

04-77260-18

Original Effective Date: 06/15/02

Reviewed: 12/07/23

Revised: 12/15/23

Subject: Proton Beam Therapy

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

[Position Statement](#)

[Billing/Coding](#)

[Reimbursement](#)

[Program Exceptions](#)

[Definitions](#)

[Related Guidelines](#)

[Other](#)

[References](#)

[Updates](#)

DESCRIPTION:

Proton beams are charged particle beams used as an alternative to conventional x-rays, gamma-rays, and other types of photon irradiation in the treatment of malignancies. Proton beam therapy requires specialized equipment in the form of accelerators (cyclotrons, synchrotrons, synchrocyclotrons, or linear accelerators) that can generate a beam of proton particles. Accurate localization of the malignancy by using tomographic scanning (with x-ray and/or magnetic resonance imaging), and precise and reproducible positioning (relative to the beam) and immobilization of the body during both tomographic scanning and treatment is also required. This type of radiation therapy allows for minimal scatter as particulate beams pass through tissue and dispose ionizing energy at precise depths (i.e., the Bragg peak), thereby minimizing tissue damage around the area being treated.

Proton beam therapy has been found to be useful in the treatment of tumors that are localized and have not spread to distant areas of the body and are not amenable to surgical excision or other conventional forms of radiation treatment. This includes tumors that are in close proximity to vital structures, which make surgery or conventional radiation therapy difficult or impossible. Because proton beam therapy can be used to precisely focus radiation on specific areas with little exposure to adjacent tissues, proton beam may be useful for treatment of tumors located near radio-sensitive structures. Proton beam therapy can be given with or without stereotactic techniques. Stereotactic approaches are frequently used for uveal and skull based tumors. Like conventional radiation therapy, proton beam therapy treatments may be delivered in a few days or up to several weeks.

Coverage for proton beam therapy is subject to the member's benefit terms, limitations and maximums. The member's contract language must be reviewed to determine coverage for proton beam therapy. Please note, this policy contains a specific "Comparative Effectiveness" coverage analysis section for Proton Beam Therapy in the treatment of Prostate Cancer. For Florida Blue policies with a definition of

Medical Necessity that contains the comparative effectiveness language, coverage for Proton Beam Therapy will be determined through application of the Comparative Effectiveness section of this medical policy.

POSITION STATEMENT:

NOTE: Coverage for proton beam therapy is subject to the member’s benefit terms, limitations and maximums. Some contracts may exclude coverage for proton beam therapy. Refer to specific contract language to determine coverage. Medical records may be required to be submitted for medical review.

NOTE: For member contracts that include comparative effectiveness language, the relative cost of proton beam therapy compared to other forms of treatment may be considered in the medical necessity determination as more particularly described in the section below entitled Comparative Effectiveness Analysis.

While proton beam therapy has been used for cancer treatment, there is limited published clinical evidence demonstrating its clinical benefit over conventional forms of radiation therapy (e.g., IMRT, brachytherapy). Because proton therapy is generally more costly than alternative therapies, comparative effectiveness evidence is needed on the safety, benefits, and health outcomes compared to other conventional forms of radiation therapy.

The intent of proton beam therapy is curative, with an expectation of a long-term benefit (greater than 2 years).

Proton beam therapy **meets the definition of medical necessity** for the following indications:

Central Nervous System	
Arteriovenous Malformation (AVM)	Proton beam therapy meets the definition of medical necessity for AVM the following: <ul style="list-style-type: none"> Intracranial AVM not amenable to surgical excision or other conventional forms of treatment; OR Intracranial AVM adjacent to critical structures such as the optic nerve, brain stem or spinal cord
Central Nervous System (CNS) Tumors	Proton beam therapy meets the definition of medical necessity for CNS tumors for the following: <p>Primary or metastatic CNS malignancies, including, but not limited to gliomas (Note: ALL of the following criteria must be met.):</p> <ul style="list-style-type: none"> When adjacent to critical structures such as the optic nerve, brain stem, or spinal cord; AND When other standard radiation techniques such as IMRT or standard stereotactic modalities would not reduce the risk of radiation damage to the critical structure
Base of Skull Tumors	

Chordoma/Chondrosarcoma	<p>Proton beam therapy meets the definition of medical necessity for chordoma, chondrosarcoma for the following:</p> <ul style="list-style-type: none"> As postoperative therapy for members who have undergone biopsy or partial resection of a chordoma or low-grade (I or II) chondrosarcoma of the basisphenoid region (e.g., skull-base chordoma or chondrosarcoma), cervical spine, or sacral/lower spine and have residual, localized tumor without evidence of metastasis
Sinonasal Cancer	<p>Proton beam therapy meets the definition of medical necessity for locally advanced sinonasal carcinoma for the following:</p> <ul style="list-style-type: none"> Tumor involves the base of skull and proton therapy is needed to spare the orbit, optic nerve, optic chiasm or brainstem
Head and Neck Cancers	<p>Proton beam therapy meets the definition of medical necessity for head and neck cancers for the following:</p> <p>Where treatment planning with conventional or advanced photon-based radiotherapy cannot meet dose-volume constraints for normal tissue radiation tolerance.</p>
Hepatocellular Carcinoma (HCC) and Intrahepatic Cholangiocarcinoma	<p>Proton beam therapy meets the definition of medical necessity for hepatocellular carcinoma for the following:</p> <ul style="list-style-type: none"> To treat unresectable hepatocellular carcinoma (HCC) or intrahepatic cholangiocarcinoma with curative intent when there is no evidence of metastatic disease.
Melanoma (Ocular Melanoma)	<p>Proton beam therapy meets the definition of medical necessity for ocular melanoma for the following:</p> <ul style="list-style-type: none"> To treat melanoma of the uveal tract (including the iris, choroid, or ciliary body) and no evidence of metastasis or extrascleral extension
Solid Tumors in Children	<p>Proton beam therapy meets the definition of medical necessity for solid tumors in children below age 18 in which radiation therapy is required.</p>
Other	<p>Proton beam therapy meets the definition of medical necessity for the following indications when ALL of the below criteria (a, b, c, and d) are met:</p> <ul style="list-style-type: none"> Benign or malignant conditions involving the base of the skull or axial skeleton Left breast tumors Lung cancer Malignant lesions of liver Peri-diaphragmatic cancer Unresectable extremity sarcoma

	<ul style="list-style-type: none"> • Unresectable retroperitoneal sarcoma • Upper abdominal cancer <p>Criteria</p> <ol style="list-style-type: none"> a) The disease is primary and non-metastatic, that is confined regionally to the primary organ (including regional lymph nodes); AND b) Dosimetric treatment planning comparisons between IMRT and proton beam therapy have been made; AND c) Dosimetric treatment planning with IMRT predicts the radiation dose to adjacent organs would be exceeded; AND d) Dosimetric treatment planning with proton beam therapy is able to reduce adjacent organ radiation exposure to a safe level
<p>Prostate Cancer</p>	<p>Note: With regard to the use of proton beam therapy for prostate cancer, even if the use of proton beam therapy meets the general medical necessity criteria below, then coverage is subject to the additional analysis of the comparative effectiveness, if applicable, in accordance with the section below entitled <u>Comparative Effectiveness Analysis for Proton Beam Therapy in the Treatment of Prostate Cancer</u>.</p> <p>Proton beam therapy meets the definition of medical necessity for the treatment of prostate cancer when the below medical necessity criteria are met.</p> <p>Either #1, #2, OR #3 must be present; AND</p> <p>Either #4 OR #5 must be present; AND</p> <p>#6 must always be present.</p> <ol style="list-style-type: none"> 1. When dose constraints to normal tissues limit the total dose of radiation safely deliverable to the tumor with other indicated methods. 2. When there is a reason to believe that doses generally thought to be above the level otherwise attainable with other methods might improve control rates. 3. In circumstances when the higher levels of precision associated with proton beam therapy as compared to other radiation methods are necessary (e.g., clinically relevant). 4. For the treatment of primary lesions, the intent of treatment must be curative. 5. For the treatment of metastatic lesions, there must be: <ul style="list-style-type: none"> • The expectation of a long-term benefit (> 2y) that could not have been attained with conventional therapy.

