MEDICAL POLICY

MEDICAL POLICY DETAILS	
Medical Policy Title	**Proton Beam Radiation Therapy**
Policy Number	**6.01.11**
Category	**Technology Assessment**
Original Effective Date	**10/18/01**
Committee Approval Date	**10/18/01, 07/18/02, 07/17/03, 06/17/04, 05/18/05, 03/16/06, 01/18/07, 12/20/07, 01/15/09, 03/18/10, 03/17/11, 02/16/12, 02/21/13, 02/20/14, 06/19/14, 02/19/15, 04/21/16, 06/15/17, 04/19/18, 05/16/19, 04/16/20, 04/15/21, 04/21/22, 06/16/22, 08/17/23**
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Archived Date	**N/A**
Archive Review Date	**N/A**
Product Disclaimer	• *If a product excludes coverage for a service, it is not covered, and medical policy criteria do not apply.* • *If a commercial product (including an Essential Plan or Child Health Plus product), medical policy criteria apply to the benefit.* • *If a Medicaid product covers a specific service, and there are no New York State Medicaid guidelines (eMedNY) criteria, medical policy criteria apply to the benefit.* • *If a Medicare product (including Medicare HMO-Dual Special Needs Program (DSNP) product) covers a specific service, and there is no national or local Medicare coverage decision for the service, medical policy criteria apply to the benefit.* • *If a Medicare HMO-Dual Special Needs Program (DSNP) product DOES NOT cover a specific service, please refer to the Medicaid Product coverage line.*

POLICY STATEMENT

I. Based upon our criteria and assessment of the peer-reviewed literature, charged particle irradiation with proton ion beams (PBT) has been medically proven to be effective and therefore, is considered a **medically appropriate** treatment for the following indications:
   A. Cancers of the Head and Neck:
      1. Chordomas or chondrosarcomas of the base of the skull, localized and in the postoperative setting; *or*
      2. Uveal melanoma, when PBT is considered preferential compared to brachytherapy; *or*
      3. Maxillary sinus or paranasal/ethmoid sinus tumors; *or*
      4. Primary cancers invading the orbit, skull base, or cavernous sinus; *or*
   B. Central Nervous System Cancers:
      1. Curative treatment of *primary central nervous system tumors or* malignancies requiring *cranial or* craniospinal irradiation (e.g., medulloblastoma, *gliomas, primary spinal cord tumors*)*;*
   C. Select cases of localized unresectable hepatocellular carcinoma or intrahepatic cholangiocarcinoma when ANY of the following criteria are met:
      1. When a single lesion is present, the lesion must be 15cm or greater in greatest dimension
      2. When two lesions are present, one lesions is greater than 10cm in greatest dimension
      3. When three lesions are present, one lesion is greater than 6cm in greatest dimension; *or*
   D. Stage IIA pure testicular seminoma;
   E. Thymoma and thymic Cancer;

F. Pediatric Cancers:
   1. Central nervous system tumors; or
   2. Other pediatric malignancies if consultation with a radiation oncologist determines an increased predicted risk of radiation-induced late effects

II. Based upon our criteria and assessment of the peer reviewed literature, charged particle irradiation with PBT has not been medically proven to be more effective than other highly-focal techniques (e.g., intensity-modulated radiation therapy [IMRT]) and, therefore, is considered **not medically necessary** for all other indications, including but not limited to prostate cancer, non-small-cell lung cancer, and esophageal cancer.

