FEP 8.01.10 Charged-Particle (Proton or Helium Ion) Radiotherapy for Neoplastic Conditions

**Effective Date:** January 15, 2019

**Related Policies:**
- 8.01.46 Intensity-Modulated Radiotherapy of the Lung
- 8.01.48 Intensity-Modulated Radiotherapy: Cancer of the Thyroid
- 8.01.49 Intensity-Modulated Radiotherapy: Abdomen and Pelvis

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**Description**

Charged-particle beams consisting of protons or helium ions are a type of particulate radiotherapy. Treatment with charged-particle radiotherapy is proposed for a large number of tumors that would benefit from the delivery of a high dose of radiation with limited scatter.

**OBJECTIVE**

The objective of this evidence review is to determine whether charged-particle irradiation with proton or helium ion beams improves the net health outcome in patients with neoplastic conditions.

**POLICY STATEMENT**

Charged-particle irradiation with proton or helium ion beams may be considered **medically necessary** in the following clinical situations:

- primary therapy for melanoma of the uveal tract (iris, choroid, or ciliary body), with no evidence of metastasis or extrascleral extension, and with tumors up to 24 mm in largest diameter and 14 mm in height.
- postoperative therapy (with or without conventional high-energy x-rays) in patients who have undergone biopsy or partial resection of chordoma or low-grade (I or II) chondrosarcoma of the basisphenoid region (skull-base chordoma or chondrosarcoma) or cervical spine. Patients eligible for this treatment have residual localized tumor without evidence of metastasis.
- in the treatment of pediatric central nervous system tumors.

Other applications of charged-particle irradiation with proton or helium ion beams are considered **investigational**. This includes, but is not limited to:

- pediatric non-central nervous system tumors,
- clinically localized prostate cancer,
- non-small-cell lung cancer at any stage or for recurrence,
- tumors of the head and neck (other than skull-based chordoma or chondrosarcoma).

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POLICY GUIDELINES

Evidence is lacking on the definition of age parameters for the use of proton beam therapy in pediatric patients. Some studies using proton beam therapy in pediatric central nervous system tumors have mostly included patients younger than 3 years of age. However, experts cite the benefit of proton beam therapy in pediatric patients of all ages (<21 years of age).

BENEFIT APPLICATION

Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).

FDA REGULATORY STATUS

Radiotherapy is a procedure and, therefore, 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 (including proton beam) are devices that require FDA oversight. The FDA’s Center for Devices and Radiological Health has indicated that the proton beam facilities constructed in the United States prior to enactment of the 1976 Medical Device Amendments were cleared for use in the treatment of human diseases on a “grandfathered” basis, while at least one that was constructed subsequently received a 510(k) marketing clearance. There are 510(k) clearances for devices used for delivery of proton beam therapy and devices considered to be accessory to treatment delivery systems, such as the Proton Therapy Multileaf Collimator (which was cleared in December 2009). Since 2001, several devices classified as medical charged-particle radiation therapy systems have received 510(k) marketing clearance. FDA product code LHN.

RATIONALE

Summary of Evidence

For individuals who have uveal melanoma(s) who receive charged-particle (proton or helium ion) radiotherapy, the evidence includes RCTs and systematic reviews. Relevant outcomes are overall survival, disease-free survival, change in disease status, and treatment-related morbidity. Systematic reviews, including a 1996 TEC Assessment and a 2013 review of randomized and nonrandomized studies, concluded that the technology is at least as effective as alternative therapies for treating uveal melanomas and is better at preserving vision. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have a skull-based tumor(s) (ie, cervical chordoma, chondrosarcoma) who receive charged-particle (proton or helium ion) radiotherapy, the evidence includes observational studies and systematic reviews. Relevant outcomes are overall survival, disease-free survival, change in disease status, and treatment-related morbidity. A 2007 systematic review found a 5-year overall survival rate of 81% with PBT compared with 44% with surgery plus photon therapy. In 2016, a systematic review of observational studies found 5-year survival rates after PBT ranging from 67% to 94%. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have pediatric central nervous system tumor(s) who receive charged-particle (proton or helium ion) radiotherapy, the evidence includes case series, nonrandomized comparative studies, and systematic reviews. Relevant outcomes are overall survival, disease-free survival, change in disease status, and treatment-related morbidity. There are few comparative studies, and they tend to have small sample sizes. The available observational studies do not provide sufficient evidence on the efficacy of charged-particle therapy compared with other treatments (eg, intensity-modulated radiotherapy). The evidence is insufficient to determine the effects of the technology on health outcomes.
For individuals who have pediatric non–central nervous system tumor(s) who receive charged-particle (proton or helium ion) radiotherapy, the evidence includes dosimetric planning studies in a small number of patients. Relevant outcomes are overall survival, disease-free survival, change in disease status, and treatment-related morbidity. For this population, there is a lack of randomized and observational studies evaluating the efficacy and safety of this technology. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have localized prostate cancer who receive charged-particle (proton or helium ion) radiotherapy, the evidence includes 2 RCTs and systematic reviews. Relevant outcomes are overall survival, disease-free survival, change in disease status, and treatment-related morbidity. A 2010 TEC Assessment addressed the use of PBT for prostate cancer and concluded that it had not been established whether PBT improves outcomes in any setting for clinically localized prostate cancer. The TEC Assessment included 2 RCTs, only one of which had a comparison group of patients that did not receive PBT. No data on the use of PBT for prostate cancer published since 2010 would alter the conclusions of the TEC Assessment. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have non-small-cell lung cancer who receive charged-particle (proton or helium ion) radiotherapy, the evidence includes case series and systematic reviews. Relevant outcomes are overall survival, disease-free survival, change in disease status, and treatment-related morbidity. A 2010 TEC Assessment, which included 8 case series, concluded that the evidence was insufficient to permit conclusions about PBT for any stage of non-small-cell lung cancer. No subsequent randomized or nonrandomized comparative studies were identified that would alter the conclusions of the TEC Assessment. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have head and neck tumors other than skull-based who receive charged-particle (proton or helium ion) radiotherapy, the evidence includes case series and a systematic review. Relevant outcomes are overall survival, disease-free survival, change in disease status, and treatment-related morbidity. The systematic review noted that the studies on charged-particle therapy were heterogenous in terms of the types of particles and delivery techniques used; further, there are no head-to-head trials comparing charged-particle therapy with other treatments. The evidence is insufficient to determine the effects of the technology on health outcomes.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