	<ul style="list-style-type: none"> • The expectation of a complete eradication of the metastatic lesion that could not have been safely accomplished with conventional therapy, as evidenced by a dosimetric advantage for proton beam radiotherapy over other forms of radiation therapy. <p>6. The member’s record must demonstrate why proton beam therapy is considered the treatment of choice for the member. Specifically, the notes in the member’s medical record must address the lower risk to normal tissue, the lower risk of disease recurrence, and the advantages of the treatment over IMRT or 3-dimensional conformal radiation. Dosimetric evidence of reduced normal tissue toxicity and/or improved tumor control must be maintained as part of the member’s medical record (the medical record may be requested as part of the review process).</p> <p>7. Florida Blue strongly supports (but does not require) *ASTRO’s recommendation that members with prostate cancer being treated with Proton Beam Therapy enroll either in an Institutional Review Board (IRB) approved clinical trial or in a multi-institutional patient registry, for evidence development. Documentation in the member’s medical record must note the reason why the member is unable to enroll in either an Institutional Review Board (IRB) approved clinical trial or in a multi-institutional patient registry for evidence development.</p> <p>As an alternative to meeting the seven (1-7) factors above, the treatment will be considered to meet the definition of medical necessity and meeting the first six (1-6) factors above if the member is enrolled in an IRB approved clinical trial or in a multi-institutional patient registry treated in a protocol that is designed for evidence development for proton beam therapy for prostate cancer treatment.</p>
Re-irradiation	Proton beam therapy meets the definition of medical necessity for the repeat irradiation of previously treated fields where the dose tolerance of surrounding normal structures would be exceeded with 3D conformal radiation or IMRT.

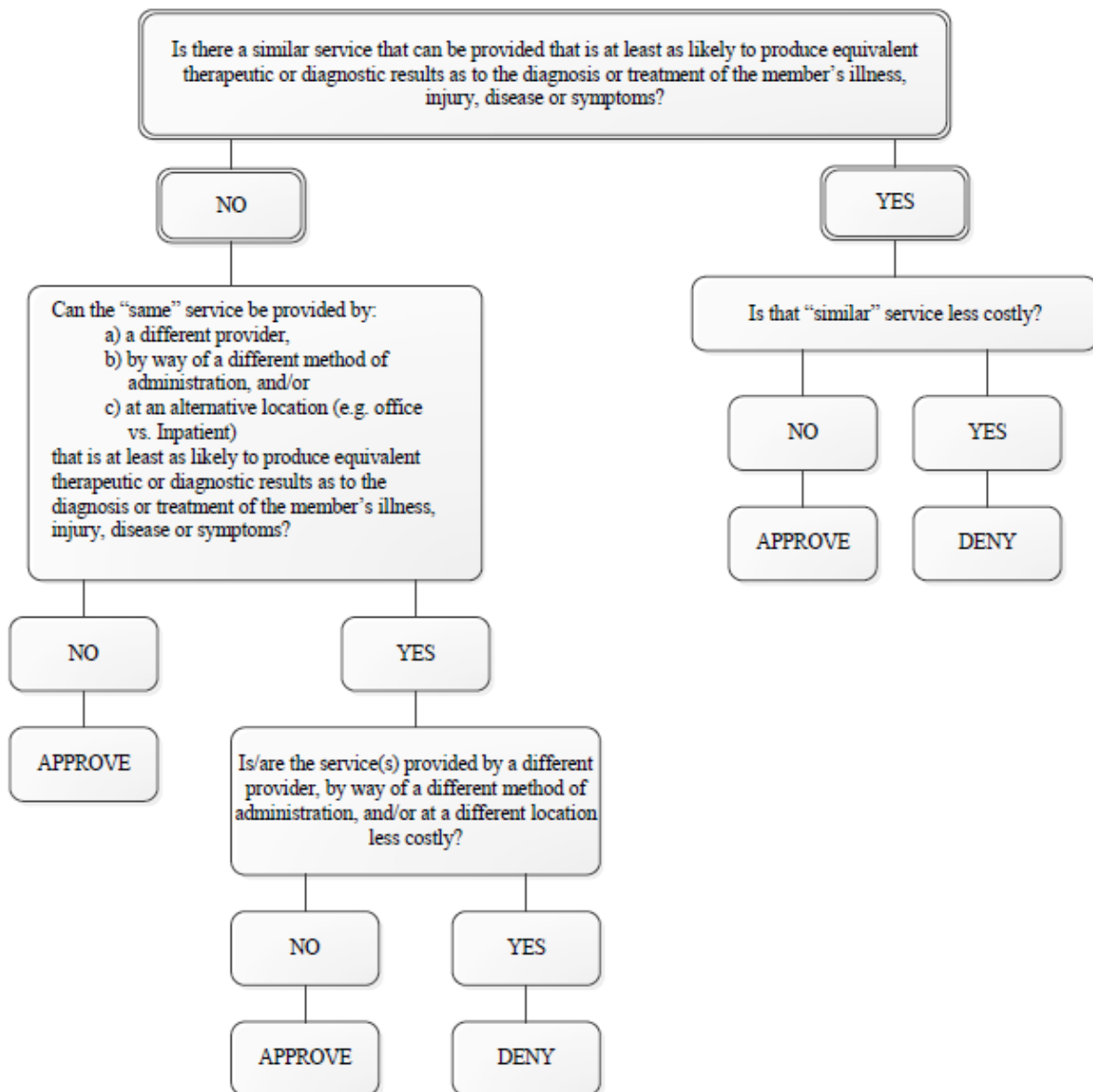
For **all other indications** not listed above, proton beam therapy is considered **experimental or investigational**, as there is insufficient evidence to support conclusions regarding the effect of proton beam therapy on health outcomes.

*American Society for Radiation Oncology (ASTRO)

COMPARATIVE EFFECTIVENESS ANALYSIS:

This section only applies to member contracts that contain a comparative effectiveness analysis within the definition of Medical Necessity. This may apply to member contracts that were issued or renewed on or after January 1, 2014.

If a service meets the medical necessity criteria set forth above in the Position Statement, then an analysis under this comparative effectiveness section should be applied, solely for coverage and payment purposes. Initially, this analysis should determine if: 1.) There is an alternate service available that produces the same or similar outcomes and/or 2.) The same service as requested or performed can be rendered at a different location of service. If there is no alternative service that produces the same or similar outcomes nor is there a different location at which the services could be rendered, then no further comparative effectiveness analysis need be completed and the service will be deemed to have met the definition of medical necessity. If, however, there are alternative services that produce the same or similar outcomes and/or there is a different location of service at which the services can be rendered, then a comparative effectiveness analysis must be conducted to determine if: a.) The same service rendered at a different location; or b.) An alternate service(s) is/are less costly. If the answer is yes, then the requested service does satisfy the requirements of this comparative effectiveness analysis and does not meet the medical necessity requirements for coverage and payment purposes. The comparative effectiveness analysis is represented by the following flowchart:



Application of Comparative Effectiveness Analysis for Proton Beam Therapy for the Treatment of Prostate Cancer

- A. Is there a similar service that can be provided that is at least as likely to produce equivalent therapeutic or diagnostic results?