Refer to Corporate Medical Policy #6.01.12 Stereotactic Radiosurgery and Stereotactic Body Radiation Therapy

Refer to Corporate Medical Policy #11.01.03 Experimental or Investigational Services

Refer to Corporate Medical Policy #11.01.10 Clinical Trials

Refer to Corporate Medical Policy #11.01.13 Out of Area/Out of Network Services

POLICY GUIDELINE

PBT is only covered when performed in specialized centers. There are numerous centers operating in the United States and additional being planned or under construction. Please refer to the National Association of Proton Centers website for more information: https://www.proton-therapy.org/map/

DESCRIPTION

Charged particle beams consisting of protons or helium ions are an alternative to conventional x-rays, and other types of photon irradiation in the treatment of malignant disease. When positively charged atomic particles called protons travel through tissue, they have a limited range, depending on the power of the proton beam. As they reach the end of their range, protons release a burst of energy within a very limited area. Controlling the power of the beam allows delivery of radiation to the tumor, but not to tissues lying behind the tumor, thereby minimizing radiation exposure to surrounding normal tissue. PBT requires specialized equipment in the form of accelerators (cyclotrons, synchrotrons, synchrocyclotrons, or linear accelerators) that can generate a beam of particles (protons or helium ions). PBT also requires accurate localization of the malignancy by using tomographic scanning (with x-ray and/or magnetic resonance imaging), precise and reproducible positioning (relative to the beam) and immobilization of the patient during both tomographic scanning and treatment.

PBT is a form of radiation therapy that can be used for either stereotactic radiosurgery or conventional fractionated radiation therapy. It can also be used without stereotactic guidance.

Per the American Society of Radiation Oncology (ASTRO) Model Policy for Proton Beam Therapy (2017), PBT may be considered reasonable when:

I. The target volume is in close proximity to one or more critical structures and a steep dose gradient outside the target must be achieved to avoid exceeding the tolerance dose to the critical structure(s).
II. A decrease in the amount of dose inhomogeneity in a large treatment volume is required to avoid an excessive dose “hotspot” within the treated volume to lessen the risk of excessive early or late normal tissue toxicity.
III. A photon-based technique would increase the probability of clinically meaningful normal tissue toxicity by exceeding and integral dose-based metric associated with toxicity.
IV. The same or an immediately adjacent area has been previously irradiated, and the dose distribution within the patient must be sculpted to avoid exceeding the cumulative tolerance dose of nearby normal tissue.

RATIONALE

Radiotherapy is a procedure and therefore is not subject to U.S. Food and Drug Administration (FDA) regulations. However, the accelerators and other equipment used to generate and deliver charged particle radiation are devices, and thus do require FDA approval. The equipment used to deliver PBT is approved as a Class II, 510(k) device by the FDA.

Cancers of the Head and Neck

Chordomas and chondrosarcomas

Chordomas and chondrosarcomas are rare malignant neoplasms of the bone. Chordomas arise from the notochord and present at the base of the skull (sphenooccipital region) for one third of the adults diagnosed. Chondrosarcomas come from the middle fossa, posterior, or anterior fossae and account for six percent of all skull base tumors. Skull base tumors are most often found adjacent to critical structures and are primarily treated with surgery and postoperative radiation therapy. Literature supporting the use of PBT in these tumors is limited. There are no randomized trials to date supporting the use of PBT over conventional treatments, however given the need to spare surrounding tissues within the central nervous system, its use is considered medically necessary in the post-operative setting.

Uveal melanoma

Uveal melanoma, although rare, is the most common primary intraocular malignancy in adults. Management is individualized and must consider tumor size, location, extension or metastases, potential disruption to vision, as well as patient preferences. It is highly radioresistant, and requires high-dose radiation, most commonly, plaque brachytherapy. Previously, charged particle beam therapy (e.g., PBT) was felt to have lower recurrence rates when compared to brachytherapy, but the use of radiosonography in the intraoperative setting has allowed for plaque localization, and has decreased the rate of recurrence, demonstrating that charged particle beam therapy and brachytherapy are equally as effective. Charged particle beam therapy has been associated with anterior eye complications, including damage to adjacent ocular structures such as the optic nerve, retina, lens, cornea and iris, and is therefore best utilized for patients who are not candidates for brachytherapy (e.g., gross extension within the orbit, no light perception).

