Washington State Health Care Authority

Proton Beam Therapy – Re-review

Public comment and response to
topic nomination and draft key questions

July 27, 2018

Health Technology Assessment Program (HTA)
Washington State Health Care Authority
PO Box 42712
Olympia, WA 98504-2712
(360) 725-5126
www.hca.wa.gov/about-hca/health-technology-assessment
shtap@hca.wa.gov

Proton Beam Therapy – Re-review

Provided by:

Aggregate Analytics, Inc.

Topic Nomination and Key Questions

Public Comments

Public Comment & Response

July 27, 2018

Responses to clinical and peer reviewers

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

Responses to public comments made during topic nomination are included Table 1.
Comments from:

- Daniel E Smith, Executive Director, Alliance for Proton Therapy Access, and Jeffrey D. Bradley, Member of Alliance for Proton Therapy Access Scientific Advisory Committee
- Deepak Khuntia, MD, Senior Vice President and Chief Medical Officer, Varian Medical Systems
- Jessica Adams, CCA, Health Policy Analyst, American Society for Radiation Oncology
- Scott Warwick, Executive Director, National Association for Proton Therapy

Responses to public comments to the DRAFT Key questions are found in Table 2.
Comments from:

- Members of the Public (Gordon Hall)
- Jessica Adams, CCA, Health Policy Analyst, American Society for Radiation Oncology (ASTRO)
- Fielding Greaves, Director State Government and Regional Affairs, AdvaMed
- Scott Warwick, Executive Director, National Association for Proton Therapy (NAPT)
- Annika Andrews, President of Seattle Cancer Care Alliance Proton Therapy Center, and Ramesh Rengan MD, PhD, Professor at University of Washington School of Medicine, Associate Member, Fred Hutchinson Cancer Research Center, Medical Director, SCCA Proton Therapy Center
- Deepak Khuntia, MD, Senior Vice President and Chief Medical Officer, Varian Medical Systems

Full text of public comments on Topic Nomination and the DRAFT Key Questions follow the tables. Attachments included with public comments related to model policies are acknowledged but were too large to append to this document and are available through the Washington State Healthcare Authority.

Table 1. Responses to comments for topic nomination

	Comment	Response
Commenter: Daniel E Smith, Executive Director, Alliance for Proton Therapy Access, and Jeffrey D. Bradley, Member of Alliance for Proton Therapy Access Scientific Advisory Committee		
	Specific comments	
Main body of Comments reproduced	"Dear Director Birch, The Alliance for Proton Therapy Access is a patient-focused advocacy organization striving to make sure all cancer patients seeking proton therapy receive fair and timely payment decisions from their health insurers. We work directly with patients and caregivers who have benefitted greatly from proton beam therapy (PBT), and with those who have had to endure health risks, anxiety, and financial hardship associated with unfair delays and denials of care after their physician recommended PBT as their best hope for survival and highest quality of life. We are writing to encourage you to broaden coverage of PBT based on clinical evidence that has been updated since the committee's publication of the 2014 Findings and Decision. The attached fact sheet summarizes key research findings that underscore the many benefits of PBT for certain cancer patients. We also ask that you provide for coverage of PBT for any indications when a patient is enrolled in a clinical trial and/or registry, as this will help generate additional clinical evidence regarding the appropriate use of PBT. Finally, we also urge you to consider the experience of patients as you re-evaluate coverage of PBT for various cancer indications. Below is an excerpt from just one of the many stories cancer patients are sharing on the Alliance website that illustrate the tremendous benefit of proton therapy, and the high costs of not getting the treatment their physician recommends. **Stephanie Wurdock Lindsey** As a four-time Super Lawyers "Rising Star," I'm used to pleading a case and making an argument on behalf of my clients. But when my doctor told me I had adenoid cystic carcinoma last year, and my insurer subsequently denied payment for the proton therapy my doctor recommended, I was speechless. Following surgery to remove the lump in my neck, my doctor said proton therapy was the best course of care. According to my medical team, proton therapy would protect the vital structures surrounding the tumor from	Thank you for your comments. The email/comment is addressed to the Health Technology Clinical Committee. Comments related to Health Technology Assessment Program policy formulation, process and/or function of the Health Technology Clinical Committee do not require a response from the evidence vendor, Aggregate Analytics, Inc.

	Comment	Response
	radiation exposure while giving me a better chance for a long, healthy life. I couldn't believe it when my insurance company denied my coverage three times, calling it "experimental" despite the wealth of evidence that it works! Even though their internal radiation oncologist agreed with my doctors that I would benefit from proton therapy, I was forced to appeal to an Independent External Review agency. I wrote a passionate plea for the services. My doctors submitted a letter, my records, and medical literature. Within 72 hours, we had our answer: THE PREVIOUS DENIAL IS HEREBY OVERTURNED. I recently completed six weeks of proton therapy treatments and am recovering well at home. My treatment was uneventful, and my side effects are mild compared to what they could have been with traditional radiation. I hope my story will help inspire other patients facing the same unfair barriers to care I faced to keep fighting for proton therapy. No cancer patient should be denied the care they have paid for and rightly deserve. We appreciate your consideration of our letter in your re-review process."	
	A document titled "Alliance for Proton Therapy Access – Proton Therapy Facts" was included with the comments and is reproduced online.	Your documents were received. All publications cited as evidence in the attachment will be considered for inclusion based on the inclusion/exclusion criteria for the evidence report.
Commenter: Deepak Khuntia, MD, Senior Vice President and Chief Medical Officer, Varian Medical Systems		
	Specific comments	
Main body of Comments reproduced	"Dear Director Birch: Varian Medical Systems is the world's leading supplier of radiotherapy products for treating cancer. Our products include medical linear accelerators, simulators, proton therapy systems, and a broad range of accessories and interconnected software tools for planning, verifying, and delivering the most advanced radiation, radiosurgical, and brachytherapy treatments. Our electronic medical record facilitates efficient management of treatment for patients undergoing medical or radiation (including proton) therapies. Varian has in-depth knowledge of the significant benefits that	Thank you for your comments. The email/comment is addressed to the Health Technology Clinical Committee. Comments related to Health Technology Assessment Program policy formulation, process and/or function of the Health Technology Clinical Committee do not require a response from the evidence vendor, Aggregate Analytics, Inc.

	Comment	Response
	radiation therapy, particularly proton beam therapy in certain indications, provides to the health of Americans. Varian appreciates the opportunity to provide comment on the re-review of proton beam therapy (PBT) as new evidence has become available since the Health Technology Clinical Committee's Findings and Decision final adoption on July 11, 2014. As new evidence has since accumulated, we encourage you to reevaluate the conditions under which coverage applies for PBT. This new clinical data supports the benefits of PBT for additional indications not covered in the 2014 Findings and Decision. As you know, PBT, a radiation therapy that uses protons rather than photons to deposit radiation energy, focuses a beam of radiation to the target tumor tissue. This technology delivers a lower dose of radiation to a patient's healthy tissue than other types of radiation therapy, making PBT particularly important in pediatric and neurological cases. Varian applauds the committee for recognizing the benefits of PBT and for its determination that PBT should be a covered benefit for the noted indications in the 2014 Findings and Decision. Based upon the mounting clinical evidence available since the publication of the Findings and Decision, Varian also recommends coverage for the following indications based upon: •Benign or malignant conditions of the base of the skull or axial skeleton including but not limited to chordomas and chondrosarcomas • Pituitary neoplasms • Malignant lesions of the head and neck • Lung cancers, especially NSCLC • Unresectable retroperitoneal sarcoma • Gastrointestinal tract tumors • Esophageal cancers • Urinary tract tumors • Tumors of the female pelvic organs • Prostate Carcinoma • Primary or metastatic tumors of the spine where the spinal cord tolerance may be exceeded with conventional treatment or where the spinal cord has previously been irradiated • Hepatocellular cancer	To the extent that literature meeting the inclusion/exclusion criteria is available for the conditions listed, they will be included in the report.

	Comment	Response
	• Patients with genetic syndromes making total volume of radiation minimization crucial such as but not limited to NF-1 patients and retinoblastoma patients • Cancers of the paranasal sinuses and other accessory sinuses • Non-metastatic retroperitoneal sarcomas In addition, PBT is indicated when: • The Dose Volume Histogram (DVH) illustrates at least one (1) or more critical structures or organs that must be considered at risk in or adjacent to the treatment volume to be protected by the use of proton beam therapy • There is documented clinical rationale that doses generally thought to be above the level otherwise attainable with other radiation methods might improve control rates; • Other radiation therapy treatment plans (e.g., photon-based treatment plans) would have a greater probability of causing clinically meaningful acute and late normal tissue toxicity; or • There is documented clinical rationale that the higher levels of precision associated with proton beam therapy compared to other radiation treatments are clinically necessary We strongly encourage coverage of PBT of these additional indications, as well as coverage of all other indications not specified as covered under the 2014 Findings and Decision when the patient is enrolled in a clinical trial and/or registry as there is a need for additional clinical evidence regarding the appropriate use of PBT for various disease sites. As you know, PBT has been utilized for many decades. However, there have been recent advancements with proton delivery systems which include spot scanning or intensity modulated proton therapy (IMPT). There are studies underway comparing the effectiveness and substantially improved dose conformity of IMPT to other forms of radiation therapy and traditional scatter proton therapy. Based upon the new evidence that has accumulated, we encourage you to reevaluate the conditions under which coverage for PBT applies. We strongly support coverage of PBT and specifically coverage of all other indications not specified as covered under the 2014 Findings and Decision, including when the patient is enrolled in a clinical trial and/or registry.	

	Comment	Response
	Please see the attached documents, the recently released American Society for Radiation Oncology (ASTRO) model policy and the National Association of Proton Therapy's (NAPT) model policy, which address coverage for PBT. We appreciate your consideration on this matter and look forward to working with you in the future on this and other issues. Sincerely, Deepak Khuntia"	
	In addition to the comments above, the commenter included two attachments titled ***"American Society for Radiation Oncology (ASTRO) model policy***" and the ***"National Association of Proton Therapy's (NAPT) model policy"***	Your documents were received. All publications cited as evidence in these documents will be considered for inclusion based on the inclusion/exclusion criteria for the evidence report.
Commenter: Jessica Adams, CCA, Health Policy Analyst, American Society for Radiation Oncology		
	Specific comments	
Main body of comments reproduced	"Good morning, The American Society for Radiation Oncology (ASTRO) issued an update to its recommendations for medical insurance coverage regarding the use of proton beam therapy to treat cancer. The updated Proton Beam Therapy Model Policy provides guidance to payers on clinical indications that are appropriate for treatment with proton therapy and should be covered by health insurance, including Medicare, Medicaid and private insurance. Based on new evidence published since the original policy was issued in 2014, the updated model policy outlines two categories of appropriate clinical indications, or diagnoses, for proton beam therapy. ASTRO publishes a distinct series of model policies to efficiently communicate correct coverage policies for radiation oncology services. We maintain updated information and inform payers of all changes to existing policies. Should you have any questions, please contact Jessica Adams, Health Policy Analyst (XXX) XXX-XXXX or via email at Jessica.adams@astro.org Thank you, Jessica"	Thank you for your comments. Your documents were received. All publications cited as evidence in these documents will be considered for inclusion based on the inclusion/exclusion criteria for the evidence report.

	Comment	Response
Commenter: Scott Warwick, Executive Director, National Association for Proton Therapy		
	Specific comments	
Main body of Comments reproduced	"To Whom It May Concern: We thank you for the opportunity to submit comments on the 2018 Health Technology Assessment Topic Selection and specifically, the re-review of proton beam therapy. By way of background, the National Association for Proton Therapy ("NAPT") is a nonprofit organization whose mission is to work collaboratively to: (i) educate and raise awareness of the clinical benefits of proton therapy among patients, providers, payers, policymakers, and other stakeholders, (ii) ensure patient choice and access to affordable proton therapy, and (iii) encourage cooperative research and innovation to advance the appropriate and cost-effective utilization of proton therapy. Its members – both hospital based and freestanding – are world-renowned cancer centers, a number of whom are National Cancer Institute (NCI) designated comprehensive cancer centers and National Comprehensive Care Network (NCCN) members including the Seattle Cancer Care Alliance Proton Therapy Center. As you proceed with the re-review process in 2018, we submit the following important points for your consideration: 1. **Model Policies and Guidelines**. Since the initial review was completed in 2014, three organizations have released revised model policies or guidelines based on their detailed review of the current literature. a. NAPT Model Policy. NAPT continuously monitors the published proton therapy evidence which it incorporates into its Model Policy. Through a consensus-based approach, a team of multidisciplinary leading cancer care leaders around the country update the Model Policy. Notably, the leadership of the Alliance for Dedicated Cancer Centers, Particle Therapy Co-Operative Group - North America and National Association for Proton Therapy endorsed the current version of the Model Policy. We are currently in the midst of updating the Model Policy for 2018 and expect to publish it in the near future. See Attachment 1 for the 2016 NAPT Model Policy and Attachment 2 for a comprehensive list of published evidence on proton beam therapy by disease site with over 820 references.	Thank you for your comments. Your documents were received. All publications cited as evidence in these documents will be considered for inclusion based on the inclusion/exclusion criteria for the evidence report. Guidelines: We attempt to identify high quality evidence-based guidelines. Reports always include information on the most updated clinical practice guidelines. CMS NCD and information from 2 bell-weather payers are routinely included in the report background. As the evidence vendor, AAI does not suggest, evaluate or discuss policy. The Health Technology Assessment Program has been made aware of the suggested model policies and suggestions related to policy as part of the public comment process.