International Particle Therapy Co-operative Group
A 2016 consensus statement by the International Particle Therapy Co-operative Group offered the following conclusion about proton therapy for non-small-cell lung cancer (NSCLC): "...Promising preliminary clinical outcomes have been reported for patients with early-stage or locally advanced NSCLC who receive proton therapy. However, the expense and technical challenges of proton therapy demand further technique optimization and more clinical studies...."34

American College of Radiology
The 2014 guidelines from the American College of Radiology on external-beam radiotherapy in stage T1 and T2 prostate cancer stated:

- "There are only limited data comparing proton-beam therapy to other methods of irradiation or to radical prostatectomy for treating stage T1 and T2 prostate cancer. Further studies are needed to clearly define its role for such treatment.
- There are growing data to suggest that hypofractionation at dose per fraction <3.0 Gy per fraction is reasonably safe and efficacious, and although the early results from hypofractionation/SBRT..."
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[stereotactic body radiation therapy] studies at dose per fraction >4.0 Gy seem promising, these approaches should continue to be used with caution until more mature, ongoing phase II and III randomized controlled studies have been completed.35

National Comprehensive Cancer Network

Prostate Cancer

National Comprehensive Cancer Network (NCCN) guidelines for prostate cancer (v.3.2018) offer the following conclusion on proton therapy: “The NCCN panel believes no clear evidence supports a benefit or decrement to proton therapy over IMRT [intensity-modulated radiotherapy] for either treatment efficacy or long-term toxicity. Conventionally fractionated prostate proton therapy can be considered a reasonable alternative to x-ray-based regimens at clinics with appropriate technology, physics, and clinical expertise.”36

Non-Small-Cell Lung Cancer

NCCN guidelines for NSCLC (v.4.2018) have been updated with the following for advanced-stage disease or palliation: “When higher doses (> 30 Gy) are warranted, technologies to reduce normal tissue irradiation (at least 3D-CRT [3-dimensional conformal radiotherapy] and including IMRT and proton therapy as appropriate) may be used.”37

Head and Neck Cancer

NCCN guidelines for head and neck cancers (v.2.2018) indicate that “Without high-quality prospective comparative data, it is premature to conclude that proton therapy has been established as superior to other established radiation techniques such as IMRT, particularly with regard to tumor control.”38 The guidelines suggest that proton therapy can be considered for cancers of the paranasal sinuses and salivary glands if normal tissue constraints cannot be met by conventional photon radiotherapy.

American Society for Radiation Oncology

The American Society for Radiation Oncology (ASTRO) (2017) updated its model policy on the medical necessity requirements for the use of proton therapy.39 ASTRO deemed the following disease sites those for which the evidence frequently supports the use of proton beam therapy:

- Ocular tumors, including intraocular melanomas
- Tumors that approach or are located at the base of the skull, including but not limited to chordoma and 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 previously been irradiated
- Hepatocellular cancer
- Primary or benign solid tumors in children treated with curative intent and occasional palliative treatment of childhood tumors
- Patients with genetic syndromes making total volume of radiation minimization crucial such as but not limited to NF-1 patients and retinoblastoma patients
- Malignant and benign primary central nervous system tumors
- Advanced (eg, T4) and/or unresectable head and neck cancers
- Cancers of the paranasal sinuses and other accessory sinuses
- Nonmetastatic retroperitoneal sarcomas
- Re-irradiation cases (where cumulative critical structure dose would exceed tolerance dose).

The model policy also made a specific statement on proton beam therapy for treating prostate cancer: “…, ASTRO believes the comparative efficacy evidence of proton beam therapy with other prostate
cancer treatments is still being developed, and thus the role of proton beam therapy for localized prostate cancer within the current availability of treatment options remains unclear."

**U.S. Preventive Services Task Force Recommendations**

Not applicable.

**Medicare National Coverage**

There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

**REFERENCES**

4. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Charged particle (proton or helium ion) irradiation for uveal melanoma and for chordoma or chondrosarcoma of the skull base or cervical spine. *TEC Assessments* 1996;Volume 11:Tab 1.  

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POLICY HISTORY

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<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Description</th>
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<tbody>
<tr>
<td>June 2013</td>
<td>Update Policy</td>
<td>Policy updated with literature search through February 6, 2014. References 5, 26, 39, 46 and 47 added. No change in policy statements.</td>
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<tr>
<td>September 2015</td>
<td>Update Policy</td>
<td>Policy updated with literature review through March 17, 2015; references 12, 22-25, 33-35, and 41-43 added. Title changed from &quot;radiation therapy&quot; to &quot;radiotherapy&quot; to be consistent with other MPRM policies. Editorial changes made to policy statement for prostate cancer with no changes to intent.</td>
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<tr>
<td>September 2016</td>
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<td>Policy updated with literature review; references 4-5, 9, and 31 added. &quot;For Neoplastic Conditions&quot; added to title. Policy statements unchanged.</td>
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