The National Comprehensive Cancer Network (NCCN) Version 2.2023 Guidelines for head and neck cancers states that "highly conformal dose distribution is important for patients whose primary tumors are located in the periocular area or invade the orbit, skull base, and/or cavernous sinus; extend intracranially or exhibit extensive perineural invasion; and who are being treated with curative intent and/or who have long life expectancies following treatment. Additionally, PBT may have the ability to spare important organs at risk, decreasing the risk for late, normal tissue damage when compared to photon-based therapy, while still achieving the primary goal of local tumor control."

Central Nervous System Cancers

The NCCN V1.2023 Clinical Practice Guidelines in Oncology for central nervous system cancers states, in efforts to diminish the dose to critical structures, proton therapy can be considered for the following malignancies requiring craniospinal radiation therapy: intracranial and spinal ependymoma, leptomeningeal metastases, high-grade glioma (isocitrate dehydrogenase (IDH)-mutant and 1p19q codeleted tumors), re-irradiation of gliomas when clinical trial options and new systemic therapy options are limited, primary spinal cord tumors, and meningiomas.

In regard to the reirradiation of gliomas, NCCN states, "Recurrence of glioma can be managed with reirradiation in select scenarios when clinical trial options and new systemic therapy options are limited. Target volumes will be defined using contrast-enhanced CT and/or MRI images. Normal tissues should include the brain, brainstem, optic nerves, and chiasm. Radiation dose should be optimized and conformed to the target volume, while diminishing dose to critical structures. Treatment may be performed with highly focused modern SRS techniques for lower volume disease; fractionated IMRT, including doses of 35 Gy in ten fractions for recurrent glioblastoma, and proton therapy to help spare previously irradiated normal brain."

Pediatric Central Nervous System Cancers

A 2016 systematic review by Leroy et al., identified several case series evaluating PBT for several types of pediatric central nervous system (CNS) tumors including craniopharyngioma, ependymoma, medulloblastoma, and CNS germinoma. Twenty-three primary studies were identified, with approximately 650 patients overall. The median/mean follow-up times were limited (range, 19-91 months). None of the studies were randomized; two were comparative, and twenty were retrospective. Most of the studies suffered from serious methodologic limitations, yielding a very low level of clinical evidence for the outcomes in all indications. Although there is no doubt that PBT reduces the radiation dose to normal tissues and organs, there was insufficient evidence to either support or refute the use of PBT in children.

Hepatocellular Carcinoma and Intrahepatic Cholangiocarcinoma

In hepatocellular cancer, radiation therapy plays a role in patients with unresectable cancers and in those patients not amenable to radiofrequency ablation. Stereotactic body radiation therapy (SBRT) has been used as well as PBT. The larger PBT series, which are from Japan, suggest excellent local control rates and modest two-to-five-year survival rates. Four retrospective studies (360 patients) and two prospective studies (64 patients) of PBT in patients with hepatocellular cancer show results similar to those achieved with SBRT. In patients with unresectable hepatocellular cancers who are not optimally treated with radiofrequency ablation or SBRT, PBT is considered medically necessary.

Pure Testicular Seminoma

Germ cell tumors (pure seminoma and nonseminomatous) account for 95% of testicular cancers. Stage I seminoma is typically treated with orchiectomy and has good outcomes in disease-free survival. Individuals with prognostic Stage II Testicular Cancer Seminoma are defined as having pure seminoma and disease spread to the lymph nodes. These individuals are typically treated with radiation therapy and/or chemotherapy and studies of overall survival comparing the two have reported different outcomes. Retrospective studies (Glaser et al, 2016, Paly et al. 2016) have assessed the five year overall survival of patients receiving radiation therapy vs. chemotherapy in Stage IIA and IIB Seminoma. The studies demonstrated that overall survival was significantly higher for individuals with IIA seminoma receiving radiation therapy vs. chemotherapy but there was no significant difference for those with stage IIB seminoma. NCCN recommends either radiation therapy or chemotherapy for both IIA and IIB Seminoma, which can include PBT, but that radiation should be "reserved for select patients with non-bulky (≤3cm) disease. It should be noted that IIB Seminoma, as defined by the American Joint Committee on Cancer (AJCC) TNM Staging Classification for Testis Cancer (2017) incorporates multiple lymph nodes, with any one mass larger than 2cm but not larger than 5cm in greatest dimension.