	Comment	Response
	b. ASTRO Model Policy. The American Society for Radiation Oncology (ASTRO) released a consensus proton beam model policy in 2014 based on their review of the existing evidence. Due to continued growth of clinical evidence supporting the use of proton therapy, ASTRO released an updated model policy - approved in June 2017 – adding additional indications to their existing recommendations for coverage. These guidelines were promulgated by leaders in the field, many of whom do not have access to protons. c. NCCN Guidelines. The National Comprehensive Cancer Network (NCCN)5 published guidelines are often used as the litmus test by payers for determining if they will approve coverage for all types of cancer treatments. Please keep in mind that the NCCN Guidelines most often consist of what is the current standard of care and often do not include emerging technologies until they have been demonstrated as becoming a standard of care. In the past, they have historically been silent on proton therapy but, over the last 18 months the guidelines have become more encouraging in their comments about the use of proton therapy, embedding proton beam therapy in the guidelines for ten different disease sites including Head & Neck cancer. See Attachment 3 for a summary of the NCCN Guidelines for Proton Beam Therapy as of April 23, 2018. We respectfully ask that you have the evidence reviewer thoroughly review the indications, conditions and referenced published evidence in the Model Policies and Guidelines as part of their due diligence. **2. Expanded Medicare Coverage**. The Medicare program is continuing to review and revise its coverage position on proton beam therapy. A number of Medicare Administrative Contractors ("MACs") have chosen to not have local coverage determinations ("LCDs"), given that these contractors have determined that proton therapy is "reasonable and necessary" for a number of cancers that afflict Medicare beneficiaries. A few MACs who still maintain local coverage determination policies have expanded their coverage for a number of indications in the last two years including Hodgkin's and B-Cell lymphomas, esophageal cancer, right side breast cancer, and high risk prostate cancers.	

	Comment	Response
	3. Examples of Coverage Models. Over the last three years, different types of coverage models have been proposed and/or implemented to further develop the clinical evidence of proton beam technology. Aetna developed and proposed a Coverage with Evidence Development model that would extend coverage for patients enrolled on clinical trials that meet high levels of clinical evidence criteria. Another proton beam therapy coverage model implemented in 2016 between the State of Texas System and M.D. Anderson Cancer Center allowed coverage for employees and their dependents on the BlueCross BlueShield of Texas UT Select plan who are eligible for any of the center's clinical trials for patients with tumors of the breast, thorax, esophagus, head & neck, or GU. We strongly encourage that these models, and others, be considered as options to provide proton beam coverage responsibly while continuing the research, collection, and on-going publication of clinical evidence. In summary, we feel that a re-review based on the current clinical evidence base is warranted. We suggest that the new clinical evidence as well as the additional sources noted above be included in the re-review to further inform your recommendations and that the language in the final guideline or report should be modified to suggest, or at a minimum support, models for expanded coverage be developed to help expand on the existing clinical data to determine the true and most effective value of proton therapy for our patients. We appreciate your consideration of our feedback on the 2018 Health Technology Assessment Topic Selection. Should you have any questions, please do not hesitate to contact Scott Warwick, NAPT Executive Director, at SWarwick@proton-therapy.org. Respectfully submitted, Scott Warwick"	
	In addition to the comments above, the commenter included three attachments: "National Association of Proton Therapy's (NAPT) 2016 model policy", an extensive reference list and "2018 NCCN Guidelines for Proton Beam Therapy".	

Table 2. Responses to comments on DRAFT Key Questions

	2017 Comments on DRAFT Key Questions	Response
Commenter: Scott Warwick, Executive Director, National Association for Proton Therapy		
Introductory Comments	Dear Committee, We thank you for the opportunity to submit comments regarding the Draft Key Questions for the 2019 Health Technology Assessment of Proton Beam Therapy. In this letter, we are submitting specific comments on the draft key questions as well as comments on the overall process and approach for the re-review of proton beam therapy. By way of background, the National Association for Proton Therapy ("NAPT") is a nonprofit organization whose mission is to work collaboratively to: (i) educate and raise awareness of the clinical benefits of proton therapy among patients, providers, payers, policymakers, and other stakeholders, (ii) ensure patient choice and access to affordable proton therapy, and (iii) encourage cooperative research and innovation to advance the appropriate and cost-effective utilization of proton therapy for certain cancers. Its members – both hospital-based and freestanding – are world renowned cancer centers, a number of whom are National Cancer Institute (NCI) designated comprehensive cancer centers and National Comprehensive Care Network (NCCN) members, including the Seattle Cancer Care Alliance Proton Therapy Center.	Thank you for your suggestions and comments.
Specific Comments – Technology of Interest	Technology of Interest - In this section, it was stated that "Because the proton beam is focused on a specific area, a greater dose of radiation may be delivered to the target neoplasm(s) while mitigating unwanted radiation delivered to surrounding tissue (Levin, 2005)." A critical benefit of proton beam therapy is its ability to treat tumors and reduce unnecessary radiation dose to critical organs and structures. As such, the last sentence in the first paragraph should be revised to state "PBT may be most promising to tumors in close proximity to organs at risk (OAR)."[1] <u>Footnote</u> [1]The original language is as follows – "PBT may be most promising for tumors close to the body surface."	**Background edits/technology of interest:** Changes have been made to the background based on all public comments received.
Specific Comments – Draft Key Questions	- In reviewing the comparative effects of proton beam therapy compared to its major alternatives, the assessment should focus not only on the potential harms but also the potential advantages associated with this type of therapy. As such, we recommend the following language for Question 3 (with proposed changes in *red italicized text*):	**Response to specific detailed comments on KQ and PICOTS** **KQ 3:** The original wording will be retained; the intent of the questions is to focus

	2017 Comments on DRAFT Key Questions	Response
	What are the comparative *clinical advantages and* harms associated with the use of proton beam therapy relative to its major alternatives, including acute (i.e., within the first 90 days after treatment) and late (>90 days) toxicities, systemic effects such as fatigue and erythema, toxicities specific to each cancer type (e.g., bladder/bowel incontinence in prostate cancer, pneumonitis in lung or breast cancer), risks of secondary malignancy, and radiation dose? - In assessing the costs and cost-effectiveness of the therapy, it is important to examine not only the costs during the actual episode of care but also the potential longer term morbidity costs due to radiation exposure of healthy tissue. As such, we recommend the following language for Question 5: What is the cost-effectiveness of proton beam therapy, short- and long-term, relative to other radiation treatment modalities and to radiation therapy alternatives or other cancer-specific treatment options (e.g., surgery, chemotherapy)? The evidence demonstrating the clinical benefits of proton beam therapy is evolving. As this occurs, different types of coverage models have been proposed and/or implemented to further develop the clinical evidence of proton beam technology. Aetna developed and proposed a Coverage with Evidence Development (CED) model that would extend coverage for patients enrolled on clinical trials that meet high levels of clinical evidence criteria. Another proton beam therapy coverage model implemented in 2016 between the State of Texas System and M.D. Anderson Cancer Center allowed coverage for employees and their dependents on the BlueCross BlueShield of Texas UT Select plan who are eligible for any of the center's clinical trials for patients with tumors of the breast, thorax, esophagus, head & neck, or GU. Additional coverage models have been proposed or implemented by the American Society of Radiation Oncology (ASTRO) and Medicare Administrative Contractors. We strongly recommend that a key question is added that examines these coverage models and others which provide proton beam coverage responsibly while continuing the research, collection, and on-going publication of clinical evidence.	on comparative harms and adverse events. Context related to clinical advantages related to harms or adverse events may be added to the background and to extent that they are described as evidence in included studies will be described with the relevant evidence. **KQ 5:** Modifications have been made based on all comments received.
Specific Comments - Proposed Inclusion and Exclusion	Under "Outcomes", we recommend adding "Patient Reported Outcomes" under the Secondary or Indirect (Intermediate) Measures as we believe that these types of outcomes are an important consideration. Under "Study Design", we recommend the following modifications:	**Coverage models and payer policies:** As the evidence vendor, AAI does not suggest, evaluate or discuss policy; thus, a KQ regarding model policies will not be included for the evidence report. The Health

2017 Comments on DRAFT Key Questions	Response
• The draft indicates that case studies in adults with < 30 patients should be excluded from the assessment. However, in specific circumstances (e.g., studies focusing on rare diseases (e.g., thymoma)), such a study population is not practical or feasible. As such, these types of case studies should be allowed as an exception when reasonably warranted. Under "Publications", we recommend the following types of publications for inclusion: • NCCN Guidelines. The National Comprehensive Cancer Network (NCCN)2 published guidelines are often used as the litmus test by payers for determining if they will approve coverage for all types of cancer treatments. Please keep in mind that the NCCN Guidelines most often consist of what is the current standard of care and often do not include emerging technologies until they have been demonstrated as becoming a standard of care. In the past, they have historically been silent on proton therapy but, over the last 24 months, the guidelines have become more encouraging in their comments about the use of proton therapy, embedding proton beam therapy in the guidelines for fourteen different disease sites including head & neck cancer.3 • Model policies from leading medical organizations. In 2017, the American Society for Radiation Oncology (ASTRO) released an updated proton beam model policy. These guidelines were promulgated by leaders in the field, many of whom do not have access to protons. The Alliance for Dedicated Cancer Centers (ADCC)4, Particle Therapy Co-Operative Group - North America (PTCOG-NA)5 and National Association for Proton Therapy have worked together through a consensus-based approach to draft and update its model policy; the last version of the model policy was released 2016. • Coverage policies from other government agencies. The Medicare program is continuing to review and revise its coverage position on proton beam therapy. A number of Medicare Administrative Contractors ("MACs") have chosen to not have local coverage determinations ("LCDs"), given that these contractors have determined that proton therapy is "reasonable and necessary" for a number of cancers that afflict Medicare beneficiaries. A few MACs who still maintain local coverage determination policies have expanded their coverage for a number of indications in the last two years including Hodgkin's and B-Cell lymphomas, esophageal	Technology Assessment Program is aware of the suggested model and suggestions related to policy as part of the public comment process. CMS NCD and information from 2 bell-weather payers are routinely included in the report background. We will review citations of evidence described in the model policy documents, compare them against the inclusion/exclusion criteria and include studies meeting the criteria into the evidence report. **Response to specific detailed comments on PICOTS inclusion/exclusion** ○ Guidelines: We attempt to identify high quality evidence-based guidelines. Reports always include information on the most updated clinical practice guidelines. ○ Model policies and coverage policies (please see above) ○ Exclusion of abstracts, editorials, letters and white papers is consistent with accepted methodology for systematic reviews and technology assessment described by AHRQ and others. These exclusions will be retained to focus on the highest quality available evidence focused on full publications from peer-reviewed literature. ○ Case series in adults with < 30 patients: The

2017 Comments on DRAFT Key Questions		Response
	cancer, right side breast cancer, and high risk prostate cancers.\ • Studies published that demonstrate toxicities to critical organs from radiation therapy techniques that are generally applicable and not specific to proton therapy. For example, Darby et al. assessed the risk of ischemic heart disease in women after radiotherapy for breast cancer.6 • White papers that are assessments of the evidence on proton beam therapy generally or for specific disease sites. Footnotes [2] The NCCN is an alliance of 27 largely academic cancer centers in the U.S. of which most are designated as Comprehensive Cancer Centers by the National Cancer Institute. [3] Guidelines that embedded proton beam therapy (as of July 17, 2018) include bone cancers, central nervous system cancers, esophageal and esophagogastric junction cancers, head and neck cancers, hepatobiliary cancers, Hodgkin Lymphoma, malignant pleural mesothelioma, uveal melanoma, Non-Hodgkin's Lymphoma (B-Cell and T-Cell), non-small cell lung cancer, prostate cancer, soft tissue sarcoma, and thymomas and thymic carcinomas. [4] The Dedicated Cancer Centers were created in response to the National Cancer Act of 1971 which declared a War on Cancer. With a singular focus on cancer, the Alliance of Dedicated Cancer Centers' state- of-the-art therapies and research activities often offer the greatest possibility of successful cancer treatment. The ADCC institutions provide multi-disciplinary cancer care, including diagnostic, surgical, medical, chemotherapy and radiation treatment. A full list of ADCC members can be found at http://www.adcc.org/page/alliance-member-institutions. [5] Particle Therapy Cooperative Group - North America (PTCOG – NA) is the North American chapter of an international non-profit scientific society. This professional membership society has been created to enhance collaboration between its members, create a platform for scientific exchange, and develop treatment guidelines, education, and training initiatives for particle therapy. [6] Studies such as Darby SC, Ewertz M, and McGale P. Risk of Ischemic Heart Disease in Women after Radiotherapy for Breast Cancer. NEJM. 2013 Mar 14;368(11):987-98.	following statement has been added: "Case series of ≥ 10 patients may be considered for very rare conditions." ○ We agree that patient-reported outcomes based on validated instruments are important. We have added Patient reported outcomes (HRQOL are generally considered PROs). ○ Studies related to toxicity from standard radiation: Comparative information on harms (including toxicities from comparator therapies such as standard radiation therapy) from included studies will be summarized in the evidence report (KQ 3). Context regarding harms and toxicities related to comparator treatments including standard radiation therapy could be added to the background.
Specific Comments – Overall Approach	Proton beam radiotherapy is a very specific form of radiotherapy that requires specialized clinical training and experience. Clinicians using this modality must have a detailed understanding of the therapy and the type of patients where	**Clinical expertise:** We have reached out to clinical experts; we always seek perspectives from clinical