For those services that meet the criteria described above in the Position Statement, yes. Proton beam therapy for the treatment of prostate cancer is merely one of many different treatments for prostate cancer. Several forms of radiation treatment alone (e.g., intensity modulated radiation therapy (IMRT), brachytherapy) are available for treatment of prostate cancer. Florida Blue, after analysis, has determined that these alternative forms of services are:

- 1.) Similar to proton beam therapy and;

- 2.) Proton beam therapy has not been documented to have equivalent or better outcomes with regard to the treatment of prostate cancer than such alternative services.

With regard to prostate cancer, there is limited published clinical evidence of proton beam demonstrating clinical equivalence or benefit over conventional forms of radiation therapy (e.g., IMRT, brachytherapy) or surgical treatments for prostate cancer. There is a need for more well-designed registries and studies with sizable comparator cohorts for data collection. As a result, there is no clinical documentation demonstrating the safety, benefits, and health outcomes compared to other conventional forms of radiation therapy or, more generally, other forms of treatment for prostate cancer.

For required documentation, refer to the [REIMBURSEMENT INFORMATION](#) section of this guideline.

BILLING/CODING INFORMATION:

CPT Coding:

Proton Delivery

77520	Proton beam delivery; simple, without compensation
77522	Proton beam delivery; simple with compensation
77523	Proton beam delivery; intermediate
77525	Proton beam delivery; complex

Planning

77295	3-dimensional radiotherapy plan, including dose-volume histograms (3D conformal treatment plan)
77301	Intensity modulated radiotherapy plan, including dose-volume histograms for target and critical structure partial tolerance specifications

HCPCS Coding:

S8030	Scleral application of tantalum ring(s) for localization of lesions for proton beam therapy
-------	---------------------------------------------------------------------------------------------

ICD-10 Diagnosis Codes That Support Medical Necessity:

C11.0 – C11.9	Malignant neoplasm of nasopharynx
C30.0	Malignant neoplasm of nasal cavity
C31.0 – C31.9	Malignant neoplasm of accessory sinuses
C41.2	Malignant neoplasm of vertebral column
C41.4	Malignant neoplasm of pelvic bones, sacrum and coccyx
C41.9	Malignant neoplasm of bone and articular cartilage, unspecified
C69.30	Malignant neoplasm of unspecified choroid
C69.40	Malignant neoplasm of unspecified ciliary body
C69.90	Malignant neoplasm of unspecified site of unspecified eye

C71.0 – C71.9	Malignant neoplasm of brain
C72.0 – C72.1	Malignant neoplasm of spinal cord, cranial nerves and other parts of central nervous system
C72.20 – C72.22	Malignant neoplasm of olfactory nerve
C72.30 – C72.32	Malignant neoplasm of optic nerve
C72.40 – C72.42	Malignant neoplasm of acoustic nerve
C72.50 – C72.59	Malignant neoplasm of unspecified cranial nerve
C72.9	Malignant neoplasm of central nervous system, unspecified
C79.31	Secondary malignant neoplasm of brain
C79.49	Secondary malignant neoplasm of other parts of nervous system
D09.8	Carcinoma in situ of other specified sites
D33.0 – D33.9	Benign neoplasm of brain and other parts of central nervous system
D42.0 – D42.9	Neoplasm of uncertain behavior of meninges
D43.0 – D43.9	Neoplasm of uncertain behavior of brain and central nervous system
D49.6	Neoplasm of unspecified behavior of brain
Q28.2	Arteriovenous malformation of cerebral vessels
Q28.3	Other malformations of cerebral vessels

LOINC Codes:

The following information may be required documentation to support medical necessity: physician history and physical, physician progress notes, plan of treatment and reason for proton beam therapy.

Documentation Table	LOINC Codes	LOINC Time Frame Modifier Code	LOINC Time Frame Modifier Codes Narrative
Physician history and physical	28626-0	18805-2	Include all data of the selected type that represents observations made six months or fewer before starting date of service for the claim
Attending physician progress note	18741-9	18805-2	Include all data of the selected type that represents observations made six months or fewer before starting date of service for the claim
Plan of treatment	18776-5	18805-2	Include all data of the selected type that represents observations made six months or fewer before starting date of service for the claim

REIMBURSEMENT INFORMATION:

Refer to section entitled [POSITION STATEMENT](#).

Required Documentation

The medical record may be requested as part of the review process.

The primary treating physician MUST submit the following information for the member:

- Documentation which supports one or more condition as noted under the position statement section of this guideline that meets the definition of medical necessity or that may be considered in the medical necessity determination.
- The member's record must demonstrate why proton beam therapy is considered the treatment of choice for the member. Specifically, the notes in the member's medical record must address the lower risk to normal tissue, the lower risk of disease recurrence, and the advantages of the treatment over IMRT or 3-dimensional conformal radiation.
- Treatment prescription that defines the goals of the member's treatment plan, including specific dose-volume parameters for the target and nearby critical structures, details of beam delivery (e.g., method of beam modulation, field arrangement, expected positional and range uncertainties).
- Treatment plan signed by the treating physician that meets the prescribed dose-volume parameters for the clinical target volume (CTV) and surrounding organs at risk (OARs).
- Description of the target setup verification methodology, including member's positioning, immobilization and use of image guidance.
- Verification of planned dose distribution via independent dose calculation or physical assessment.
- Dosimetric evidence of reduced normal tissue toxicity and/or improved tumor control must be maintained as part of the member's medical record.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Advantage products: The following Local Coverage Determination (LCD) was reviewed on the last guideline review date: Proton Beam Radiotherapy, (L33937) located at fcso.com.

DEFINITIONS:

Adjacent: near close or adjoining.

Benign: not cancerous. Benign tumors may grow larger but do not spread to other parts of the body. Also called nonmalignant.

Central nervous system (CNS) tumors (children): masses of abnormal cells in the brain or spinal cord that have grown out of control. Examples of CNS tumors in children (e.g., glioma, craniopharyngioma, infratentorial, ependymoma, medulloblastoma).

Craniopharyngioma: a rare, benign (not cancer) brain tumor that usually forms near the pituitary gland and the hypothalamus. Craniopharyngiomas are slow-growing and do not spread to other parts of the brain or to other parts of the body. However, they may grow and press on nearby parts of the brain, including the pituitary gland, hypothalamus, optic chiasm, optic nerves, and fluid-filled spaces in the brain. This may cause problems with growth, vision, and making certain hormones. Craniopharyngiomas usually occur in children and young adults.

Conventional forms of treatment (AVM): includes (e.g., surgery, embolization, radiation therapy, stereotactic radiosurgery).

Conventional forms of treatment (prostate cancer): includes (e.g., surgery, chemotherapy, radiation therapy).

Dosimetry: the calculation of the radiation dose to be delivered to the tumor. The physician chooses the energy level and modality of photon or electron beams to be used for each simulated port, even if only one treatment area is concerned. Once the tentative treatment fields have been determined, the dosimetry of the treatment portals can be calculated. Special dosimetry uses measuring and monitoring devices when the physician deems it necessary to calculate the total amount of radiation that a patient has received at any given point. The results determine whether to uphold or alter the current treatment plan.