Thymomas and thymic carcinomas

Thymomas and thymic carcinoma, also collectively referred to as thymic epithelial tumors (TETs), are very rare neoplasms (0.13 cases per 100,000 person years) located in the anterior mediastinum. Thymomas specifically are associated with autoimmune paraneoplastic diseases (e.g., myasthenia gravis, hypogammaglobulinemia, autoimmune pure red cell aplasia) but the clinical behavioral of all TETs can vary from indolent to metastatic and aggressive, with a five-year survival for inoperable locally advanced carcinoma of 36%; and 24% for metastatic thymoma and thymic carcinoma. The anterior mediastinum holds the heart, lungs, and esophagus, critical organs that are areas of concern for toxicity following radiation therapy, including the risk for secondary malignancies, cardiovascular disease, hypothyroidism, cerebrovascular accidents, pulmonary sequelae, and muscle atrophy.

Given the rare nature of the disease, literature is limited to small case and cohort studies. A 2016 dosimetry comparison by Parikh, et al, demonstrated that PBT delivered significantly lower mean doses of radiation to the lung (.61 Gy vs. 8.13 Gy; P=0.2), esophagus (5.39 vs 20.62 Gy; P=.003) and heart (6.00 vs 10.44 Gy; P=.007) when compared to intensity modulated radiation therapy (IMRT), while adjuvantly treating thymomas in 4 patients at a single proton therapy center.

The NCCN V1.2023 guidelines for thymomas and thymic carcinomas were updated to consider proton therapy use as appropriate, and state that compared to IMRT, it has been shown to improve the dosimetry allowing better sparing of the normal organs (lungs, heart, and esophagus) with favorable local control and toxicity, removing the verbiage, "for certain patients." This is a Category 2A recommendation.

Prostate cancer

Data published concerning the use of PBT in large numbers of patients with localized prostate cancer results comparable to those obtained with alternative techniques. A 2008 comparative effectiveness review of therapies for clinically localized prostate cancer by the Agency for Healthcare Research and Quality (AHRQ) indicated that, based on nonrandomized comparisons, the absolute rates of outcomes after proton radiation appear similar to other treatments. However, the clinical utility of dose escalation using PBT, compared to doses similar to those currently used in intensity modulated radiation therapy (IMRT) (e.g.,79-81 Gy), is still not known and further studies are needed. The American Society for Radiation Oncology (ASTRO) published a guideline for clinically localized prostate cancer in 2017 which states, "limited information exists in relation to the comparative effectiveness of proton therapy compared to other radiation techniques or other modalities of treatment. Clinicians should inform localized prostate cancer patients who are

considering proton beam therapy that it offers no clinical advantage over other forms of definitive treatment" (Moderate Recommendation; Evidence Level: Grade C).

Other indications
Case series with small sample size that addresses PBT in the treatment of esophageal, non-small-cell lung cancer (NSCLC) and invasive bladder carcinoma indicate favorable results, but these studies have limitations of small sample size and short follow-up period. Small retrospective studies indicate that the use of PBT appears promising for the treatment of Stage I non-small-cell lung cancer; however, prospective clinical trials with larger study populations and longer follow-up periods are needed.