	2017 Comments on DRAFT Key Questions	Response
	this treatment approach may or may not be clinically appropriate. A thorough review or assessment of the evidence on this type of technology requires well-informed engagement. We ask the Washington State Health Care Authority to strongly consider engaging a board-certified radiation oncologist with multiple years of clinical experience at an operating proton therapy center as part of the assessment. As a representative of the vast majority of operating proton beam therapy centers in the United States, the NAPT would willingly provide a list of physician candidates to serve in this capacity.	experts on specific clinical questions and have them involved with peer review. As necessary or appropriate we will reach out for names of additional experts.
Concluding Comments	We appreciate your consideration of our feedback on the Key Draft Questions for the 2019 Health Technology Assessment of Proton Beam Therapy. Should you have any questions, please do not hesitate to contact me at the contact information provided below. Respectfully submitted, Scott Warwick Executive Director National Association for Proton Therapy	
Commenter: Fielding Greaves, Director State Government and Regional Affairs, AdvaMed		
Introductory communication	Hello, Please accept our attached comments to the HTAP PBT Re-review proceeding. Please let me know if you have any problems opening the document. Please let me know if you have any questions. Best, Fielding	Thank you for your comments. Your communication was received.
Main body of Comments reproduced	Dear Director Birch: The Advanced Medical Technology Association (AdvaMed), the national association of medical technology providers, is deeply concerned about the process involved with the Health Technology Assessment Program (program) as it relates to the current proceeding examining Proton Beam Therapy (PBT). We urge you to provide the public with more time to comment or extend the comment period so that the public can study these complex questions, develop thorough, comprehensive responses and meaningfully engage with program staff to best serve the interests of the program. AdvaMed member companies produce the medical devices, diagnostic products, and health information systems that are transforming health care through earlier disease detection,	Thank you for your comments. Comments related to Health Technology Assessment Program policy formulation, process and/or function of the Health Technology Clinical Committee do not require a response from the evidence vendor, Aggregate Analytics, Inc. The timelines for the HTA process, including those

2017 Comments on DRAFT Key Questions	Response
less invasive procedures and more effective treatments. AdvaMed encourages public policies that assure patient access to the benefits of medical technology. AdvaMed has been very interested in Washington's health technology assessment program since its inception. During the legislative debate that led to the creation of the program and the assessment program's subsequent activities, AdvaMed has advocated for efforts to ensure transparency and adequate public comment. AdvaMed appreciates the opportunity to provide comment on the draft key questions regarding the re-review of PBT by the Health Technology Assessment and the need to finalize this initial step in a timely manner. Although this proceeding considers only questions for consideration, the questions stand to deeply influence the program's ultimate conclusions and we urge the program to extend this and future comment periods to fall in line with other customary comment periods to ensure adequate public participation. For federal rulemaking 30-60 days is the normal minimum comment period. 180 days is provided for complex rules. California provides for a minimum comment period of 45 days for all rulemaking. However, the current public comment period for the PBT questions provides only 15 days, beginning with publication on July 3 and ending today, July 18. AdvaMed is concerned that this short comment period (just 10 business days) will limit the depth and value of public consideration and comment that may be provided to the program. We understand that significant new evidence has become available since the initial review of PBT in 2014 and the current two-week public comment period fails to provide enough time to effectively respond to the draft key questions. AdvaMed respectfully requests a delay in the deadline for the public comment submissions to the draft key questions as we look to carefully and thoughtfully respond to the program's questions. Thank you for considering our concerns. Please contact me if you have any questions. Sincerely, Fielding Greaves Director, State Government & Regional Affairs	related to public comment are the purview of the HTAP program not the evidence vendor.

2017 Comments on DRAFT Key Questions		Response
Commenter: Annika Andrews, President of Seattle Cancer Care Alliance Proton Therapy Center, and Ramesh Rengan MD PhD, Professor at University of Washington School of Medicine, Associate Member, Fred Hutchinson Cancer Research Center, Medical Director, SCCA Proton Therapy Center		
Introductory Comments	Good afternoon, Please see attachment for comments from the SCCA Seattle Proton Therapy Center, with respect to the Public Comments on draft key questions for the Re-review of Proton Beam Therapy. Very Sincerely, Kristen M Southwick Dear Committee: We would like to thank the Washington State Health Care Authority for the opportunity to comment on the "Draft Key Questions and Background" for the re-review of proton beam therapy. With this letter, we are submitting comments regarding the process and approach of this review, as well as specific comments and edits concerning the draft key questions	Thank you for your suggestions and comments. Background edits: Changes have been made to the background.
Specific Comments – Process/Approach	• Proton beam therapy is a highly specialized form of radiotherapy that requires specialized clinical training and experience in order to use this modality for the treatment of cancer patients. As such, a thorough review of this methodology requires well-informed engagement including, but not limited to: • The enlistment of an ABR (American Board of Radiology) board-certified radiation oncologist with a minimum of 5 years of clinical experience at an operating proton center to aid in the evidentiary review • The engagement of experienced faculty from the University of Washington Department of Radiation Oncology so that they can speak to the specific needs of the patient population in the state of Washington with respect to proton beam therapy. As you may know, there is only one operating proton center in the state of Washington (and broader Pacific Northwest), and this center is staffed solely by physicians from the University of Washington (UW), Department of Radiation Oncology who have no financial interest in the center. • The inclusion of dosimetric studies in your evidentiary review. It should be noted that proton beam therapy is the standard of care for our most vulnerable patient population, pediatric cancer patients. The evidentiary	**Process, approach comments** ○ Clinical expertise: We have reached out to clinical experts, including one from UW; we always seek perspectives from clinical experts on specific clinical questions and have them involved with peer review. They also may provide important stakeholder information/perspective. Comments made from stakeholders during the public comment periods are evaluated and considered. ○ Inclusion of dosimetric studies: Per the previous report, dosimetry and planning studies will be included for context. To the extent that they directly answer the key questions, particularly with regard to

2017 Comments on DRAFT Key Questions		Response
	basis for establishing proton beam therapy as the standard of care for treating children with cancer is dosimetric studies. (We do not have randomized trials in children, comparing standard radiation exposure to protons, because it would be unethical.) The current clinical "gold" standard in Radiation Oncology is to perform a dosimetric comparison in order to identify the optimal radiotherapeutic modality for the treatment of a given patient. Dosimetric comparisons are an essential part of clinical decision making and therefore it is standard practice to review dosimetric studies when evaluating treatment options for adults. • The inclusion of consensus-based treatment guidelines, such as from the National Comprehensive Cancer Network, as part of the evidentiary support for your review. We would also recommend inclusion of existing model policies from relevant medical societies and consensus-based organizations, such as (1) the American Society for Radiation Oncology model policy for proton beam radiotherapy, and (2) the Alliance of Dedicated Cancer Centers, Particle Therapy Co-Operative Group, and National Association for Proton Therapy model policy for proton beam radiotherapy. We also respectfully request that your contracted reviewer engages with these and other key stakeholders (such as the National Cancer Institute and patient representatives) as part of their research and deliberative processes.	treating children, information will be included as evidence. ○ Guidelines: We always attempt to identify high quality evidence-based guidelines. Reports always include information on the most updated clinical practice guidelines. ○ Reports do not include information on model policies as policy evaluation, determination or discussion is not the purview of the evidence vendor. We will review citations of evidence described in the model policy documents, compare them against the inclusion/exclusion criteria and include studies meeting the criteria into the evidence report. The HTAP has is aware of the model policies attached by commenters. ○ CMS NCD and information from at 2 bell-weather payers is routinely included in the report background.
Specific Comments – Attachment with Edits; Final Comments	**Specific, detailed comments to the "Draft Key Questions and Background" released on your website are enclosed in a red-lined version of the document that is included as Attachment 1.** We respectfully recommend the additions set forth in Attachment 1. We look forward to working with the Health Technology Clinical Committee as they move forward in this important re-review of proton beam therapy. Thanks again for allowing us to provide comments. Ramesh Rengan MD PhD Professor, University of Washington School of Medicine Associate Member, Fred Hutchinson Cancer Research Center	**The attached revisions to our Draft Key Questions are appended at the end of this document. Responses to these revisions are described here.** **Suggested KQ revisions**: ○ KQ1. Suggested re-wording to "clinical advantages" vs. impact. The original wording will be retained as it as it was used in the original report as an answerable question to denote emphasis on

2017 Comments on DRAFT Key Questions	Response
Medical Director, SCCA Proton Therapy Center Annika Andrews President, SCCA Proton Therapy Center	evaluation of evidence. Context related to clinical advantages may be added to the background and to extent that they are described in included studies as part of the evidence may be described with relevant evidence. ○ KQ5. Has been revised based on evaluation of all comments received. ○ Addition of KQ 6 regarding model policies: As the evidence vendor, AAI does not suggest policy or include evaluations of policy; thus, this KQ will not be included by the evidence vendor. The Health Technology Assessment Program is aware of the attachments and suggestions related to policy. Citations listed in the models will be evaluated against the inclusion/exclusion criteria. **PICOTS table revisions** ○ FDA "cleared" vs. "approved": We will use both terms. [Definitions from the FDA website Cleared medical devices: These medical devices are ones that FDA has determined to be substantially equivalent to (similar) another legally marketed device. A premarket notification submission is referred to as a 510(k) and must be submitted to FDA to review and provide clearance. The U.S. Food and Drug Administration (FDA) examines, tests, and

2017 Comments on DRAFT Key Questions	Response
	approves a wide range of items for medical use, including drugs and medical appliances. In the simplest terms, "FDA approval" means that the FDA has decided the benefits of the approved item outweigh the potential risks for the item's planned use. https://www.fda.gov/ForConsumers] ○ Added immunotherapy to comparators ○ Added patient reported outcomes (HRQOL are generally considered PROs) ○ Dosimetry, planning and simulation studies: Per the previous report, dosimetry and planning studies will be included for context. To the extent that they directly answer the key questions, particularly with regard to treating children, information will be described with the evidence. Studies of simulation that do not include actual clinical outcomes data will be excluded. ○ Case series in adults with < 30 patients: The following statement has been added: Case series of ≥ 10 patients may be considered for very rare conditions. ○ Studies prior to 2014: For purposes of this update report, it is assumed that the relevant highest quality studies meeting the inclusion criteria were represented in the prior report and will not be re-

2017 Comments on DRAFT Key Questions	Response
	evaluated or re-reviewed for this update report. ○ Studies related to toxicity from standard radiation: Comparative information on harms (including toxicities from comparator therapies such as standard radiation therapy), will be include in the evidence report. Context regarding harms and toxicities related to comparator treatments including standard radiation therapy could be added to the background. ○ Relevant clinical guidelines are routinely included in the report background; we attempt to focus on high quality, evidence-based guidelines. Similarly, relevant CMS NCDs and summaries of 2 bellwether payer policies will be included in the report. As the evidence vendor, it is not AAI's role to suggest policy; as such, model policies will not be included in the evidence report. The HTAP program is aware of model polices submitted as part of public comment. Citations of evidence contained in the model policies will be evaluated against the *a priori* inclusion/exclusion criteria; citations meeting the inclusion criteria will be incorporated into the evidence report. ○ Exclusion of abstracts, editorials, letters and white papers is consistent with accepted methodology for systematic reviews and technology assessment

2017 Comments on DRAFT Key Questions		Response
		described by AHRQ and others; these exclusions will be retained to focus on the highest quality available evidence as described in the PICOTS table.
Commenter: Jessica Adams, CCA, Health Policy Analyst, American Society for Radiation Oncology (ASTRO)		
Main body of Comments reproduced	Dear Washington State Health Care Authority, The American Society for Radiation Oncology (ASTRO) would like to provide input on the Proton Beam Therapy Health Technology Assessment (HTA). ASTRO members are medical professionals, who practice at hospitals and cancer treatment centers in the United States and around the globe, and make up the radiation therapy treatment teams that are critical in the fight against cancer. These teams often include radiation oncologists, medical physicists, medical dosimetrists, radiation therapists, oncology nurses, nutritionists and social workers, and treat more than one million cancer patients each year. We believe this multi-disciplinary membership makes us uniquely qualified to provide input on the inherently complex issues related to Medicare payment policy and coding for radiation oncology services. In 2017, ASTRO issued an update to its recommendations for medical insurance coverage regarding the use of proton beam therapy to treat cancer. The updated Proton Beam Therapy Model Policy provides guidance to payers on clinical indications that are appropriate for treatment with proton therapy and should be covered by health insurance, including Medicare, Medicaid and private insurance. Based on new evidence published since the original policy was issued in 2014, the updated model policy outlines two categories of appropriate clinical indications, or diagnoses, for proton beam therapy. ASTRO publishes a distinct series of model policies to efficiently communicate correct coverage policies for radiation oncology services. We maintain updated information and inform payers of all changes to existing policies. Also attached is a recent paper on the use of proton therapy in children. It is a thorough review of the existing data and addresses your questions regarding the use of proton therapy for pediatric cancers.	Thank you for your comments. Your documents and publications were received. All publications cited as evidence will be considered for inclusion based on the inclusion/exclusion criteria for the evidence report. As the evidence vendor, it is not AAI's role to suggest, evaluate or discuss policy; as such, model policies will not be included in the evidence report. The HTAP program is aware of model polices submitted as part of public comment. Citations of evidence contained in the model policies will be evaluated against the a priori inclusion/exclusion criteria; citations meeting the inclusion criteria will be incorporated into the evidence report.