Extrascleral extension: occurring outside of the scleral or orbit (eye).

IRB (Institutional Review Board): a group of individuals (e.g., scientists, physicians, clergy, patient advocates) that reviews and approves the detailed plan for clinical trials.

Malignant: cancerous. Malignant tumors can invade and destroy nearby tissue and spread to other parts of the body.

Metastatic: having to do with metastasis, which is the spread of cancer from the primary site (place where it started) to other places in the body.

Nonmalignant (non-metastatic): not cancerous. Nonmalignant tumors may grow larger but do not spread to other parts of the body. Also called benign.

Plaque brachytherapy: an eye and vision-sparing method to treat patients with intraocular tumors.

Regional: in oncology, describes the body area right around a tumor.

Solid tumor: an abnormal mass of tissue that usually does not contain cysts or liquid areas. Solid tumors may be benign (not cancer), or malignant (cancer). Different types of solid tumors are named for the type of cells that form them (e.g., sarcomas, carcinomas, and lymphomas). Examples of solid tumors in children (e.g., brain tumor, neuroblastoma, rhabdomyosarcoma, Wilms' tumor, osteosarcoma).

Stereotactic modalities: Stereotactic radiosurgery (SRS), stereotact body radiotherapy (SBRT).

Tumor: a new growth of tissue in which the multiplication of cells is uncontrolled and progressive; also called neoplasm (benign or malignant).

RELATED GUIDELINES:

None applicable.

OTHER:

Other names used to report proton beam:

Charged Particle Radiation Therapy

Charged Particle Radiotherapy

Hadron therapy

Helium Ion Radiation Therapy
Particle Beam Therapy
Proton Beam Radiation Therapy
Proton Beam Radiotherapy
Proton Radiation Therapy
Proton Radiotherapy
Proton Therapy

REFERENCES:

1. ASTRO Proton Beam Therapy (PBT) Model Policy, June 2017.
2. ACR–ASTRO Practice Guideline for the Performance of Proton Beam Radiation Therapy, Amended 2014.
3. Allen AM, Pawlicki T, Dong L et al. An evidence-based review of proton beam therapy: the report of ASTRO's emerging technology committee. *Radiotherapy and Oncology* 2012, 103(1): 8-11.
4. Al-Shahi R, Warlow CP. Interventions for Treating Brain Arteriovenous Malformations in Adults. *The Cochrane Database of Systematic Review* 2006, Issue 1. Art. No.: CD003436.pub2. DOI: 10.1002/14651858. CD003436.pub2.
5. American Brachytherapy Society consensus guidelines for plaque brachytherapy of uveal melanoma and retinoblastoma The American Brachytherapy Society - Ophthalmic Oncology Task Force, 2013.
6. Archambeau JO, Slater JD, Slater JM et al. Role for Proton Beam Irradiation in Treatment of Pediatric CNS Malignancies. *International Journal of Radiation Oncology Biology Physics* 1992; 22(2): 287-294.
7. Arimoto T, Kitagawa T, Tsujii H et al. High-Energy Proton Beam Radiation Therapy for Gynecologic Malignancies. *Cancer* 1991; 68 (1): 79-83.
8. Austin-Seymour M, Lunzenrider J, Goiten M et al. Fractionated Proton Radiation Therapy of Chordoma and Low-Grade Chondrosarcoma of the Base of the Skull. *Journal of Neurology* 1989; 70(1): 13-17.
9. Austin-Seymour M, Munzenrider J, Goitein M et al. Fractionated Proton Radiation Therapy of Chorodoma and Low-Grade Chondrosarcoma of the Base of the Skull. *Journal of Neurosurgery* 1989; 70: 13-17.
10. American Society of Radiation Oncology (ASTRO) Proton Beam Therapy Model Policy, 05/20/14.
11. Austin-Seymour M, Munzenrider J, Goitein M et al. Fractionated Proton Radiation Therapy of Cranial and Intracranial Tumors. *American Journal of Clinical Oncology* 1990; 13(4): 327-330.
12. Australia and New Zealand Horizon Scanning Network-Technology Assessment-Proton Beam Therapy for the Treatment of Cancer, June 2006 [Cochrane Database].
13. Beltran C, Roca M, Merchant TE. On the benefits and risks of proton therapy in pediatric craniopharyngioma. *International Journal of Radiation Oncology, Biology, Physics* 2012; 82(2): e281-e287.
14. Badiyan SN, Rutenberg MS, Hoppe BS et al. Clinical outcomes of patients with Recurrent lung cancer reirradiated with proton therapy on the Proton Collaborative Group and University of Florida Proton Therapy Institute Prospective Registry Studies. *Pract Radiat Oncol.* 2019 Jul-Aug;9(4):280-288 [Abstract].
15. Bishop AJ, Greenfield B, Mahajan A et al. Proton beam therapy versus conformal photon radiation therapy for childhood craniopharyngioma: multi-institutional analysis of outcomes, cyst dynamics, and toxicity. *International Journal of Radiation Oncology, Biology, Physics* 2014; 90(2): 354-361.

16. Blue Cross Blue Shield Association Evidence Positioning System®. 8.01.10 Charged-Particle (Proton or Helium Ion) Radiotherapy for Neoplastic Conditions, 06/23.
17. Bonnet RB, Bush D, Cheek GA et al. Effects of Proton and Combined Proton/Photon Beam Radiation on Pulmonary Function in Patients with Resectable but Medically Inoperable Non-small Cell Lung Cancer. *Chest* 2001(current as of 05/22/06); 120(6): 1803-1810.
18. Brada M Pijls-Johannesma M, De Ruyscher D. Proton therapy in clinical practice: current clinical evidence. *Journal of Clinical Oncology* 2007; 25(8): 965-970.
19. Bryant C, Smith TL, Henderson RH et al. Five-Year Biochemical Results, Toxicity, and Patient-Reported Quality of Life After Delivery of Dose-Escalated Image Guided Proton Therapy for Prostate Cancer. *International Journal of Radiation Oncology, Biology, Physics* 2016; 95(1): 422-434.
20. Bush DA, McAllister CJ, Loreda LN et al. Fractionated Proton Beam Radiotherapy for Acoustic Neuroma. *Neurosurgery* 2002; 50(2): 270-275.
21. Bush DA, Slater JD, Bonnet R et al. Proton-Beam Radiotherapy for Early-Stage Lung Cancer. *Chest* 1999; 116(5): 1313-1319.
22. Bush DA, Slater JD, Shin BB et al. Hypofractionated Proton Beam Radiotherapy for Stage I Lung Cancer. *Chest* 2004; 126(4): 1198-1203.
23. Chang JY, Liu HH, Komaki R. *Current Oncology Reports* 2005; 7:255-259.
24. Chiba T, Tokuuye K, Matsuzaki Y et al. Proton Beam Therapy for Hepatocellular Carcinoma: A Retrospective Review of 162 Patients. *Clinical Cancer Research* 2005; 11(10): 3799-3805.
25. Clair WH, Adams JA, Bues M et al. Advantage of Protons Compared to Conventional X-Ray or IMRT in the Treatment of a Pediatric Patient with Medulloblastoma. *International Journal of Radiation Oncology Biology Physics* 2004; 58 (3): 727-734.
26. Colaco RJ, Hoppe BS, Flampouri S et al. Rectal toxicity after proton therapy for prostate cancer: an analysis of outcomes of prospective studies conducted at the university of Florida Proton Therapy Institute. *International Journal of Radiation Oncology, Biology, Physics* 2015; 91(1): 172-181.
27. Courdi A, Caujolle JP, Grange JD et al. Results of Proton Therapy of Uveal Melanomas Treated in Nice. *International Journal of Radiation Oncology, Biology, Physics* 1999; 45(1): 5-11.
28. Dagan R, Bryant C, Li Z, et al. Outcomes of Sinonasal Cancer Treated with Proton Therapy. *Int J Radiat Oncol Biol Phys*. 2016 May 1;95(1): 377-385. [Abstract]
29. Dagan R, Uezono H, Bryant C, et al. Long-term Outcomes from Proton Therapy for Sinonasal Cancers. *Int J Part Ther*. 2021 Jun 25;8(1): 200-212.
30. DeLaney TF, Trofimov AV, Engelsman M et al. Advanced-Technology Radiation Therapy in the Management of Bone and Soft Tissue Sarcomas. *Cancer Control* 2005; 12(1): 27-35.
31. Fan M, Kang JJ, Lee A, et al. Outcomes and toxicities of definitive radiotherapy and reirradiation using 3-dimensional conformal or intensity-modulated (pencil beam) proton therapy for patients with nasal cavity and paranasal sinus malignancies. *Cancer*. 2020 Jan 1;126(9): 1905-1916.
32. First Coast Services Options, Inc. LCD for Proton Beam Radiotherapy (L33937), 12/16/19.
33. Fitzek M M, Thornton AF, Rabinov JD et al. Accelerated Fractionated Proton/Photon Irradiation to 90 Cobalt Gray Equivalent for Glioblastoma Multiforme: Results of a Phase II Prospective Trial. *Journal of Neurosurgery* 1999; 91: 251-260.
34. Fitzek MM, Linggood RM, Adams J et al. Combined Proton and Photon Irradiation for Craniopharyngioma: Long-Term Results of the Early Cohort of Patients Treated at Harvard Cyclotron Laboratory and Massachusetts General Hospital. *International Journal of Radiation Oncology, Biology, Physics* 2006; 64(5): 1348-1354.