ASTRO has published a model policy, most recently updated in 2017. It states that PBT is considered reasonable in instances where sparing the surrounding normal tissue cannot be achieved with photon-based radiotherapy and is of added clinical benefit to the patient. The policy lists four examples of when PBT might be preferred over conventional radiotherapy, which include reducing the potential for toxicity to critical nearby structures. In addition to meeting criteria in one of the four listed examples, the radiation oncologist must determine the patient's suitability for PBT allowing for reproducible delivery, adequate definition of the target volumes and organs at risk; equipment capability; physician, physicist, and staff training; and adequate quality assurance procedures. Normal tissue dose volume histograms (DVHs) must be demonstrably improved with a PBT plan, to validate coverage. Coverage decisions must extend beyond ICD-10 codes to incorporate considerations of clinical scenario and medical necessity with appropriate documentation, which may include comparative dose volume histograms. On the basis of the medical necessity requirements and published clinical data, disease sites that frequently support the use of PBT include the following: ocular tumors, including intraocular melanomas; tumors that approach or are located at the base of the skull (e.g., chordoma, chondrosarcomas); primary or metastatic tumors of the spine (where the spinal cord tolerance may be exceeded with conventional treatment or where the spinal cord has been previously irradiated); primary hepatocellular cancer and primary or benign solid tumors in children treated with curative intent and occasional palliative treatment, when at least one of four example criteria is met, malignant and benign primary CNS tumors, advanced (e.g.,T4) and/or unresectable head and neck cancers, cancers of the paranasal sinuses and other accessory sinuses, non-metastatic retroperitoneal sarcomas, and re-irradiation cases. PBT may also be appropriate for patients with genetic syndromes that make total volume of irradiation minimization crucial, such as, but not limited to NF-1 patients and retinoblastoma patients. PBT would be considered as part of "coverage with evidence development" (CED) for indications that include, but not limited to the following: non- T4 and resectable head and neck malignancies; thoracic malignancies; abdominal malignancies; and pelvic malignancies, including non-metastatic rectal, anal, bladder and cervical cancers, non-metastatic prostate cancer, and breast cancer. In the treatment of prostate cancer, the use of PBT is evolving as the comparative efficacy evidence is still being developed. PBT for primary treatment of prostate cancer should only be performed within the context of a prospective clinical trial or registry.

CODES

- *Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract.*
- *CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.*
- *Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.*
- *Code Key: Experimental/Investigational = (E/I), Not medically necessary/ appropriate = (NMN).*

CPT Codes

Code	Description
77520	Proton treatment delivery; simple, without compensation
77522	Proton treatment delivery; simple, with compensation
77523	Proton treatment delivery; intermediate
77525	Proton treatment delivery; complex

HCPCS Codes

Code	Description
No codes	

ICD10 Codes

Code	Description
C22.0-C22.8	Malignant neoplasm of liver and intrahepatic bile ducts (code range)
C30.0-C31.9	Malignant neoplasm of nasal cavity, middle ear, accessory sinuses (code range)
C40.80-C40.82	Malignant neoplasm of overlapping sites of bone and articular cartilage of limb (code range)
C40.90-C40.92	Malignant neoplasm of unspecified bones and articular cartilage of limb (code range)
C41.0-C41.9	Malignant neoplasm of bone and articular cartilage of other and unspecified sites (code range)
C61	Malignant neoplasm of prostate
C69.30-C69.42	Malignant neoplasm of choroid or ciliary body (code range)
C72.20-C72.9	Malignant neoplasm of spinal cord, cranial nerves and other parts of central nervous system (code range)
C78.30-C78.39	Secondary malignant neoplasm of other and unspecified respiratory organs (code range)
C79.32	Secondary malignant neoplasm of cerebral meninges
C79.40-C79.49	Secondary malignant neoplasm of other and unspecified parts of nervous system (code range)
C79.51-C79.52	Secondary malignant neoplasm of bone or bone marrow (code range)
D02.3	Carcinoma in situ of other parts of respiratory system
D07.5	Carcinoma in situ of prostate

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*Key Article

KEY WORDS

Charged particle radiation therapy, conformal proton beam radiation, proton beam radiation, proton beam therapy, intensity-modulated proton beam therapy, pencil beam scanning.

CMS COVERAGE FOR MEDICARE PRODUCT MEMBERS

There is currently a Local Coverage Determination (LCD) for Proton Beam Therapy. Please refer to the following LCD website for Medicare members: https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=35075&ContrId=298&ver=34&ContrVer=1&CntrctrSelected=298*1&Cntrctr=298&s=41&DocType=1&bc=AAQAAAIAAAAA&.