	2017 Comments on DRAFT Key Questions	Response
	Should you have any questions, please contact Jessica Adams, Health Policy Analyst (XXX) XXX-XXXX or via email at Jessica.adams@astro.org. Regards, Jessica	
Commenter: Deepak Khuntia, MD, Senior Vice President and Chief Medical Officer, Varian Medical Systems		
Email communication	Dear Director Birch: On behalf of Varian Medical Systems, please find attached our comment letter and supporting attachments to the Health Technology Assessment Program's key draft questions regarding the re-review of proton beam therapy. Sincerely, Keelin McGee	Thank you, your communication was received.
Main Body of Comments	Dear Director Birch: Varian Medical Systems is the world's leading supplier of radiotherapy products for treating cancer. Our products include medical linear accelerators, simulators, proton therapy systems, and a broad range of accessories and interconnected software tools for planning, verifying, and delivering the most advanced radiation, radiosurgical, and brachytherapy treatments. Our electronic medical record facilitates efficient management of treatment for patients undergoing medical or radiation (including proton) therapies. Varian has in-depth knowledge of the significant benefits that radiation therapy, particularly proton beam therapy (PBT) in certain indications, provides to the health of Americans. Varian appreciates the opportunity to comment on the draft key questions regarding the re-review of PBT by the Health Technology Assessment Program. However, Varian is concerned about the quick turnaround to provide thoughtful comments to the draft key questions published on July 3, 2018. As new evidence has become available since the initial review of PBT in 2014, we do not feel as though the two-week public comment period provides enough time to effectively respond to the draft key questions. Varian respectfully requests a delay in the deadline for the public comment submissions to the draft key questions as we look to carefully and thoughtfully respond to the Health Technology Assessment's questions.	Thank you for your comments. The timelines for the HTA process, including those related to public comment are the purview of the HTAP program. As the evidence vendor, it is not AAI's role to suggest policy; as such, model policies will not be included in the evidence report. The HTAP program is aware of the model polices submitted as part of public comment. Citations of evidence contained in the model policies will be evaluated against the a priori inclusion/exclusion criteria; citations meeting the inclusion criteria will be incorporated into the evidence report

2017 Comments on DRAFT Key Questions	Response
As previously submitted by Varian, new clinical evidence has become available since the publication of the 2014 Findings and Decision and we again attach the American Society for Radiation Oncology's (ASTRO) Model Policies: Proton Beam Therapy (PBT) approved in June 2017 and the National Association for Proton Therapy's (NAPT) Model Policy: Coverage of Proton Beam Therapy published in March 2015. The attached model policies from ASTRO and NAPT provide new clinical data which support the benefits of PBT for additional indications not covered in the 2014 Findings and Decision. We strongly encourage coverage of PBT of these additional indications, as well as coverage of all other indications not specified as covered under the 2014 Findings and Decision when the patient is enrolled in a clinical trial and/or registry as there is a need for additional clinical evidence regarding the appropriate use of PBT for various disease sites. Varian appreciates your consideration on this matter and again, we request a delay in the deadline for the public comment submission to the key draft questions. We look forward to working with you in the future on this and other issues. Sincerely, Deepak Khuntia, MD Senior Vice President and Chief Medical Officer Varian Medical Systems	

We are also grateful to the following individuals for providing general public comment (i.e., not addressing evidence, project scope, or draft key questions) on the topic of proton beam therapy:

Gordon Hall

Alliance for Proton Therapy Access
4515 Drummond Avenue
Chevy Chase, MD 20815
(202) 999-8923

March 19, 2018

Sue Birch
Director
Health Care Authority
P.O. Box 42712
Olympia, WA 98504-2712

RE: Re-review of the Health Technology Assessment Program's Proton Beam Therapy Technology Assessment

Dear Director Birch,

The Alliance for Proton Therapy Access is a patient-focused advocacy organization striving to make sure all cancer patients seeking proton therapy receive fair and timely payment decisions from their health insurers. We work directly with patients and caregivers who have benefitted greatly from proton beam therapy (PBT), and with those who have had to endure health risks, anxiety, and financial hardship associated with unfair delays and denials of care after their physician recommended PBT as their best hope for survival and highest quality of life.

We are writing to encourage you to broaden coverage of PBT based on clinical evidence that has been updated since the committee's publication of the 2014 Findings and Decision. The attached fact sheet summarizes key research findings that underscore the many benefits of PBT for certain cancer patients.

We also ask that you provide for coverage of PBT for any indications when a patient is enrolled in a clinical trial and/or registry, as this will help generate additional clinical evidence regarding the appropriate use of PBT.

Finally, we also urge you to consider the experience of patients as you re-evaluate coverage of PBT for various cancer indications. Below is an excerpt from just one of the many stories cancer patients are sharing on the Alliance website that illustrate the tremendous benefit of proton therapy, and the high costs of not getting the treatment their physician recommends.

> **Stephanie Wurdock Lindsey**
> *As a four-time Super Lawyers "Rising Star," I'm used to pleading a case and making an argument on behalf of my clients. But when my doctor told me I had adenoid cystic carcinoma last year, and my insurer subsequently denied payment for the proton therapy my doctor recommended, I was speechless.*
>
> *Following surgery to remove the lump in my neck, my doctor said proton therapy was the best course of care. According to my medical team, proton therapy would protect the vital structures surrounding the tumor from radiation exposure while giving me a better chance for a long, healthy life.*

I couldn't believe it when my insurance company denied my coverage three times, calling it "experimental" despite the wealth of evidence that it works! Even though their internal radiation oncologist agreed with my doctors that I would benefit from proton therapy, I was forced to appeal to an Independent External Review agency.

I wrote a passionate plea for the services. My doctors submitted a letter, my records, and medical literature. Within 72 hours, we had our answer: THE PREVIOUS DENIAL IS HEREBY OVERTURNED.

I recently completed six weeks of proton therapy treatments and am recovering well at home. My treatment was uneventful, and my side effects are mild compared to what they could have been with traditional radiation. I hope my story will help inspire other patients facing the same unfair barriers to care I faced to keep fighting for proton therapy. No cancer patient should be denied the care they have paid for and rightly deserve.

We appreciate your consideration of our letter in your re-review process.

Sincerely,

[redacted]

Daniel E. Smith
Executive Director
Alliance for Proton Therapy Access

[redacted]

Jeffrey D. Bradley, MD, FACR, FASTRO (Member, Alliance for Proton Therapy Access Scientific Advisory Committee)
Professor
S. Lee Kling Endowed Chair in Radiation Oncology
Medical Director, S. Lee Kling Center for Proton Therapy
Washington University School of Medicine and The Alvin J. Siteman Cancer Center

Attachment: Alliance for Proton Therapy Access. Proton Therapy Facts (2017)

Alliance for Proton Therapy Access

Proton Therapy Facts

Proton therapy is a medically necessary, FDA-cleared treatment for cancer patients. In the early days of proton therapy, because of technological limitations, the therapy was used for a limited number of conditions and demonstrated considerable value for pediatric populations, patients with tumors affecting the brain and skull-base, paranasal sinuses, eye tumors and arteriovenous malformations. With technological advances, the data show considerable promise and improvement in side effects of patients with cancers of the breast, esophagus, liver, lung and head and neck.

For many cancer patients, proton therapy is prescribed by their physician and is the optimal and most effective treatment option. Studies have shown that proton therapy can help increase survival, reduce the risk of secondary cancers, result in fewer acute and long-term conditions as well as debilitating short-term side effects and improve quality of life for individuals undergoing cancer treatment.

Outlined below are key research findings that underscore the many benefits of proton therapy for certain cancer patients:

SECONDARY CANCERS:

- When compared with photon radiation, proton therapy allows for an increased dose of radiation to a cancerous tumor while decreasing the dose to adjacent critical structures. The use of proton radiation therapy has *not* been associated with an increased risk of secondary malignancies compared with photon therapy.[1]
- Compared with intensity-modulated radiation therapy (IMRT), proton therapy can reduce the risk of a patient developing a secondary cancer by 26 to 39 percent. [2]

HEAD AND NECK CANCERS (CANCERS OF THE OROPHARYNX NASOPHARYANX & SKULL-BASE CHORDOMAS):

- With proton therapy, unnecessary radiation doses can be avoided in head and neck cancer patients, resulting in significant improvement in quality of life during and after treatment.[3]
- Patients with cancers of the oropharynx and nasopharynx had less swallowing dysfunction following proton therapy, and were approximately 60 percent less likely to need a feeding tube.[4]
- Proton therapy reduces the rates of feeding tube dependency and severe weight loss for patients with oropharyngeal cancers and improves survival for patients with paranasal and nasal cavity malignancies.[5]
- Proton beam therapy is “an effective treatment modality for skull base chordomas.”[6]
- Compared with historical photon therapy data, proton therapy results in better local control and overall survival treatments for patients with chordomas and chondrosarcomas of the spine.[7]

[1] *Chung C S, Yock T I, et al. Incidence of Second Malignancies Among Patients Treated With Proton Versus Photon Radiation. Int J Radiation Oncol Biol Phys*, Vol. 87, No. 1, pp. 46e52, 2013
[2] Fontenot JD, Lee AK, Newhauser WD. Risk of secondary malignant neoplasms from proton therapy and intensity-modulated x-ray therapy for early-state prostate cancer. *Int J Radiat Oncol Biol Phys* 2009;74:616-22
[3] Blanchard P, et al. Intensity-modulated proton beam therapy (IMPT) versus intensity-modulated photon therapy (IMRT) for patients with oropharynx cancer - A case matched analysis. *Radiother Oncol.* 2016;120(1):48-55.
[4] Blanchard P, et al. “Intensity modulated proton beam therapy (IMPT) versus intensity modulated photon therapy (IMRT) for oropharynx cancer patients – a case matched analysis” Radiother Oncol; 2016: 120:48-55
[5] Patel SH, et al. Lancet Oncol. 2014;15(9):1027-38
[6] Ares C, et al. Effectiveness and safety of spot scanning proton radiation therapy for chordomas and chondrosarcomas of the skull base: first long-term report. Int J Radiat Oncol Biol Phys. 2009;75(4):1111-8.
[7] Indelicato DJ, Rotondo RL, Begosh-Mayne D, et al. “A prospective outcomes study of proton therapy for chordomas and chondrosarcomas of the spine.” Int J Radiat Oncol Biol Phys 2016;95:297-303.

Alliance for Proton Therapy Access

BREAST CANCER:

- Proton therapy after mastectomy or breast-conserving surgery significantly reduces cardiac exposure to radiation[8] and improves target coverage for the internal mammary nodes, which may positively impact long-term survival in breast cancer patients.[9]

NON-SMALL CELL LUNG CANCER (NSCLC):

- Virtual clinical studies have shown that, compared with photon-based radiation therapy, proton therapy can spare critical structures of excess radiation, particularly the heart, lungs, esophagus and spinal cord.[10]
- One study found that among NSCLC patients, those who received proton therapy reported less severe patient-reported symptoms such as fatigue, pain, drowsiness and lack of appetite than those receiving IMRT or 3D Conformal Radiation Therapy (3DCRT).[11]
- Other studies of proton therapy patients have demonstrated promising clinical outcomes in reducing toxic effects compared to IMRT.[12] Another study found that patients with locally advanced NSCLC also demonstrated an "excellent overall survival rate with tolerable toxicity" after undergoing proton therapy treatment with lower rates of toxicity than would be expected with photon therapy treatment.[13]

PEDIATRIC CANCER:

- Data show pediatric cancer patients benefit from reduced integral dose with protons compared with photons. Patients with tumors in the central nervous system, head and neck and some abdominal locations have a reduction of radiation dosage to normal tissues and potentially fewer late toxicities if treated with protons compared with photons.[14]

ESOPHAGEAL CANCER:

- In a study of nearly 450 patients with esophageal cancer, those who received proton therapy had fewer gastrointestinal and pulmonary toxicities than those receiving photon therapy." [15]
- In patients with locally advanced esophageal cancer, proton therapy has been shown to be associated with improved survival rates compared to modulated radiation therapy.[16]
- Another study found that patients with esophageal cancer who underwent proton beam therapy treatment had significantly fewer postoperative complications and spent fewer days in the hospital compared to patients who underwent other types of radiation therapy.[17]

LIVER CANCER:

- In liver cancer, contemporary data for proton therapy are highly promising. In a recent phase II trial including a large number of patients with advanced liver disease, median progression-free survival was 36 months, with a 60 percent three-year progression-free survival rate for patients.[18]
- In a randomized trial of transarterial chemoembolization (TACE) versus proton therapy, proton therapy was superior on multiple metrics. For example, the total hospitalization days within 30 days of the procedures for the entire cohort was 166 versus 24, in favor of protons.[19]

[8] Lin LL, et al. Proton beam versus photon beam dose to the heart and left anterior descending artery for left-sided breast cancer. Acta Oncol. 2015;54(7):1032-9.
[9] Bradley J A, Dagan D, et al. Initial Report of a Prospective Dosimetric and Clinical Feasibility Trial Demonstrates the Potential of Protons to Increase the Therapeutic Ratio in Breast Cancer Compared With Photons. Int J Radiation Oncol Biol Phys, Vol. 95, No. 1, pp. 411e421, 2016
[10] Chang J Y, Jabbour S K, et al. Consensus Statement on Proton Therapy in Early-Stage and Locally Advanced Non Small Cell Lung Cancer. Int J Radiation Oncol Biol Phys, Vol. 95, No. 1, pp. 505-516, 2016
[11] Wang XS, Shi Q, Williams LA, et al. Prospective study of patient-reported symptom burden in patients with non-small-cell lung cancer undergoing proton or photon chemoradiation therapy. J Pain Symptom Manage 2016;51:832-838.
[12] Chang, Joe Y. "Proton beam radiotherapy and concurrent chemotherapy for unresectable stage III non–small-cell lung cancer: final results of a phase 2 study." Journal of the American Medical Association. 2017.
[13] Nguyen QN, Ly NB, Komaki R, et al. "Long-term outcomes after proton therapy, with concurrent chemotherapy, for state II-III inoperable non-small cell lung cancer" Radiother Oncol 2015;115:367-372.
[14] Ladra MM, et al. Preliminary results of a phase II trial of proton radiotherapy for pediatric rhabdomyosarcoma. J Clin Oncol. 2014;32(33):3762-70.
[15] Wang J, et al. Int J Radiat Oncol Biol Phys. 2013;86(5):885-91
[16] Mian, Xi. "Comparative outcomes after definitive chemoradiotherapy using proton beam therapy versus intensity modulated radiation therapy for esophageal cancer: a retrospective, single-institutional analysis." Int J Radiation Oncol Biol Phys. 2017
[17] Lin SH, Merrell K W, Shen J, et al. "Multi-institutional analysis of radiation modality use and postoperative outcomes of neoadjuvant chemoradiation of esophageal cancer." Radiother Oncol 2017:123:376-381.
[18] Bush, D. A., Kayali, Z., Grove, R. & Slater, J. D. The safety and efficacy of high-dose proton beam radiotherapy for hepatocellular carcinoma: a phase 2 prospective trial. Cancer 117, 3053rafety and ef
[19] Bush DA, Smith JC, Slater JD, Volk ML, Reeves ME, Cheng J: Randomized Clinical Trial Comparing Proton Beam Radiation Therapy with Transarterial Chemoembolization for Hepatocellular Carcinoma: Results of an Interim Analysis, Int J Radiat Oncol Biol Phys, 95(1):477-482, 2016

Alliance for Proton Therapy Access

Proton Therapy Facts

Proton therapy is a medically necessary, FDA-cleared treatment for cancer patients. In the early days of proton therapy, because of technological limitations, the therapy was used for a limited number of conditions and demonstrated considerable value for pediatric populations, patients with tumors affecting the brain and skull-base, paranasal sinuses, eye tumors and arteriovenous malformations. With technological advances, the data show considerable promise and improvement in side effects of patients with cancers of the breast, esophagus, liver, lung and head and neck.