35. Fitzek MM, Thornton AF, Harsh G et al. Dose-Escalation with Proton/Photon Irradiation for Daumas-Duport Lower-Grade Glioma: Results of an Institutional Phase I/II Trial. *International Journal of Radiation Oncology, Biology, Physics* 2001; 51(1):131-137.
36. Fontenot JD, Lee AK, Newhauser WD. Risk of secondary malignant neoplasms from proton therapy and intensity-modulated x-ray therapy for early-stage prostate cancer. *International Journal of Radiation Oncology, Biology, Physics* 2009; 74(2): 616-622.
37. Frank SJ, Blanchard P, Lee JJ et al. Comparing intensity-modulated proton therapy with intensity-modulated photon therapy for oropharyngeal cancer: the journey from clinical trial concept to activation. *Semin Radiat Oncol.* 2018;28(2):108-113.
38. Fu KK, Pajak TF, Trotti A et al. A Radiation Therapy Oncology Group (RTOG) Phase III Randomized Study to Compare Hyperfractionation and Two Variants of Accelerated Fractionation to Standard Fractionation Radiotherapy for Head and Neck Squamous Cell Carcinomas: First Report of RTOG 9003. *International Journal of Radiation Oncology, Biology, Physics* 2000; 48(1): 7-16.
39. Fuss M, Hug EB, Schaefer RA et al. Proton Radiation Therapy (PRT) for Pediatric Optic Pathway Gliomas: Comparison with 3D Planned Conventional Photons and a Standard Photon Technique. *International Journal of Radiation Oncology, Biology, Physics* 1999; 45(5): 117-1126.
40. Goitein M. Should randomized clinical trials be required for proton radiotherapy? *Journal of Clinical Oncology* 2008; 26(2): 175-176.
41. Gragoudas ES, Lane AM. Uveal Melanoma: Proton Beam Irradiation. *Ophthalmology Clinics of North America* 2005; 18(1): 111-118.
42. Grewal AS, Schonewolf C, Min EJ, et al. Four-Year Outcomes from a Prospective Phase II Clinical Trial of Moderately Hypofractionated Proton Therapy for Localized Prostate Cancer. *Int J Radiat Oncol Biol Phys.* 2019 Nov 15;105(4):713-722. [Abstract]
43. Gunn GB, Blanchard P, Garden AS, et al. Clinical outcomes and patterns of disease recurrence after intensity modulated proton therapy for oropharyngeal squamous carcinoma. *Int J Radiat Oncol Biol Phys* 2016;95(1):360-367.
44. Hall EJ. Intensity-modulated radiation therapy, protons, and the risk of second cancers. *International Journal of Radiation Oncology Biology Physics* 2006; 65(1): 1-7.
45. Hata M, Miyanaga N, Tokuyue K et al. Proton Beam Therapy for Invasive Bladder Cancer: A Prospective Study of Bladder-Preserving Therapy with Combined Radiotherapy and Intra-Arterial Chemotherapy. *International Journal of Radiation Oncology, Biology, Physics* 2006; 64(5): 1371-1379.
46. Hata M, Tokuyue K, Kagei K et al. Hypofractionated high-dose proton beam therapy for stage I non-small-cell lung cancer: preliminary results of a phase I/II clinical study. *International Journal of Radiation Oncology, Biology, Physics* 2007; 68 (3): 786-793.
47. Hata M, Tokuyue K, Sugahara S et al. Proton Beam Therapy for Hepatocellular Carcinoma with Limited Treatment Options. *Cancer* August 2006; 107(3): 591-598.
48. Hata M, Tokuyue K, Sugahara S et al. Proton Beam Therapy for Hepatocellular Carcinoma with Limited Treatment Options. *Cancer* August 2005; 104(4): 794-801.
49. Henderson RH, Bryant C, Hoppe BS, et al. Five-year outcomes from a prospective trial of image-guided accelerated hypofractionated proton therapy for prostate cancer. *Acta Oncol.* 2017 Jul;56(7):963-970.
50. Henderson RH, Hoppe BS, Marcus RB et al. Urinary functional outcomes and toxicity five years after proton therapy for low- and intermediate-risk prostate cancer: results of two prospective trials. *Acta Oncologica* 2013; 52(3): 463-469.
51. Holliday EB, Kocak-Uzel E, Feng L, et al. Dosimetric advantages of intensity-modulated proton therapy for oropharyngeal cancer compared with intensity-modulated radiation: A case-matched control analysis. *Med Dosim.* 2016 Autumn;41(3):189-94. [Abstract]

