it is often an important component of clinical decision-making for our specialty.	*We understand the concerns regarding our exclusion of dosimetric data, particularly in cancer types unlikely to see much in the way of additional collection of comparative data such as pediatric tumors. However, as we note in the report, the uncertainties that remain regarding proton physics and biology make comparisons of simulated outcomes problematic, and would only be addressed through comparisons of actual clinical outcomes. Our approach is consistent with that of other evidence review organizations in this regard.*
Laura I. Thevenot, Chief Executive Officer, American Society for Radiation Oncology (ASTRO)		
1	While PBT is not a new technology, there is a need for clinical evidence development and comparative effectiveness analyses for its use to treat assorted disease sites. Since clinical data is still in the process of being gathered and published, dosimetric comparisons may be helpful in demonstrating potential benefits of PBT for certain indications until additional patient results are available.	*Thank you for your comments. Please see our response to comment 3 on the previous page.*

	Comment	Response
2	For these indications, ASTRO strongly supports acquiring information for PBT under the paradigm of coverage with evidence development (CED) requirements for patients treated on clinical trials or within prospective registries. The role of the payer community in supporting future research is vital in the field of radiation oncology. ASTRO recommends cooperation and the establishment of partnerships between payers and institutions as we believe collecting data in these settings is essential to reaching an informed consensus. Without this support, we fear there will be minimal maturation and refinement of the appropriate clinical scenarios for this potentially valuable technology.	*Please see our response to comment 1 on the previous page.*
3	The technology assessment failed to acknowledge the multiple levels of ongoing efforts to better define the benefits and harms of PBT including numerous institutional registries, randomized controlled studies, and the incorporation of PBT into co-operative group studies. Even though we generally agree with the interpretations of the data, the influx of additional clinical results will require a reevaluation of this topic in the coming years. In the near future, more prospective data with a larger cohort of patients are expected to be released which we hope will better inform the appropriate use of this technology. Furthermore, previously published studies will have had the opportunity to release more data on the long-term benefits and harms of PBT with extended follow-up patient results.	*While it will likely be the case that the evidence will need to be revisited in the future, the focus of this evidence review was on the evidence that is available currently. Major ongoing studies are acknowledged in Section 6 of the report.*
4	In addition, the cost analysis assessment only included the expenses involved in treatment delivery and did not adequately describe the limitations of this cohort of studies. The evaluation did not consider the downstream costs of salvage treatment or caring for acute and late toxicities and complications. As this technology continues to develop with hypofractioned schemes and intensity modulated proton beam therapy (IMPT), the expenses may change. Additional cost comparative data is necessary to make the determination to address key question five.	*The section summarizing previously-published economic studies included several that examined the downstream costs and effects of PBT and alternative treatment options. The budget impact analysis focused on the recent radiation therapy experience at one of the HCA's agencies, and was intended to assess the potential change in annual treatment expenditures that might be experienced with proton beam therapy. Because the HCA dataset was limited, the revised Section 8 also explores the potential change in expenditures using national Medicare payment estimates for therapy, including planning, simulation, and treatment. We agree that further economic study should focus on both immediate and downstream treatment-related costs and effects of PBT and its alternatives, provided there are clinical data to distinguish treatment options for particular cancer types.*

March 10, 2014

Christine Valkyrie Masters
Program Specialist
Health Technology Assessment
Washington State Health Care Authority
P.O. Box 42712
Olympia, WA 98504-2712

BY ELECTRONIC SUBMISSION to shtap@hca.wa.gov

Dear Ms. Masters:

The American Society for Radiation Oncology[1] (ASTRO), appreciates the opportunity to comment on the Washington State Health Care Authority Health Technology Assessment Program Draft Evidence Report on proton beam therapy (PBT), published on February 7, 2014.

Overall, ASTRO agrees with the determination of health benefits as interpreted by current available data. As the report suggested, additional clinical data comparing PBT to other treatments, including various other radiation therapies, is needed to better establish the role of this evolving therapy.

While PBT is not a new technology, there is a need for clinical evidence development and comparative effectiveness analyses for its use to treat assorted disease sites. Since clinical data is still in the process of being gathered and published, dosimetric comparisons may be helpful in demonstrating potential benefits of PBT for certain indications until additional patient results are available. For these indications, ASTRO strongly supports acquiring information for PBT under the paradigm of coverage with evidence development (CED) requirements for patients treated on clinical trials or within prospective registries. The role of the payer community in supporting future research is vital in the field of radiation oncology. ASTRO recommends cooperation and the establishment of partnerships between payers and institutions as we believe collecting data in these settings is essential to reaching an informed consensus. Without this support, we fear there will be minimal maturation and refinement of the appropriate clinical scenarios for this potentially valuable technology.