For many cancer patients, proton therapy is prescribed by their physician and is the optimal and most effective treatment option. Studies have shown that proton therapy can help increase survival, reduce the risk of secondary cancers, result in fewer acute and long-term conditions as well as debilitating short-term side effects and improve quality of life for individuals undergoing cancer treatment.

Outlined below are key research findings that underscore the many benefits of proton therapy for certain cancer patients:

SECONDARY CANCERS:

- When compared with photon radiation, proton therapy allows for an increased dose of radiation to a cancerous tumor while decreasing the dose to adjacent critical structures. The use of proton radiation therapy has *not* been associated with an increased risk of secondary malignancies compared with photon therapy.[1]
- Compared with intensity-modulated radiation therapy (IMRT), proton therapy can reduce the risk of a patient developing a secondary cancer by 26 to 39 percent. [2]

HEAD AND NECK CANCERS (CANCERS OF THE OROPHARYNX NASOPHARYANX & SKULL-BASE CHORDOMAS):

- With proton therapy, unnecessary radiation doses can be avoided in head and neck cancer patients, resulting in significant improvement in quality of life during and after treatment.[3]
- Patients with cancers of the oropharynx and nasopharynx had less swallowing dysfunction following proton therapy, and were approximately 60 percent less likely to need a feeding tube.[4]
- Proton therapy reduces the rates of feeding tube dependency and severe weight loss for patients with oropharyngeal cancers and improves survival for patients with paranasal and nasal cavity malignancies.[5]
- Proton beam therapy is “an effective treatment modality for skull base chordomas.”[6]
- Compared with historical photon therapy data, proton therapy results in better local control and overall survival treatments for patients with chordomas and chondrosarcomas of the spine.[7]

[1] *Chung C S, Yock T I, et al. Incidence of Second Malignancies Among Patients Treated With Proton Versus Photon Radiation. Int J Radiation Oncol Biol Phys*, Vol. 87, No. 1, pp. 46e52, 2013
[2] Fontenot JD, Lee AK, Newhauser WD. Risk of secondary malignant neoplasms from proton therapy and intensity-modulated x-ray therapy for early-state prostate cancer. *Int J Radiat Oncol Biol Phys* 2009;74:616-22
[3] Blanchard P, et al. Intensity-modulated proton beam therapy (IMPT) versus intensity-modulated photon therapy (IMRT) for patients with oropharynx cancer - A case matched analysis. *Radiother Oncol.* 2016;120(1):48-55.
[4] Blanchard P, et al. “Intensity modulated proton beam therapy (IMPT) versus intensity modulated photon therapy (IMRT) for oropharynx cancer patients – a case matched analysis” Radiother Oncol; 2016: 120:48-55
[5] Patel SH, et al. Lancet Oncol. 2014;15(9):1027-38
[6] Ares C, et al. Effectiveness and safety of spot scanning proton radiation therapy for chordomas and chondrosarcomas of the skull base: first long-term report. Int J Radiat Oncol Biol Phys. 2009;75(4):1111-8.
[7] Indelicato DJ, Rotondo RL, Begosh-Mayne D, et al. “A prospective outcomes study of proton therapy for chordomas and chondrosarcomas of the spine.” Int J Radiat Oncol Biol Phys 2016;95:297-303.

Alliance for Proton Therapy Access

BREAST CANCER:

- Proton therapy after mastectomy or breast-conserving surgery significantly reduces cardiac exposure to radiation[8] and improves target coverage for the internal mammary nodes, which may positively impact long-term survival in breast cancer patients.[9]

NON-SMALL CELL LUNG CANCER (NSCLC):

- Virtual clinical studies have shown that, compared with photon-based radiation therapy, proton therapy can spare critical structures of excess radiation, particularly the heart, lungs, esophagus and spinal cord.[10]
- One study found that among NSCLC patients, those who received proton therapy reported less severe patient-reported symptoms such as fatigue, pain, drowsiness and lack of appetite than those receiving IMRT or 3D Conformal Radiation Therapy (3DCRT).[11]
- Other studies of proton therapy patients have demonstrated promising clinical outcomes in reducing toxic effects compared to IMRT.[12] Another study found that patients with locally advanced NSCLC also demonstrated an "excellent overall survival rate with tolerable toxicity" after undergoing proton therapy treatment with lower rates of toxicity than would be expected with photon therapy treatment.[13]

PEDIATRIC CANCER:

- Data show pediatric cancer patients benefit from reduced integral dose with protons compared with photons. Patients with tumors in the central nervous system, head and neck and some abdominal locations have a reduction of radiation dosage to normal tissues and potentially fewer late toxicities if treated with protons compared with photons.[14]

ESOPHAGEAL CANCER:

- In a study of nearly 450 patients with esophageal cancer, those who received proton therapy had fewer gastrointestinal and pulmonary toxicities than those receiving photon therapy." [15]
- In patients with locally advanced esophageal cancer, proton therapy has been shown to be associated with improved survival rates compared to modulated radiation therapy.[16]
- Another study found that patients with esophageal cancer who underwent proton beam therapy treatment had significantly fewer postoperative complications and spent fewer days in the hospital compared to patients who underwent other types of radiation therapy.[17]

LIVER CANCER:

- In liver cancer, contemporary data for proton therapy are highly promising. In a recent phase II trial including a large number of patients with advanced liver disease, median progression-free survival was 36 months, with a 60 percent three-year progression-free survival rate for patients.[18]
- In a randomized trial of transarterial chemoembolization (TACE) versus proton therapy, proton therapy was superior on multiple metrics. For example, the total hospitalization days within 30 days of the procedures for the entire cohort was 166 versus 24, in favor of protons.[19]

[8] Lin LL, et al. Proton beam versus photon beam dose to the heart and left anterior descending artery for left-sided breast cancer. Acta Oncol. 2015;54(7):1032-9.
[9] Bradley J A, Dagan D, et al. Initial Report of a Prospective Dosimetric and Clinical Feasibility Trial Demonstrates the Potential of Protons to Increase the Therapeutic Ratio in Breast Cancer Compared With Photons. Int J Radiation Oncol Biol Phys, Vol. 95, No. 1, pp. 411e421, 2016
[10] Chang J Y, Jabbour S K, et al. Consensus Statement on Proton Therapy in Early-Stage and Locally Advanced Non Small Cell Lung Cancer. Int J Radiation Oncol Biol Phys, Vol. 95, No. 1, pp. 505-516, 2016
[11] Wang XS, Shi Q, Williams LA, et al. Prospective study of patient-reported symptom burden in patients with non-small-cell lung cancer undergoing proton or photon chemoradiation therapy. J Pain Symptom Manage 2016;51:832-838.
[12] Chang, Joe Y. "Proton beam radiotherapy and concurrent chemotherapy for unresectable stage III non–small-cell lung cancer: final results of a phase 2 study." Journal of the American Medical Association. 2017.
[13] Nguyen QN, Ly NB, Komaki R, et al. "Long-term outcomes after proton therapy, with concurrent chemotherapy, for state II-III inoperable non-small cell lung cancer" Radiother Oncol 2015;115:367-372.
[14] Ladra MM, et al. Preliminary results of a phase II trial of proton radiotherapy for pediatric rhabdomyosarcoma. J Clin Oncol. 2014;32(33):3762-70.
[15] Wang J, et al. Int J Radiat Oncol Biol Phys. 2013;86(5):885-91
[16] Mian, Xi. "Comparative outcomes after definitive chemoradiotherapy using proton beam therapy versus intensity modulated radiation therapy for esophageal cancer: a retrospective, single-institutional analysis." Int J Radiation Oncol Biol Phys. 2017
[17] Lin SH, Merrell K W, Shen J, et al. "Multi-institutional analysis of radiation modality use and postoperative outcomes of neoadjuvant chemoradiation of esophageal cancer." Radiother Oncol 2017:123:376-381.
[18] Bush, D. A., Kayali, Z., Grove, R. & Slater, J. D. The safety and efficacy of high-dose proton beam radiotherapy for hepatocellular carcinoma: a phase 2 prospective trial. Cancer 117, 3053rafety and ef
[19] Bush DA, Smith JC, Slater JD, Volk ML, Reeves ME, Cheng J: Randomized Clinical Trial Comparing Proton Beam Radiation Therapy with Transarterial Chemoembolization for Hepatocellular Carcinoma: Results of an Interim Analysis, Int J Radiat Oncol Biol Phys, 95(1):477-482, 2016

varian

Varian Medical Systems
3100 Hansen Way
Palo Alto, CA 94304
650.493.4000
800.544.4636
varian.com

March 19, 2018

Sue Birch
Director
Washington State Health Care Authority
P.O. Box 42712
Olympia, WA 98504-2712

Re: Re-review of the Health Technology Assessment Program's Proton Beam Therapy Technology Assessment

Dear Director Birch:

Varian Medical Systems is the world's leading supplier of radiotherapy products for treating cancer. Our products include medical linear accelerators, simulators, proton therapy systems, and a broad range of accessories and interconnected software tools for planning, verifying, and delivering the most advanced radiation, radiosurgical, and brachytherapy treatments. Our electronic medical record facilitates efficient management of treatment for patients undergoing medical or radiation (including proton) therapies. Varian has in-depth knowledge of the significant benefits that radiation therapy, particularly proton beam therapy in certain indications, provides to the health of Americans.

Varian appreciates the opportunity to provide comment on the re-review of proton beam therapy (PBT) as new evidence has become available since the Health Technology Clinical Committee's Findings and Decision final adoption on July 11, 2014. As new evidence has since accumulated, we encourage you to reevaluate the conditions under which coverage applies for PBT. This new clinical data supports the benefits of PBT for additional indications not covered in the 2014 Findings and Decision.

As you know, PBT, a radiation therapy that uses protons rather than photons to deposit radiation energy, focuses a beam of radiation to the target tumor tissue. This technology delivers a lower dose of radiation to a patient's healthy tissue than other types of radiation therapy,[1] making PBT particularly important in pediatric and neurological cases.

Varian applauds the committee for recognizing the benefits of PBT and for its determination that PBT should be a covered benefit for the noted indications in the 2014 Findings and Decision. Based upon the mounting clinical evidence available since the publication of the Findings and Decision, Varian also recommends coverage for the following indications based upon:

- Benign or malignant conditions of the base of the skull or axial skeleton including but not limited to chordomas and chondrosarcomas
- Pituitary neoplasms
- Malignant lesions of the head and neck
- Lung cancers, especially NSCLC
- Unresectable retroperitoneal sarcoma
- Gastrointestinal tract tumors

[1] American Society for Radiation Oncology (ASTRO). Model Policies: Proton Beam Therapy (PBT). ASTRO: June 2017.

varian

- Esophageal cancers
- Urinary tract tumors
- Tumors of the female pelvic organs
- Prostate Carcinoma
- Primary or metastatic tumors of the spine where the spinal cord tolerance may be exceeded with conventional treatment or where the spinal cord has previously been irradiated
- Hepatocellular cancer
- Patients with genetic syndromes making total volume of radiation minimization crucial such as but not limited to NF-1 patients and retinoblastoma patients
- Cancers of the paranasal sinuses and other accessory sinuses
- Non-metastatic retroperitoneal sarcomas[2] [3]

In addition, PBT is indicated when:

- The Dose Volume Histogram (DVH) illustrates at least one (1) or more critical structures or organs that must be considered at risk in or adjacent to the treatment volume to be protected by the use of proton beam therapy
- There is documented clinical rationale that doses generally thought to be above the level otherwise attainable with other radiation methods might improve control rates;
- Other radiation therapy treatment plans (e.g., photon-based treatment plans) would have a greater probability of causing clinically meaningful acute and late normal tissue toxicity; or
- There is documented clinical rationale that the higher levels of precision associated with proton beam therapy compared to other radiation treatments are clinically necessary.[4]

We strongly encourage coverage of PBT of these additional indications, as well as coverage of all other indications not specified as covered under the 2014 Findings and Decision when the patient is enrolled in a clinical trial and/or registry as there is a need for additional clinical evidence regarding the appropriate use of PBT for various disease sites.

As you know, PBT has been utilized for many decades. However, there have been recent advancements with proton delivery systems which include spot scanning or intensity modulated proton therapy (IMPT). There are studies underway comparing the effectiveness and substantially improved dose conformity of IMPT to other forms of radiation therapy and traditional scatter proton therapy.

Based upon the new evidence that has accumulated, we encourage you to reevaluate the conditions under which coverage for PBT applies. We strongly support coverage of PBT and specifically coverage of all other indications not specified as covered under the 2014 Findings and Decision, including when the patient is enrolled in a clinical trial and/or registry.