52. Hoppe BS, Michalski JM, Mendenhall NP et al. Comparative effectiveness study of patient-reported outcomes after proton therapy or intensity-modulated radiotherapy for prostate cancer. *Cancer* 2014; 120(7): 1076-1082.
53. Hoppe BS, Nichols RC, Henderson RH et al. Erectile function, incontinence, and other quality of life outcomes following proton therapy for prostate cancer in men 60 years old and younger. *Cancer* 2012; 118(18): 4619-4626.
54. Hughes JR, Parsons JL. FLASH Radiotherapy: Current Knowledge and Future Insights Using Proton-Beam Therapy. *Int J Mol Sci.* 2020 Sep 5;21(18):6492.
55. Igaki H, Tokuyue K, Okumura T et al. Clinical Results of Proton Beam Therapy for Skull Base Chordoma. *International Journal of Radiation Oncology, Biology, Physics* 2004; 60(4): 1120-1126.
56. Indelicato DJ, Bradley JA, Rotondo RL, et al. Outcomes following proton therapy for pediatric ependymoma. *Acta Oncol* 2018;57(5):644-648.
57. Indelicato DJ, Rotondo RL, Uezono H, et al. Outcomes following proton therapy for pediatric low-grade glioma. *Int J Radiat Oncol Biol Phys* 2019; 23:23.
58. Jereczek-Fossa BA, Krengli M, Orecchi R. Particle Beam Radiotherapy for Head and Neck Tumors: Radiobiological Basis and Clinical Experience. *Head and Neck* 2006; 28(8): 750-760.
59. Kaeashima M, Furuse J, Nishio T et al. Phase II Study of Radiotherapy Employing Proton Beam for Hepatocellular Carcinoma. *Journal of Clinical Oncology* 2005; 23(9): 1839-1846.
60. Kahalley LS, Douglas Ris M, Mahajan A et al. Prospective, longitudinal comparison of neurocognitive change in pediatric brain tumor patients treated with proton radiotherapy versus surgery only. *Neuro Oncol.* 2019 Jun 10;21(6):809-818.
61. Kil WJ, Nichols RC, Hoppe BS et al. Hypofractionated passively scattered proton radiotherapy for low- and intermediate-risk prostate cancer is not associated with post-treatment testosterone suppression. *Acta Oncologica* 2013; 52(3): 492-497.
62. Kim JK, Leeman JE, Riaz N, et al. Proton Therapy for Head and Neck Cancer. *Curr Treat Options Oncol.* 2018 May 9;19(6):28. [Abstract]
63. Kline NE, Sevier N. Solid tumors in children. *Journal of Pediatric Nursing* 2003 Apr; 18(2): 96-102.
64. Kodjikian L, Roy P, Rouberol F et al. Survival After Proton-Beam Irradiation of Uveal Melanomas. *American Journal of Ophthalmology* 2004; 137(6): 1002-1010.
65. Kong FS. What happens when proton meets randomization: is there a future for proton therapy? *J Clin Oncol* 2018; 36(18): 1777-1779.
66. Konski A, Speier W, Hanlon A et al. Is proton beam therapy cost effective in the treatment of adenocarcinoma of the prostate? *Journal of Clinical Oncology* 2007; 25(24): 3603-3608.
67. Koyama S, Tsujii H. Proton Beam Therapy with High-Dose Irradiation for Superficial and Advanced Esophageal Carcinomas. *Clinical Cancer Research* 2003; 9: 3571-3577.
68. Liao Z, Lee JJ, Komaki R et al. Bayesian adaptive randomization Trial of passive scattering proton therapy and intensity-modulated photon radiotherapy for locally advanced non-small-cell lung cancer. *J Clin Oncol.* 2018;36(18):1813-1822.
69. Lin SH, Hobbs BP, Verma V, et al. Randomized Phase IIB Trial of Proton Beam Therapy Versus Intensity-Modulated Radiation Therapy for Locally Advanced Esophageal Cancer. *J Clin Oncol.* 2020 May 10;38(14):1569-1579.
70. Mak AC, Morrison WH, Garden AS et al. Base-Of-Tongue Carcinoma: Treatment Results Using Concomitant Boost Radiotherapy. *International Journal of Radiation Oncology, Biology, Physics* 1995; 33(2): 289-296.
71. Matsuzaki Y, Osuga T, Saito Y et al. A New, Effective, and Safe Therapeutic Option Using Proton Irradiation for Hepatocellular Carcinoma. *Gastroenterology* 1994; 106:1032-1041.

72. McAllister B, Archambeau JO, Nguyen MC et al. Proton Therapy for Pediatric Cranial Tumors: Preliminary Report on Treatment and Disease-Related Morbidities. *International Journal of Radiation Oncology Biology Physics* 1997; 39(2): 455-460.
73. McDonald MW, Liu Y, Moore MG et al. Acute toxicity in comprehensive head and neck radiation for nasopharynx and paranasal sinus cancers: cohort comparison of 3D conformal proton therapy and intensity modulated radiation therapy. *Radiat Oncol* 2016; 11:32.
74. McGee L, Mendenhall NP, Henderson RH et al. Outcomes in men with large prostates (≥ 60 cm³) treated with definitive proton therapy for prostate cancer. *Acta Oncologica* 2013; 52(3): 470-476.
75. Mendenhall NP, Hoppe BS, Nichols RC et al. Five-year outcomes from 3 prospective trials of image-guided proton therapy for prostate cancer. *International Journal of Radiation Oncology, Biology, Physics* 2014; 88(3): 596-602.
76. Mendenhall NP, Li Z, Hoppe BS et al. Early outcomes from three prospective trials of image-guided proton therapy for prostate cancer. *International Journal of Radiation Oncology, Biology, Physics* 2012; 82(1): 213-221.
77. Mendenhall NP, Malyapa RS, Su Z, Yeung D et al. Proton therapy for head and neck cancer: rationale, potential indications, practical considerations, and current clinical evidence. *Acta Oncologica* 2011 Aug; 50(6): 763-71.
78. Mohan R, Grosshans D. Proton therapy - Present and future. *Adv Drug Deliv Rev.* 2017 Jan 15;109: 26-44.
79. Mutter RW, Choi JI, Jimenez RB, et al. Proton Therapy for Breast Cancer: A Consensus Statement from the Particle Therapy Cooperative Group Breast Cancer Subcommittee. *Int J Radiat Oncol Biol Phys.* 2021 Oct 1;111(2):337-359.
80. Valery R, Mendenhall NP, Nichols RC et al. Hip fractures and pain following proton therapy for management of prostate cancer. *Acta Oncologica* 2013; 52(3): 486-491.
81. Mendenhall WM, Mendenhall CM, Lewis SB et al. Skull Base Chordoma. *Head and Neck* 2005; 27(2): 159-165.
82. Miralbell R, Lomax A, Russo M. Potential Role of Proton Therapy in the Treatment of Pediatric Medulloblastoma/Primitive Neuro-Ectodermal Tumors: Spinal Theca Irradiation. *International Journal of Radiation Oncology, Biology, Physics* 1997; 38(4): 805-811.
83. Moreno AC, Frank SJ, Garden AS et al. Intensity modulated proton therapy (IMPT)-the future of IMRT for head and neck cancer. *Oral Oncol* 2019; 88-66-74.
84. Nakajima K, Iwata H, Ogino H, et al. Clinical outcomes of image-guided proton therapy for histologically confirmed stage I non-small cell lung cancer. *Radiat Oncol* 2018;13(1):199.
85. Nakayama H, Sugahara S, Tokita M et al. Proton beam therapy for hepatocellular carcinoma: the University of Tsukuba experience. *Cancer* 2009; 115(23): 5499-5506.
86. National Brain Tumor Society Tumor Types: Understanding Brain Tumors, 2017.
87. National Cancer Institute Childhood Craniopharyngioma Treatment (PDQ®) Health Professional Version, Updated: Sept 28, 2017.
88. National Cancer Institute Prostate Cancer Treatment (PDQ®) Health Professional Version, Updated: Sept 20, 2019.
89. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Breast Cancer, Version 1.2019.
90. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Head and Neck Cancer Version 1.2024.
91. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Non-Small Cell Lung Cancer, Version 5.2019.

92. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Prostate Cancer, Version 4.2019.
93. Neff B, Thayer RT, Storey L et al. Chondrosarcoma of the Skull Base. *Laryngoscope* 2002 January; 112(1): 134-139.
94. Nguyen PL, Trofimov A, Zietman AL. Proton-beam vs intensity-modulated radiation therapy. Which is best for treating prostate cancer? *Oncology* 2008; 22(7): 748-54; discussion 754-757.
95. Nihel K, Ogino T, Ishikura S et al. High-Dose Proton Beam Therapy for Stage I Non-Small-Cell Lung Cancer. *International Journal of Radiation Oncology, Biology, Physics* 2006; 65(1): 107-111.
96. Olsen DR, Bruland OS, Frykholm G et al. Proton therapy: A systematic review of clinical effectiveness. *Radiotherapy and Oncology* 2007; 83(2): 123-132.
97. Pan HY, Jiang J, Hoffman KE, et al. Comparative toxicities and cost of intensity-modulated radiotherapy, proton radiation, and stereotactic body radiotherapy among younger men with prostate cancer. *J Clin Oncol* 2018;36(18):1823-1830.
98. Phan J, Sio TT, Nguyen TP, et al. 2016. Reirradiation of Head and Neck Cancers with Proton Therapy: Outcomes and Analyses. *Int J Radiat Oncol Biol Phys*. 2016 Sep 1;96(1):30-41. [Abstract]
99. Pollack IF. Pediatric Brain Tumors. *Seminars in Surgical Oncology* 1999; 16:73-90.
100. Pommier P, Liebsch NJ, Deschier D G et al. Proton Beam Radiation Therapy for Skull Base Adenoid Cystic Carcinoma. *Archives of Otolaryngology-Head & Neck Surgery* 2006 Nov; 132(11): 1242-1249.
101. Prostate Cancer National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology, Version 2.2014.
102. Romesser PB, Cahlon O, Scher ED, et al. Proton beam reirradiation for recurrent head and neck cancer: multi-institutional report on feasibility and early outcomes. *Int J Radiat Oncol Biol Phys* 2016;95(1):386-395.
103. Romesser PB, Cahlon O, Scher ED, et al. Proton beam radiation therapy results in significantly reduced toxicity compared with intensity-modulated radiation therapy for head and neck tumors that require ipsilateral radiation. *Radiother Oncol*. 2016;118(2):286-92.
104. Saw CB, Celi JC, Huq MS. *Therapeutic Radiation Physics Primer*. *Hematology Oncology Clinics of North America* 2006; 20: 25-43.
105. Schulte RW, Fargo RA, Meinass HJ et al. Analysis of Head Motion Prior to and During Proton Beam Therapy. *International Journal of Radiation Oncology, Biology, Physics* 2000; 47(4): 1105-1110.
106. Semenova J. Proton beam radiation therapy in the treatment of pediatric central nervous system malignancies: a review of the literature. *Journal of Pediatric Oncology Nursing* 2009; 26(3): 142-149.
107. Sheets NC, Goldin GH, Meyer AM et al. Intensity-modulated radiation therapy, proton therapy, or conformal radiation therapy and morbidity and disease control in localized prostate cancer. *JAMA* 2012; 307(15): 1611-1620.
108. Shipley WU, Verhey Lj, Munzenrider JE et al. Advanced Prostate Cancer: The Results of a Randomized Comparative Trial of High Dose Irradiation Boosting with Conformal Protons Compared with Conventional Dose Irradiation Using Photons Alone. *International Journal of Radiation Oncology, Biology, Physics* 1995; 32(1): 3-12.
109. Silander H, Pellettieri L, Enbald P et al. Fractionated, Stereotactic Proton Beam Treatment of Cerebral Arteriovenous Malformations. *Acta Neurologica Scandinavica* 2004; 109(2): 85-90.
110. Sio TT, Lin HK, Shi Q et al. Intensity modulated proton therapy versus intensity modulated photon radiation therapy for oropharyngeal cancer: first comparative results of patient-reported outcomes. *Int J Radiat Oncol Biol Phys* 2016;95(4):1107-1114.
111. Slater, JD. Clinical Applications of Proton Radiation Treatment at Loma Linda University: Review of a Fifteen-Year Experience. *Technology in Cancer Research and Treatment* April 2006; 5(2): 81-89.

112. Smith AR. Vision 20/20: Proton therapy. *Medical Physics* 2009; 36(2): 556-568.
113. Smith RP, Heron DE, Huq MS, et al. Modern Radiation Treatment Planning and Delivery-From Rontgen to Real Time. *Hematology Oncology Clinics of North America* 2006; 20: 45-62.
114. Soares HP, Kumar A, Daniels S et al. Evaluation of New Treatments in Radiation Oncology-Are They Better Than Standard Treatment? *Journal of the American Medical Association* 2005; 293(8): 970-978.
115. Suit H, Kooy H, Trofimov A et al. Should positive phase III clinical trial data be required before proton beam therapy is more widely adopted? No. *Radiotherapy and Oncology* 2008; 86(2): 148-153.
116. Tatsuzaki H, Urie MM, Linggod R. Comparative Treatment Planning: Proton vs. X-ray Beams Against Glioblastoma Multiforme. *International Journal of Radiation Oncology, Biology, Physics* 1992; 22(2): 265-273.
117. The National Association for Proton Therapy: Proton Therapy Fact Sheet, 2016.
118. Trofimov A, Nguyen PL, Coen JJ et al. Radiotherapy treatment of early-stage prostate cancer with IMRT and protons: a treatment planning comparison. *International Journal of Radiation Oncology, Biology, Physics* 2007; 69(2): 444-453.
119. Trikalinos TA, Terasawa T, Ip S, et al. Particle Beam Radiation Therapies for Cancer. Technical Brief No. 1. (Prepared by Tufts Medical Center Evidence-based Practice Center under Contract No. HHS-290-07-10055.) Rockville, MD: Agency for Healthcare Research and Quality. Revised November 2009.
120. Tsujii H, Tsuji H, Inada T et al. Clinical Results of Fractionated Proton Therapy. *International Journal of Radiation Oncology Biology Physics* 1993; 25(1): 49-60.
121. Wambersie A, Gregoire V, Brucher JM. Potential Clinical Gain of Proton (and Heavy Ion) Beams for Brain Tumors in Children. *International Journal of Radiation Oncology, Biology, Physics* 1992; 22(2): 275-286.
122. Wang L, Fossati P, Paganetti H, et al. The Biological Basis for Enhanced Effects of Proton Radiation Therapy Relative to Photon Radiation Therapy for Head and Neck Squamous Cell Carcinoma. *Int J Part Ther.* 2021 Jun 25;8(1):3-13.
123. Weber DC, Lomax AJ, Rutz HP et al. Spot-Scanning Proton Radiation Therapy for Recurrent Residual or Untreated Intracranial Meningiomas. *Radiotherapy & Oncology* 2004; 71(3): 251-258.
124. Wenkel E, Thornton AF, Finkelstein D et al. Benign Meningioma: Partially Resected, Biopsied and Recurrent Intracranial Tumors Treated with Combined Proton and Photon Radiotherapy. *International Journal of Radiation Oncology, Biology, Physics* 2000; 48(5): 1363-1369.
125. Wilt TJ, Shamliyan T, Taylor B, et al Comparative Effectiveness of Therapies for Clinically Localized Prostate Cancer. Comparative Effectiveness Review No. 13. (Prepared by Minnesota Evidence-based Practice Center under Contract No. 290-02-0009.) Rockville, MD: Agency for Healthcare Research and Quality, February 2008.
126. Yang P, Xu T, Gomez DR, et al. Patterns of local-regional failure After intensity modulated radiation therapy or passive scattering proton therapy with concurrent chemotherapy for non-small cell lung cancer. *Int J Radiat Oncol Biol Phys.* 2019 Jul;103(1):123-131.
127. Yee D, Halperin R, Hanson J et al. Phase I Study of Hypofractionated Dose-Escalated Thoracic Radiotherapy for Limited-Stage Small-Cell Lung Cancer. *International Journal of Radiation Oncology, Biology, Physics* 2006; 65(2): 466-473.
128. Yu JB, Soulos PR, Herrin J et al. Proton versus intensity-modulated radiotherapy for prostate cancer: patterns of care and early toxicity. *Journal of the National Cancer Institute* 2013; 105(1): 25-32.