[1] *ASTRO is the premier radiation oncology society in the world, with more than 10,000 members who are physicians, nurses, biologist, physicists, radiation therapists, dosimetrists and other health care professionals that specialize in treating patients with radiation therapies. As the leading organization in radiation oncology, the Society is dedicated to improving patient care through professional education and training, support for clinical practice and health policy standards, advancement of science and research, and advocacy. ASTRO publishes two medical journals, International Journal of Radiation Oncology, Biology, Physics (www.redjournal.org) and Practical Radiation Oncology (www.practicalradonc.org); developed and maintains an extensive patient website, www.rtanswers.org; and created the Radiation Oncology Institute (www.roinstitute.com), a non-profit foundation to support research and education efforts around the world that enhance and confirm the critical role of radiation therapy in improving cancer treatment. To learn more about ASTRO, visit www.astro.org.*

The technology assessment failed to acknowledge the multiple levels of ongoing efforts to better define the benefits and harms of PBT including numerous institutional registries, randomized controlled studies, and the incorporation of PBT into co-operative group studies. Even though we generally agree with the interpretations of the data, the influx of additional clinical results will require a reevaluation of this topic in the coming years. In the near future, more prospective data with a larger cohort of patients are expected to be released which we hope will better inform the appropriate use of this technology. Furthermore, previously published studies will have had the opportunity to release more data on the long-term benefits and harms of PBT with extended follow-up patient results.

In addition, the cost analysis assessment only included the expenses involved in treatment delivery and did not adequately describe the limitations of this cohort of studies. The evaluation did not consider the downstream costs of salvage treatment or caring for acute and late toxicities and complications. As this technology continues to develop with hypofractioned schemes and intensity modulated proton beam therapy (IMPT), the expenses may change. Additional cost comparative data is necessary to make the determination to address key question five.

In summary, ASTRO agrees that in general, prospective studies and randomized controlled trials are the most reliable way of assessing the efficacy and safety of new technologies. We support accruing these patient results, when feasible, to best determine the benefits and harms associated with treatments. The payer community will need to support these efforts with coverage for evidence development for PBT until enough data is gathered to make an informed decision.

We appreciate your consideration of our comments and look forward to the May 16, 2014 public meeting on this topic.

Sincerely,

Laura I. Thevenot
Chief Executive Officer

UW Medicine
DEPARTMENT OF
RADIATION ONCOLOGY
CANCER CENTER

March 10, 2014

Washington State Health Care Authority
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Re: Technology Assessment of Proton Beam Radiotherapy

Dear Sir/Madam;

We would like to thank the Washington State Health Care Authority for their recent Technological Assessment of Proton Beam Radiotherapy. We have reviewed the published draft report thoroughly and would like to submit the enclosed commentary regarding this review.

We would like to congratulate the HTA on an exhaustive review of proton beam radiotherapy and overall feel that the assessment was well-balanced in its overall analysis and conclusions it drew based upon the review of published clinical data. However, we would like to highlight the following points to consider:

The report mentions on several occasions the utter lack of strong clinical data upon which their conclusions are based- and we completely agree on this point. Therefore, we would want to emphasize that this report should truly be a clarion call to gather additional clinical data and that this **cannot be achieved without payer partnership**. In their position of authority, the HTA should highlight the critical need for payers to develop coverage agreements for proton beam radiotherapy so that we may obtain the clinical data required to evaluate proton beam radiotherapy. This report is supportive of future research, but does not emphasize the central role that the payer must play in order to obtain these data. Indeed, this requires a shift in the traditional mindset of some payers to not pay for treatment that is deemed 'experimental'. Unlike a new drug, where industry support can be used to obtain the clinical data to drive the treatment paradigm, this model cannot be applied to proton beams or other technological advancements.

From the standpoint of clinical data, it should also be noted that not all disease sites are candidates for investigation by clinical trial or RCTs. This underscores the importance of data registries that should serve as a complement to (and not a replacement of) clinical trials for disease indications not covered by the clinical trial paradigm. Again, payers could take a leadership role in helping to fund these registries as they are costly and difficult to support. Despite our best efforts, the oncologic community treats 97% of adult cancer patients outside of the clinical trial mechanism. We strive to do better in the proton community, but it will never be 100%.

From a methodological standpoint, we respectfully disagree with the exclusion of dosimetric comparisons, especially in the setting of a paucity of clinical data. In the absence of clinical data, the

first tool that radiation oncologists have at their disposal to guide clinical practice are dosimetric comparisons. We perform these on a daily basis in order to guide our daily practice (one set of critical organ constraints vs another, IMRT vs 3D-CRT, etc). Although we agree that there are many weaknesses to dosimetric comparisons, it is often an important component of clinical decision making for our specialty and the peer-reviewed literature utilizing dose comparisons should have been included in this report when clinical data was lacking or to augment the existing data. Much of the establishment of protons for pediatric tumors has been initially based upon dosimetric data alone. If these dosimetric data had been not been utilized for this initial assessment, proton therapy's efficacy and reduction of harm in pediatric cancers may not have become established. As such, we feel that proton dosimetric data should have been included in the Washington HTA report.

In summary, we feel that the substance of the review based upon the clinical literature is reasonable. We would just suggest that additional data may have been included to better inform their recommendations and that the language should be modified to emphasize the need for payer partnership and for coverage agreements to be developed in order to obtain the clinical data required to determine the true and most effective value of proton therapy for our patients.

Thanks again for allowing us to provide comments,

[redacted]

Ramesh Rengan MD PhD
Medical Director, SCCA Proton Therapy

[redacted]

Nina Mayr MD
Chair, Department of Radiation Oncology