Please see the attached documents, the recently released American Society for Radiation Oncology (ASTRO) model policy and the National Association of Proton Therapy's (NAPT) model policy, which address coverage for PBT.

We appreciate your consideration on this matter and look forward to working with you in the future on this and other issues.

---

[2] ASTRO Model Policies. June 2017.
[3] National Association of Proton Therapy (NAPT). Model Policy: Coverage of Proton Beam Therapy. NAPT: March 30, 2015.
[4] NAPT Model Policy. March 30, 2015.

varian

Sincerely,

[redacted]

Deepak Khuntia, MD
Senior Vice President and Chief Medical Officer
Varian Medical Systems

Attachments: American Society for Radiation Oncology (ASTRO). Model Policies: Proton Beam Therapy (PBT). ASTRO: June 2017.
National Association of Proton Therapy (NAPT). Model Policy: Coverage of Proton Beam Therapy. NAPT: March 30, 2015.

[redacted]

From: Jessica Adams <jessica.adams@astro.org>
Sent: Monday, March 26, 2018 7:40 AM
To: HCA ST Health Tech Assessment Prog
Subject: 2018 health technologies - Proton Beam Therapy
Attachments: Proton Beam Therapy Model Policy.pdf

Follow Up Flag: Follow up
Flag Status: Completed

Good morning,

The American Society for Radiation Oncology (ASTRO) issued an update to its recommendations for medical insurance coverage regarding the use of proton beam therapy to treat cancer. The updated Proton Beam Therapy Model Policy provides guidance to payers on clinical indications that are appropriate for treatment with proton therapy and should be covered by health insurance, including Medicare, Medicaid and private insurance.

Based on new evidence published since the original policy was issued in 2014, the updated model policy outlines two categories of appropriate clinical indications, or diagnoses, for proton beam therapy. ASTRO publishes a distinct series of model policies to efficiently communicate correct coverage policies for radiation oncology services. We maintain updated information and inform payers of all changes to existing policies.

Should you have any questions, please contact Jessica Adams, Health Policy Analyst (703) 839-7396 or via email at Jessica.adams@astro.org.

Thank you,
Jessica

Jessica Adams, CCA
Health Policy Analyst
American Society for Radiation Oncology
251 18th Street South, 8th Floor
Arlington, VA 22202
703-839-7396 direct
703-502-1550 main
Jessica.Adams@astro.org
www.astro.org

VIA electronic mail to: shtap@hca.wa.gov

April 23, 2018

Re: Health Technology Assessment Topic Selection, 2018

Health Technology Assessment Program
Washington State Health Care Authority
626 8th Avenue • P.O. Box 45502
Olympia, WA 98504-5502

To Whom It May Concern:

We thank you for the opportunity to submit comments on the 2018 Health Technology Assessment Topic Selection and specifically, the re-review of proton beam therapy.

By way of background, the National Association for Proton Therapy ("NAPT") is a nonprofit organization whose mission is to work collaboratively to: (i) educate and raise awareness of the clinical benefits of proton therapy among patients, providers, payers, policymakers, and other stakeholders, (ii) ensure patient choice and access to affordable proton therapy, and (iii) encourage cooperative research and innovation to advance the appropriate and cost-effective utilization of proton therapy. Its members – both hospital based and freestanding – are world-renowned cancer centers, a number of whom are National Cancer Institute (NCI) designated comprehensive cancer centers and National Comprehensive Care Network (NCCN) members including the Seattle Cancer Care Alliance Proton Therapy Center.[1]

As you proceed with the re-review process in 2018, we submit the following important points for your consideration.

1. **Model Policies and Guidelines**. Since the initial review was completed in 2014, three organizations have released revised model policies or guidelines based on their detailed review of the current literature.
   a. NAPT Model Policy. NAPT continuously monitors the published proton therapy evidence which it incorporates into its Model Policy. Through a consensus-based approach, a team of multidisciplinary leading cancer care leaders around the country update the Model Policy. Notably, the leadership of the Alliance for Dedicated Cancer Centers[2], Particle Therapy Co-Operative Group - North America[3] and National Association for Proton Therapy endorsed the current version of the Model Policy.[4] We are currently in the midst of updating the Model Policy for 2018 and expect to publish it in the near future. See **Attachment 1** for the 2016 NAPT Model Policy and **Attachment 2** for a comprehensive list of published evidence on proton beam therapy by disease site with over 820 references.
   b. ASTRO Model Policy. The American Society for Radiation Oncology (ASTRO) released a consensus proton beam model policy in 2014 based on their review of the existing evidence. Due to continued growth of clinical evidence supporting the use of proton therapy, ASTRO

[1] NAPT website can be found at www.proton-therapy.org.
[2] The Dedicated Cancer Centers were created in response to the National Cancer Act of 1971 which declared a War on Cancer. With a singular focus on cancer, the Alliance of Dedicated Cancer Centers' state- of-the-art therapies and research activities often offer the greatest possibility of successful cancer treatment. The ADCC institutions provide multi-disciplinary cancer care, including diagnostic, surgical, medical, chemotherapy and radiation treatment. A full list of ADCC members can be found at http://www.adcc.org/page/alliance-member-institutions.
[3] Particle Therapy Cooperative Group - North America (PTCOG – NA) is the North American chapter of an international non-profit scientific society. This professional membership Society has been created to enhance collaboration between its members, create a platform for scientific exchange, and develop treatment guidelines, education, and training initiatives for particle therapy. The Society --in collaboration with PTCOG International--established a particle therapy journal. A full list of PTCOG institutional members can be found at http://ptcog-na.org/institution_membership.html.
[4] http://www.proton-therapy.org/documents/2016_model_policy.pdf

released an updated model policy - approved in June 2017 – adding additional indications to their existing recommendations for coverage. These guidelines were promulgated by leaders in the field, many of whom do not have access to protons.

c. NCCN Guidelines. The National Comprehensive Cancer Network (NCCN)[5] published guidelines are often used as the litmus test by payers for determining if they will approve coverage for all types of cancer treatments. Please keep in mind that the NCCN Guidelines most often consist of what is the current standard of care and often do not include emerging technologies until they have been demonstrated as becoming a standard of care. In the past, they have historically been silent on proton therapy but, over the last 18 months the guidelines have become more encouraging in their comments about the use of proton therapy, embedding proton beam therapy in the guidelines for ten different disease sites including Head & Neck cancer. See **Attachment 3** for a summary of the NCCN Guidelines for Proton Beam Therapy as of April 23, 2018.

We respectfully ask that you have the evidence reviewer thoroughly review the indications, conditions and referenced published evidence in the Model Policies and Guidelines as part of their due diligence.

2. **Expanded Medicare Coverage**. The Medicare program is continuing to review and revise its coverage position on proton beam therapy. A number of Medicare Administrative Contractors ("MACs") have chosen to not have local coverage determinations ("LCDs"), given that these contractors have determined that proton therapy is "reasonable and necessary" for a number of cancers that afflict Medicare beneficiaries. A few MACs who still maintain local coverage determination policies have expanded their coverage for a number of indications in the last two years including Hodgkin's and B-Cell lymphomas, esophageal cancer, right side breast cancer, and high risk prostate cancers.

3. **Examples of Coverage Models**. Over the last three years, different types of coverage models have been proposed and/or implemented to further develop the clinical evidence of proton beam technology. Aetna developed and proposed a Coverage with Evidence Development model that would extend coverage for patients enrolled on clinical trials that meet high levels of clinical evidence criteria. Another proton beam therapy coverage model implemented in 2016 between the State of Texas System and M.D. Anderson Cancer Center allowed coverage for employees and their dependents on the BlueCross BlueShield of Texas UT Select plan who are eligible for any of the center's clinical trials for patients with tumors of the breast, thorax, esophagus, head & neck, or GU. ***We strongly encourage that these models, and others, be considered as options to provide proton beam coverage responsibly while continuing the research, collection, and on-going publication of clinical evidence***.

In summary, we feel that a re-review based on the current clinical evidence base is warranted. We suggest that the new clinical evidence as well as the additional sources noted above be included in the re-review to further inform your recommendations and that the language in the final guideline or report should be modified to suggest, or at a minimum support, models for expanded coverage be developed to help expand on the existing clinical data to determine the true and most effective value of proton therapy for our patients.

* * * * *

[5] The NCCN is an alliance of 27 largely academic cancer centers in the U.S. of which most are designated as Comprehensive Cancer Centers by the National Cancer Institute.

We appreciate your consideration of our feedback on the 2018 Health Technology Assessment Topic Selection. Should you have any questions, please do not hesitate to contact Scott Warwick, NAPT Executive Director, at SWarwick@proton-therapy.org.

Respectfully submitted,

Scott Warwick
Executive Director

From: GL HALL
To: HCA ST Health Tech Assessment Prog
Subject: Proton Beam Therapy
Date: Tuesday, July 3, 2018 4:17:24 PM

I had this treatment 8 years ago at Loma Linda, CA since it was not available in the Northwest at the time, plus your insurance would not cover it!

Mine was for prostate cancer. My two older brothers had the traditional treatment for this cancer and it did not work and they are dead! I am still alive after 8 years so it seems it has a place in treatment options for folks? It's not only good for men, but it also can treat cancers in women and other cancers in general. Maybe it costs more now, but I would think the long term life saving it does must be worth something and plus the insurance companies should save a lot from cancers returning from the other treatment options and all the costs that must come from the retreating?

Let's get it approved!!!!

Gordon Hall

[redacted]

From: Jessica Adams <jessica.adams@astro.org>
Sent: Wednesday, July 18, 2018 11:41 AM
To: HCA ST Health Tech Assessment Prog
Subject: Proton Beam Therapy – re-review
Attachments: Proton therapy for pediatric malignancies.pdf; WA State HCA PBT Policy.pdf

Follow Up Flag: Follow up
Flag Status: Flagged

Dear Washington State Health Care Authority,

The American Society for Radiation Oncology (ASTRO) would like to provide input on the Proton Beam Therapy Health Technology Assessment (HTA). ASTRO members are medical professionals, who practice at hospitals and cancer treatment centers in the United States and around the globe, and make up the radiation therapy treatment teams that are critical in the fight against cancer. These teams often include radiation oncologists, medical physicists, medical dosimetrists, radiation therapists, oncology nurses, nutritionists and social workers, and treat more than one million cancer patients each year. We believe this multi-disciplinary membership makes us uniquely qualified to provide input on the inherently complex issues related to Medicare payment policy and coding for radiation oncology services.

In 2017, ASTRO issued an update to its recommendations for medical insurance coverage regarding the use of proton beam therapy to treat cancer. The updated Proton Beam Therapy Model Policy provides guidance to payers on clinical indications that are appropriate for treatment with proton therapy and should be covered by health insurance, including Medicare, Medicaid and private insurance.

Based on new evidence published since the original policy was issued in 2014, the updated model policy outlines two categories of appropriate clinical indications, or diagnoses, for proton beam therapy. ASTRO publishes a distinct series of model policies to efficiently communicate correct coverage policies for radiation oncology services. We maintain updated information and inform payers of all changes to existing policies.

Also attached is a recent paper on the use of proton therapy in children. It is a thorough review of the existing data and addresses your questions regarding the use of proton therapy for pediatric cancers.

Should you have any questions, please contact Jessica Adams, Health Policy Analyst (703) 839-7396 or via email at Jessica.adams@astro.org.

Regards,
Jessica

Jessica Adams, CCA
Health Policy Analyst
American Society for Radiation Oncology
251 18th Street South, 8th Floor
Arlington, VA 22202
703-839-7396 direct
703-502-1550 main
Jessica.Adams@astro.org
www.astro.org

July 18, 2018

Sue Birch
Director, Health Technology Assessment Program
P.O. Box 42712
Olympia, WA 98504-2712

Dear Director Birch:

The Advanced Medical Technology Association (AdvaMed), the national association of medical technology providers, is deeply concerned about the process involved with the Health Technology Assessment Program (program) as it relates to the current proceeding examining Proton Beam Therapy (PBT). We urge you to provide the public with more time to comment or extend the comment period so that the public can study these complex questions, develop thorough, comprehensive responses and meaningfully engage with program staff to best serve the interests of the program.

AdvaMed member companies produce the medical devices, diagnostic products, and health information systems that are transforming health care through earlier disease detection, less invasive procedures and more effective treatments. AdvaMed encourages public policies that assure patient access to the benefits of medical technology. AdvaMed has been very interested in Washington's health technology assessment program since its inception. During the legislative debate that led to the creation of the program and the assessment program's subsequent activities, AdvaMed has advocated for efforts to ensure transparency and adequate public comment.

AdvaMed appreciates the opportunity to provide comment on the draft key questions regarding the re-review of PBT by the Health Technology Assessment and the need to finalize this initial step in a timely manner. Although this proceeding considers only questions for consideration, the questions stand to deeply influence the program's ultimate conclusions and we urge the program to extend this and future comment periods to fall in line with other customary comment periods to ensure adequate public participation. For federal rulemaking 30-60 days is the normal minimum comment period. 180 days is provided for complex rules. California provides for a minimum comment period of 45 days for all rulemaking. However, the current public comment period for the PBT questions provides only 15 days, beginning with publication on July 3 and ending today, July 18. AdvaMed is concerned that this short comment period (just 10 business days) will limit the depth and value of public consideration and comment that may be provided to the program.

We understand that significant new evidence has become available since the initial review of PBT in 2014 and the current two-week public comment period fails to provide enough time to effectively respond to the draft key questions. AdvaMed respectfully requests a delay in the deadline for the public comment submissions to the draft key questions as we look to carefully and thoughtfully respond to the program's questions.

Thank you for considering our concerns. Please contact me if you have any questions.