129. Zietman AL, DeSilvio ML, Slater JD et al. Comparison of Conventional-Dose vs High-Dose Conformal Radiation Therapy in Clinically Localized Adenocarcinoma of the Prostate. Journal of the American Medical Association (JAMA) 2005; 294(10): 1233-1239.
130. Zurlo A, Lomax A Hoess A et al. The Role of Proton Therapy in the Treatment of Large Irradiation Volumes: A Comparative Planning Study of Pancreatic and Biliary Tumors. International Journal of Radiation Oncology, Biology, Physics. 2000; 48(1): 277-88.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Medical Policy and Coverage Committee on 12/7/23.

06/15/02	Reviewed; proton beam delivery information separated from Radiation Treatment Delivery and Radiation Treatment Management MCG; added one additional diagnosis code.
07/15/03	Annual review. Added rationale to support investigational statement.
01/15/04	Added S8030, and updated references.
09/15/04	Scheduled review, and updated references.
06/15/05	Scheduled review. Revised when services are covered. Added localized prostate cancer to the when services are covered. Revised when services are not covered. Added ICD-9 diagnosis 185 (malignant neoplasm of the prostate). Added charge particle radiation therapy and helium ion radiation therapy to the other section, and updated references.
04/15/07	Deleted "Radiation" from MCG title. Revised WHEN SERVICES ARE COVERED; expanded covered indications to include: intraocular melanomas, benign or malignant conditions involving the base of the skull or axial skeleton, including but not limited to chordomas and chondrosarcomas, benign or malignant central nervous system tumors, including primary and variant forms of medulloblastoma, astrocytoma, glioblastoma, arteriovenous malformations, acoustic neuroma, craniopharyngioma, benign and atypical meningiomas and pineal gland tumors, solid tumors in children, malignant lesions of the head and neck, malignant lesions of the para nasal sinus, and other accessory sinuses, malignant advanced state-non-metastatic tumors of the bladder, advanced pelvic tumors, malignant lesions of the cervix, left breast tumors, adrenal tumors, skin cancer with perineural/cranial nerve invasion, unresectable retroperitoneal sarcoma, unresectable extremity sarcoma, lung cancer, upper abdominal cancer, peridiaphragmatic cancer, malignant lesions of liver, malignant lesions of biliary tract, malignant lesions of anal canal, and malignant lesions of rectum. Expanded ICD-9 diagnoses for proton beam therapy to include: 141.0, 142.0, 142.1, 142.2, 143.0, 143.1, 144.0 – 144.9, 145.0 – 145.9, 146.0 – 146.9, 147.0 – 147.9, 148.0 – 148.9, 149.0, 149.1, 154.0 – 154.8, 155.0 – 155.2, 157.0 – 157.9, 158.0, 160.0 – 160.9, 161.0 – 161.9, 162.0 – 162.9, 164.0, 164.1, 164.2, 164.3, 170.0 – 170.9, 171.0 – 171.9, 173.0 – 173.9, 174.0 – 174.6, 180.0 – 180.8, 183.0, 184.0, 188.0 – 188.9, 189.0, 190.0 – 190.9, 191.0 – 191.9, 192.0, 192.1, 192.2, 192.3, 192.8, 193, 194.1, 194.3, 194.4, 195.1, 195.2, 195.3, 197.0, 197.7, 198.3, 225.0-225.8, 227.3, 227.4, 237.0, 237.1, 237.5, 237.6, and 747.81. Revised code descriptor for 198.5. Added guideline specific definitions. Added Charged Particle Radiotherapy and Proton Beam Radiotherapy to OTHER section, and updated references.

06/15/07	Reformatted guideline.
04/15/08	Scheduled review. Revised experimental or investigational statement, and updated references.
04/15/09	Scheduled review. No change in position statements, and updated references.
08/15/10	Revised position statement, deleted malignant advanced state, non-metastatic tumors of the bladder, advanced pelvic tumors, malignant lesions of the cervix, pancreatic tumors, adrenal tumors, skin cancer with perineural/cranial nerve invasion, upper abdominal cancer, malignant lesions of: biliary tract, anal canal, and rectum. Deleted ICD-9 diagnoses codes: 141.0, 142.0, 142.1, 142.2, 143.0, 143.1, 144.0 – 144.9, 145.0 – 145.9, 146.0 – 146.9, 147.0 – 147.9, 148.0 – 148.9, 149.0, 149.1, 154.0 – 154.8, 157.0 – 157.9, 164.0, 164.1, 164.2, 164.3, 171.0 – 171.9, 173.0 – 173.9, 180.0 – 180.8, 183.0, 184.0, 188.0 – 188.9, 189.0, 193, 194.1, 195.1, 195.2, and, 195.3. Added program exception for Medicare Advantage products; covered indications and ICD-9 codes that support medical necessity. Updated references.
02/01/11	Revision; related ICD-10 codes added.
10/15/11	Annual review; maintain position statements. Added uveal tract (iris, ciliary body, choroid) to intraocular melanomas). Added definition for axial skeleton. Updated references.
05/01/16	Revision; updated description, added medical necessity criteria for: benign or malignant conditions involving the base of the skull or axial skeleton, left breast tumors, lung cancer, malignant lesions of liver, peri-diaphragmatic cancer, unresectable extremity sarcoma, unresectable retroperitoneal sarcoma, and upper abdominal cancer; added medical necessity position statement and criteria for prostate cancer, added comparative effectiveness analysis statement and flowchart; added comparative effective analysis statement for proton beam therapy for the treatment of prostate cancer, updated ICD-10 codes; updated program exception; added LOINC codes; updated references.
08/15/16	Updated program exceptions.
12/15/16	Revision; updated references.
02/15/18	Review; revised position statement. Added position statement for central nervous system (CNS) tumors in children. Updated definitions and references.
11/10/19	Revision; added sinonasal cancer and criteria for locally advanced sinonasal carcinoma, when tumor involves base of skull and proton beam therapy is needed. Deleted tumor size restrictions for ocular melanoma of the uveal tract, pediatric central nervous system tumors and proton beam therapy and IMRT statement. Added ICD-10 diagnosis code: (C11.0-C11.9, C30.0, C31.0-C31.9). Added CPT code (77301, 77295). Updated research summary and references.
03/15/21	Review/revision. Added hepatocellular carcinoma (HCC), intrahepatic cholangiocarcinoma and criteria. Solid tumors in children: Added radiation therapy. Updated references.
05/15/23	Review; no change in position statement. Updated references.
12/15/23	Review; added head and neck cancers. Updated references.