Sincerely,

[redacted]

Fielding Greaves
Director, State Government & Regional Affairs

The National Association for Proton Therapy

MEMBERS
Ackerman Cancer Center
California Protons Cancer Therapy Center
Cincinnati Children's / UC Health Proton Therapy Center
Emory Proton Therapy Center
Georgetown Lombardi Comprehensive Cancer Center at Medstar Georgetown University Hospital
Hampton University Proton Therapy Institute
Inova Schar Cancer Institute Proton Therapy Center
James M. Slater, M.D. Proton Treatment and Research Center at Loma Linda University Medical Center
The Marjorie and Leonard Williams Center for Proton Therapy at Orlando Health UF Health Cancer Center
Maryland Proton Treatment Center
Mayo Clinic Proton Beam Therapy Program – Phoenix
Mayo Clinic Proton Beam Therapy Program – Rochester
MD Anderson Proton Therapy Center
Miami Cancer Institute at Baptist Health South Florida
New York Proton Center
Northwestern Medicine Chicago Proton Center
ProCure Proton Therapy Center – New Jersey
ProCure Proton Therapy Center – Oklahoma
Proton Therapy Center at Beaumont Hospital Cancer Institute
Provision CARES Proton Therapy Center – Knoxville
Provision CARES Proton Therapy Center – Nashville
The Roberts Proton Therapy Center at the University of Pennsylvania
Seattle Cancer Care Alliance Proton Therapy Center
S. Lee Kling Proton Therapy Center at the Siteman Cancer Center
Texas Center for Proton Therapy
University Hospitals Seidman Cancer Center, Case Medical Center
The University of Florida Health Proton Therapy Institute
Willis-Knighton Health System

8400 Westpark Drive, 2nd Fl.
McLean, VA 22102
(202) 495-3133
www.proton-therapy.org

VIA electronic mail to: shtap@hca.wa.gov

July 18, 2018

Re: Draft Key Questions for Proton Beam Therapy

Health Technology Assessment Program
Washington State Health Care Authority
626 8th Avenue • P.O. Box 45502
Olympia, WA 98504-5502

Dear Committee,

We thank you for the opportunity to submit comments regarding the Draft Key Questions for the 2019 Health Technology Assessment of Proton Beam Therapy. In this letter, we are submitting specific comments on the draft key questions as well as comments on the overall process and approach for the re-review of proton beam therapy.

By way of background, the National Association for Proton Therapy ("NAPT") is a nonprofit organization whose mission is to work collaboratively to: (i) educate and raise awareness of the clinical benefits of proton therapy among patients, providers, payers, policymakers, and other stakeholders, (ii) ensure patient choice and access to affordable proton therapy, and (iii) encourage cooperative research and innovation to advance the appropriate and cost-effective utilization of proton therapy for certain cancers. Its members – both hospital-based and freestanding – are world-renowned cancer centers, a number of whom are National Cancer Institute (NCI) designated comprehensive cancer centers and National Comprehensive Care Network (NCCN) members, including the Seattle Cancer Care Alliance Proton Therapy Center.

Specific Comments on "Draft Key Questions and Background"

- Technology of Interest
  - In this section, it was stated that "Because the proton beam is focused on a specific area, a greater dose of radiation may be delivered to the target neoplasm(s) while mitigating unwanted radiation delivered to surrounding tissue (Levin, 2005)." A critical benefit of proton beam therapy is its ability to treat tumors and reduce unnecessary radiation dose to critical organs and structures. As such, the last sentence in the first paragraph should be revised to state "PBT may be most promising to tumors in close proximity to organs at risk (OAR)."[1]

[1] The original language is as follows – "PBT may be most promising for tumors close to the body surface."

- Draft Key Questions
  - In reviewing the comparative effects of proton beam therapy compared to its major alternatives, the assessment should focus not only on the potential harms but also the potential advantages associated with this type of therapy. As such, we recommend the following language for Question 3 (with proposed changes in *red italicized* text):

    > What are the comparative *clinical advantages and* harms associated with the use of proton beam therapy relative to its major alternatives, including acute (i.e., within the first 90 days after treatment) and late (>90 days) toxicities, systemic effects such as fatigue and erythema, toxicities specific to each cancer type (e.g., bladder/bowel incontinence in prostate cancer, pneumonitis in lung or breast cancer), risks of secondary malignancy, and radiation dose?

  - In assessing the costs and cost-effectiveness of the therapy, it is important to examine not only the costs during the actual episode of care but also the potential longer term morbidity costs due to radiation exposure of healthy tissue. As such, we recommend the following language for Question 5:

    > What is the cost-effectiveness of proton beam therapy*, short- and long-term,* relative to *other radiation treatment modalities and* to radiation therapy alternatives or other cancer-specific treatment options (*e.g.*, surgery, chemotherapy)?

  - The evidence demonstrating the clinical benefits of proton beam therapy is evolving. As this occurs, different types of coverage models have been proposed and/or implemented to further develop the clinical evidence of proton beam technology. Aetna developed and proposed a Coverage with Evidence Development (CED) model that would extend coverage for patients enrolled on clinical trials that meet high levels of clinical evidence criteria. Another proton beam therapy coverage model implemented in 2016 between the State of Texas System and M.D. Anderson Cancer Center allowed coverage for employees and their dependents on the BlueCross BlueShield of Texas UT Select plan who are eligible for any of the center's clinical trials for patients with tumors of the breast, thorax, esophagus, head & neck, or GU. Additional coverage models have been proposed or implemented by the American Society of Radiation Oncology (ASTRO) and Medicare Administrative Contractors. We strongly recommend that a key question is added that examines these coverage models and others which provide proton beam coverage responsibly while continuing the research, collection, and on-going publication of clinical evidence.

- Proposed Inclusion and Exclusion
  - Under "Outcomes", we recommend adding "Patient Reported Outcomes" under the Secondary or Indirect (Intermediate) Measures as we believe that these types of outcomes are an important consideration.
  - Under "Study Design", we recommend the following modifications:
    - The draft indicates that case studies in adults with < 30 patients should be excluded from the assessment. However, in specific circumstances (*e.g.*, studies focusing on rare diseases (*e.g.*, thymoma)), such a study population is not practical or feasible. As such, these types of case studies should be allowed as an exception when reasonably warranted.
  - Under "Publications", we recommend the following types of publications for inclusion:

- NCCN Guidelines. The National Comprehensive Cancer Network (NCCN)[2] published guidelines are often used as the litmus test by payers for determining if they will approve coverage for all types of cancer treatments. Please keep in mind that the NCCN Guidelines most often consist of what is the current standard of care and often do not include emerging technologies until they have been demonstrated as becoming a standard of care. In the past, they have historically been silent on proton therapy but, over the last 24 months, the guidelines have become more encouraging in their comments about the use of proton therapy, embedding proton beam therapy in the guidelines for fourteen different disease sites including head & neck cancer.[3]
- Model policies from leading medical organizations. In 2017, the American Society for Radiation Oncology (ASTRO) released an updated proton beam model policy. These guidelines were promulgated by leaders in the field, many of whom do not have access to protons. The Alliance for Dedicated Cancer Centers (ADCC)[4], Particle Therapy Co-Operative Group - North America (PTCOG-NA)[5] and National Association for Proton Therapy have worked together through a consensus-based approach to draft and update its model policy; the last version of the model policy was released 2016.
- Coverage policies from other government agencies. The Medicare program is continuing to review and revise its coverage position on proton beam therapy. A number of Medicare Administrative Contractors ("MACs") have chosen to not have local coverage determinations ("LCDs"), given that these contractors have determined that proton therapy is "reasonable and necessary" for a number of cancers that afflict Medicare beneficiaries. A few MACs who still maintain local coverage determination policies have expanded their coverage for a number of indications in the last two years including Hodgkin's and B-Cell lymphomas, esophageal cancer, right side breast cancer, and high risk prostate cancers.
- Studies published that demonstrate toxicities to critical organs from radiation therapy techniques that are generally applicable and not specific to proton therapy. For example, Darby et al. assessed the risk of ischemic heart disease in women after radiotherapy for breast cancer[6].
- White papers that are assessments of the evidence on proton beam therapy generally or for specific disease sites.

---

[2] The NCCN is an alliance of 27 largely academic cancer centers in the U.S. of which most are designated as Comprehensive Cancer Centers by the National Cancer Institute.

[3] Guidelines that embedded proton beam therapy (as of July 17, 2018) include bone cancers, central nervous system cancers, esophageal and esophagogastric junction cancers, head and neck cancers, hepatobiliary cancers, Hodgkin Lymphoma, malignant pleural mesothelioma, uveal melanoma, Non-Hodgkin's Lymphoma (B-Cell and T-Cell), non-small cell lung cancer, prostate cancer, soft tissue sarcoma, and thymomas and thymic carcinomas.

[4] The Dedicated Cancer Centers were created in response to the National Cancer Act of 1971 which declared a War on Cancer. With a singular focus on cancer, the Alliance of Dedicated Cancer Centers' state- of-the-art therapies and research activities often offer the greatest possibility of successful cancer treatment. The ADCC institutions provide multi-disciplinary cancer care, including diagnostic, surgical, medical, chemotherapy and radiation treatment. A full list of ADCC members can be found at http://www.adcc.org/page/alliance-member-institutions.

[5] Particle Therapy Cooperative Group - North America (PTCOG – NA) is the North American chapter of an international non-profit scientific society. This professional membership society has been created to enhance collaboration between its members, create a platform for scientific exchange, and develop treatment guidelines, education, and training initiatives for particle therapy.

[6] Studies such as Darby SC, Ewertz M, and McGale P. Risk of Ischemic Heart Disease in Women after Radiotherapy for Breast Cancer. *NEJM*. 2013 Mar 14;368(11):987-98.

Overall Process and Approach

Proton beam radiotherapy is a very specific form of radiotherapy that requires specialized clinical training and experience. Clinicians using this modality must have a detailed understanding of the therapy and the type of patients where this treatment approach may or may not be clinically appropriate. A thorough review or assessment of the evidence on this type of technology requires well-informed engagement. We ask the Washington State Health Care Authority to strongly consider engaging a board-certified radiation oncologist with multiple years of clinical experience at an operating proton therapy center as part of the assessment. As a representative of the vast majority of operating proton beam therapy centers in the United States, the NAPT would willingly provide a list of physician candidates to serve in this capacity.

* * * * *

We appreciate your consideration of our feedback on the Key Draft Questions for the 2019 Health Technology Assessment of Proton Beam Therapy. Should you have any questions, please do not hesitate to contact me at the contact information provided below.

Respectfully submitted,

Scott Warwick
Executive Director
National Association for Proton Therapy
8400 Westpark Drive, 2nd Floor
McLean, VA 22102
swarwick@proton-therapy.org
Office – 202.495.3124
Mobile – 865.384.7636

Seattle Cancer Care Alliance
Fred Hutch · Seattle Children's · UW Medicine
Proton Therapy Center

July 18, 2018

Washington State Health Care Authority
Health Technology Clinical Committee
626 8th Avenue • P.O. Box 45502
Olympia, WA 98504-5502

Sent via email: shtap@hca.wa.gov

Re: Comments on Draft Key Questions and Background for Proton Beam Therapy Re-Review

Dear Committee:

We would like to thank the Washington State Health Care Authority for the opportunity to comment on the "Draft Key Questions and Background" for the re-review of proton beam therapy. With this letter, we are submitting comments regarding the process and approach of this review, as well as specific comments and edits concerning the draft key questions:

Process / Approach Comments

Proton beam therapy is a highly specialized form of radiotherapy that requires specialized clinical training and experience in order to use this modality for the treatment of cancer patients. As such, a thorough review of this methodology requires well-informed engagement including, but not limited to:

- The **enlistment of an ABR (American Board of Radiology) board-certified radiation oncologist with a minimum of 5 years of clinical experience at an operating proton center** to aid in the evidentiary review.

- The **engagement of experienced faculty from the University of Washington Department of Radiation Oncology** so that they can speak to the specific needs of the patient population in the state of Washington with respect to proton beam therapy. As you may know, there is only one operating proton center in the state of Washington (and broader Pacific Northwest), and this center is staffed solely by physicians from the University of Washington (UW), Department of Radiation Oncology who have no financial interest in the center.

- The **inclusion of dosimetric studies in your evidentiary review.** It should be noted that proton beam therapy is the standard of care for our most vulnerable patient population, pediatric cancer patients. The evidentiary basis for establishing proton beam therapy as the standard of care for treating children with cancer is dosimetric studies. (We do not have randomized trials in children, comparing standard radiation exposure to protons, because it would be unethical.) The **current clinical "gold" standard in Radiation Oncology is to perform a dosimetric comparison in order to identify the optimal radiotherapeutic modality for the treatment of a given patient.** Dosimetric comparisons are an essential part of clinical decision making and therefore it is standard practice to review dosimetric studies when evaluating treatment options for adults.

- The **inclusion of consensus-based treatment guidelines**, such as from the National Comprehensive Cancer Network, as part of the evidentiary support for your review. We would also recommend inclusion of **existing model policies from relevant medical societies and consensus-based organizations**, such as (1) the American Society for Radiation Oncology model policy for proton beam radiotherapy, and (2) the Alliance of Dedicated Cancer Centers, Particle Therapy Co-Operative Group, and National Association for Proton Therapy model policy for proton beam radiotherapy. We also respectfully request that your contracted reviewer engages with these and other key stakeholders (such as the National Cancer Institute and patient representatives) as part of their research and deliberative processes.

Specific, detailed comments to the "Draft Key Questions and Background" released on your website are enclosed in a red-lined version of the document that is included as Attachment 1.

We respectfully recommend the additions set forth in Attachment 1.

We look forward to working with the Health Technology Clinical Committee as they move forward in this important re-review of proton beam therapy.

Thanks again for allowing us to provide comments.

[redacted]

Ramesh Rengan MD PhD
Professor, University of Washington School of Medicine
Associate Member, Fred Hutchinson Cancer Research Center
Medical Director, SCCA Proton Therapy Center

[redacted]

Annika Andrews
President, SCCA Proton Therapy Center

Washington State Health Care Authority

Attachment 1
Comments included in Red, from Seattle Cancer Care Alliance Proton Therapy, dated July 18, 2018

Draft Key Questions and Background

Proton Beam Therapy – re-review

Comments accepted on the draft key questions until close of business, July 18, 2018

Background:

Clinical need and target population

Overall, it's estimated that 1.7 million new cases of cancer are diagnosed yearly and cancerous conditions are responsible for over half a million deaths per year. Treatment options for cancerous and noncancerous conditions vary depending on the type and stage of cancer and can include radiation therapy, chemotherapy, targeted therapy (e.g. inhibitor drugs), immunotherapy (including monoclonal antibodies) and surgery. In recent years the use of proton beam therapy (PBT) has expanded to include a variety of conditions including a number of cancer types, noncancerous brain tumors and cancerous conditions afflicting the central nervous system as well as eyes, lungs, liver, prostate, spine, and pelvis.

Technology of interest

The use of protons for radiotherapy has a history of over 60 years of clinical use. In conventional radiotherapy, photons deliver radiation across tissue depths on the way toward the target tumor and beyond. In contrast, PBT, which is a form of external beam radiotherapy, deposits peak radiation energy more precisely at or around the target followed by sharp decline in energy output to deeper tissues via a phenomenon known as the Bragg peak (Larsson, 1958). Because the proton beam is focused on a specific area, a greater dose of radiation may be delivered to the target neoplasm(s) while mitigating unwanted radiation delivered to surrounding tissue (Levin, 2005). PBT use was initially directed towards conditions where sparing sensitive adjacent normal tissues was considered to be of utmost importance (such as cancerous or noncancerous malformations of the brain stem, eye, or spinal cord) or for many pediatric tumors because of the particular risk of pronounced acute and long-term toxicity in pediatric patients (Thorp, 2010). PBT may be most promising for tumors in proximity to vital organs ~~close to the body surface~~.

In the past two decades, the number of centers offering PBT has increased to over 20, with more planned or under construction, even given the high cost of facility construction and operation. Despite increasing availability of PBT and its potential for precise delivery of radiation therapy, its effectiveness compared with other forms of therapy and with the emerging techniques, such as intensity modulated radiation therapy (IMRT) is evolving ~~unclear~~.

Policy context/reason for selection:

This topic was originally reviewed in 2014. It is being re-reviewed in 2018 due to newly available published evidence.

Objectives

The aim of this report is to update the 2014 HTA on proton beam therapy (PBT) by systematically reviewing, critically appraising and analyzing new research evidence on the safety and efficacy of PBT, as a primary or as a salvage therapy (i.e., for recurrent disease or failure of initial therapy), for the treatment of multiple cancer types, as well as selected noncancerous conditions in adults and children.

DRAFT key questions (from previous report):

1. What is the comparative impact of proton beam therapy (PBT) treatment with curative intent on survival, disease progression, health-related quality of life, and other patient outcomes versus radiation therapy alternatives and other cancer-specific treatment options (e.g., surgery, chemotherapy) for the following conditions:
    a. Cancers
        i. Bone tumors
        ii. Brain, spinal, and paraspinal tumors
        iii. Breast cancer
        iv. Esophageal cancer
        v. Gastrointestinal cancers
        vi. Gynecologic cancers
        vii. Head and neck cancers (including skull base tumors)
        viii. Liver cancer
        ix. Lung cancer
        x. Lymphomas
        xi. Ocular tumors
        xii. Pediatric cancers (e.g., medulloblastoma, retinoblastoma, Ewing's sarcoma)
        xiii. Prostate cancer
        xiv. Soft tissue sarcomas
        xv. Seminoma
        xvi. Thymoma
        xvii. Other cancers
    b. Noncancerous Conditions
        i. Arteriovenous malformations
        ii. Hemangiomas
        iii. Other benign tumors (e.g., acoustic neuromas, pituitary adenomas)
2. What is the comparative impact of salvage treatment (including treatment for recurrent disease) with proton beam therapy versus major alternatives on survival, disease progression, health-related quality of life, and other patient outcomes versus radiation therapy alternatives and other cancer-specific treatment options (e.g., surgery, chemotherapy) for the condition types listed in key question 1?

3. What are the comparative clinical advantages and harms associated with the use of proton beam therapy relative to its major alternatives, including acute (i.e., within the first 90 days after treatment) and late (>90 days) toxicities, systemic effects such as fatigue and erythema, toxicities specific to each cancer type (e.g., bladder/bowel incontinence in prostate cancer, pneumonitis in lung or breast cancer), risks of secondary malignancy, and radiation dose?

4. What is the differential effectiveness and safety of proton beam therapy according to factors such as age, sex, race/ethnicity, disability, presence of comorbidities, tumor characteristics (e.g., tumor volume and location, proliferative status, genetic variation) and treatment protocol (e.g., dose, duration, timing of intervention, use of concomitant therapy)?

5. What is the comparative cost-effectiveness of proton beam therapy when accounting for both the short- and long-term morbidity cost of excess radiation exposure to normal tissue, relative to radiation therapy alternatives and other cancer-specific treatment options (e.g., surgery, chemotherapy,)?

6. What current models exist for payer partnership and coverage agreements, including coverage with evidence development?[1]

Draft scope based on previous report key questions:

PROPOSED inclusion and exclusion

Study Component	Inclusion	Exclusion
Population	Adults and children undergoing treatment of primary or recurrent disease to include: • Cancers (bone, brain/spinal/paraspinal, breast, esophageal, gastrointestinal, gynecologic, head and neck, liver, lung, ocular, pediatric, and prostate cancers; lymphomas, sarcomas, seminomas, thymomas, other cancers) • Noncancerous conditions (arteriovenous malformations, hemangiomas, other benign tumors)	• Conditions not amenable to proton-beam therapy or for which proton beam therapy would be contra-indicated
Interventions	Proton beam therapy (PBT) use as a • Curative therapy • Primary or monotherapy • "Salvage" treatment (e.g. following failure of initial therapy or disease recurrence) • "Boost" mechanism to conventional radiation • Combination therapy with other treatments (e.g., chemotherapy, surgery)	• Non-FDA cleared devices/therapies
Comparator	• Other radiation therapy alternatives (e.g.,	• Technologies or treatments that

[1] There are challenges to obtaining the clinical data required to determine the true and most effective value of proton therapy for our patients. In addition, there are existing models that work well in other regions.

Study Component	Inclusion	Exclusion
	intensity-modulated radiation therapy (IMRT), stereotactic radiation techniques ~~and~~ other external beam therapies, ~~and~~ brachytherapy, and immunotherapy) • Other treatment alternatives specific to each condition type treated; may include chemotherapy, surgical procedures, and other devices (e.g., laser therapy for ocular tumors) • Dose/fractionation comparison (will be included for completeness as was done in prior report) but not formally evaluated as evidence	are not widely available or are no longer routinely used • Non-FDA cleared devices/therapies
Outcomes	**Clinical outcomes**: <u>Primary</u> • Overall survival/disease-free survival • All-cause and/or disease-related mortality • Direct measures of tumor regression, control or recurrence • Incidence of metastases <u>Secondary or indirect (intermediate) measures</u> • Health-related quality of life (HrQoL) • Patient Reported Outcomes (PRO) • Requirements for subsequent therapy • Other outcomes specific to particular conditions (e.g., visual acuity for ocular tumors, shunt requirements for arteriovenous malformations) • Intermediate measures of recurrence such as biochemical measures **Safety outcomes**: • Treatment-related harms, with a focus on adverse effects requiring medical attention, to include: ♦ Generalized effects (e.g., fatigue, erythema) ♦ Localized toxicities specific to each condition (e.g., urinary incontinence in prostate cancer, pulmonary toxicity in lung or breast cancer) to include consideration of: ▪ Early (≤90 days post-treatment) ▪ Late (>90 days post-treatment) • Secondary malignancy risk due to radiation exposure **Economic outcomes**:	• Non-clinical outcomes

Study Component	Inclusion	Exclusion
	• Long term and short-term comparative cost-effectiveness measures (e.g. ICER)	
Study Design	• Dosimetry, planning, and simulation studies.[2] • Focus will be on high quality (low risk of bias) comparative studies for questions 1-4 • Case series will be considered but will not be the primary focus of evaluation for each key question • Case series in children with <10 patients will be considered if no comparative studies are available • Case series designed specifically to evaluate safety may be included • Formal, full economic studies will be sought for question 5. Studies using modeling may be used to determine cost-effectiveness	• ~~Dosimetry, planning, and simulation studies~~ • Studies of low quality (high risk of bias) • Comparative studies with fewer than 10 per treatment arm • Case reports • Case series in adults with <30 patients unless disease populations reasonably warrant exceptions (e.g., rare diseases)[3] • Studies comparing modes of therapy; dose comparisons may be included for completeness/context per previous report
Publication	• Studies published in English in peer reviewed journals, technology assessments or publically available FDA reports • Studies published subsequent to the 2014 report (previous report search date through February 2014), unless studies published prior to 2014 are of highest quality of evidence and were omitted from the previous report • For question 5, full formal economic analyses (e.g., cost-effectiveness, cost-utility studies) published in English in a peer reviewed journal • Studies published that demonstrate toxicities to critical organs from standard radiation therapy techniques (e.g. *Risk of Ischemic Heart Disease in Women after Radiotherapy for Breast Cancer*, Darby et al. NEJM) • **Guidelines** including the National Comprehensive Cancer Network (NCCN) guidelines, where protons are embedded within disease-specific guidelines for	• ~~Abstracts, editorials, letters~~ • Duplicate publications of the same study that do not report different outcomes or follow-up times • Single reports from multicenter trials • ~~White papers~~ • Narrative reviews • Articles identified as preliminary reports when full results are published in later versions • Incomplete economic evaluations such as costing studies

[2] Payors uniformly require dosimetric comparison data in order to substantiate approval for protons and other advanced radiation modalities. Further, we perform these dosimetric comparisons on a daily basis in order to determine the best approach for the patient (one set of critical organ constraints vs. another, IMRT vs. 3D-CRT, etc.). The fundamental tenet of radiation oncology is to minimize radiation exposure to normal tissue. Dosimetric analyses represent the only current standard available to quantify that exposure to guide clinical decision making. Therefore, we feel that these represent core data that should be utilized in your review.

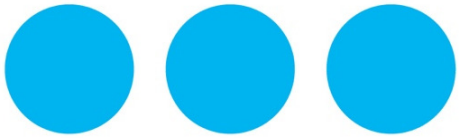
[3] Because of the rarity of certain diseases, it is not practical to study large populations. Exceptions should be made to be able to best represent special populations.

Study Component	Inclusion	Exclusion
	radiation oncology treatment • **Model Policies** from leading medical institutions including o American Society for Radiation Oncology (ASTRO) o Alliance of Dedicated Cancer Centers, Particle Therapy Co-Operative Group and National Association for Proton Therapy o **Coverage Policies** of other Government agencies (e.g., Medicare), commercial payers	

Public comment and response

Submit comments to the HTA program at shtap@hca.wa.gov.

For additional information on public comments.



Varian Medical Systems
3100 Hansen Way
Palo Alto, CA 94304
650.493.4000
800.544.4636
varian.com

July 18, 2018

Sue Birch
Director
Health Technology Assessment Program
P.O. Box 42712
Olympia, WA 98504-2712

Re: Re-review of the Health Technology Assessment Program's Proton Beam Therapy Technology Assessment

Dear Director Birch:

Varian Medical Systems is the world's leading supplier of radiotherapy products for treating cancer. Our products include medical linear accelerators, simulators, proton therapy systems, and a broad range of accessories and interconnected software tools for planning, verifying, and delivering the most advanced radiation, radiosurgical, and brachytherapy treatments. Our electronic medical record facilitates efficient management of treatment for patients undergoing medical or radiation (including proton) therapies. Varian has in-depth knowledge of the significant benefits that radiation therapy, particularly proton beam therapy (PBT) in certain indications, provides to the health of Americans.

Varian appreciates the opportunity to comment on the draft key questions regarding the re-review of PBT by the Health Technology Assessment Program. However, Varian is concerned about the quick turnaround to provide thoughtful comments to the draft key questions published on July 3, 2018. As new evidence has become available since the initial review of PBT in 2014, we do not feel as though the two-week public comment period provides enough time to effectively respond to the draft key questions. Varian respectfully requests a delay in the deadline for the public comment submissions to the draft key questions as we look to carefully and thoughtfully respond to the Health Technology Assessment's questions.

As previously submitted by Varian, new clinical evidence has become available since the publication of the 2014 Findings and Decision and we again attach the American Society for Radiation Oncology's (ASTRO) Model Policies: Proton Beam Therapy (PBT) approved in June 2017 and the National Association for Proton Therapy's (NAPT) Model Policy: Coverage of Proton Beam Therapy published in March 2015.

The attached model policies from ASTRO and NAPT provide new clinical data which support the benefits of PBT for additional indications not covered in the 2014 Findings and Decision. We strongly encourage coverage of PBT of these additional indications, as well as coverage of all other indications not specified as covered under the 2014 Findings and Decision when the patient is enrolled in a clinical trial and/or registry as there is a need for additional clinical evidence regarding the appropriate use of PBT for various disease sites.

Varian appreciates your consideration on this matter and again, we request a delay in the deadline for the public comment submission to the key draft questions. We look forward to working with you in the future on this and other issues.

varian

Sincerely,

[redacted]

Deepak Khuntia, MD
Senior Vice President and Chief Medical Officer
Varian Medical Systems

Attachments: American Society for Radiation Oncology (ASTRO). Model Policies: Proton Beam Therapy (PBT). ASTRO: June 2017.
National Association for Proton Therapy (NAPT). Model Policy: Coverage of Proton Beam Therapy. NAPT: March 30, 2015.