Clinical Policy: Proton and Neutron Beam Therapiesy

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Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Proton beam therapy (PBT) is a form of external beam radiation therapy (EBRT) that utilizes protons (positively charged subatomic particles) to precisely target a specific tissue mass. Proton beams can penetrate deep into tissues to reach tumors, while delivering less radiation to surrounding tissues. This may make PBT more effective for inoperable tumors, or for those areas in which damage to healthy tissue would pose an unacceptable risk.

Neutron beam therapy (NBT) is a less widely available form of EBRT that utilizes neutrons. Its clinical use is very limited due to difficulties in the delivery of this treatment modality.

Policy/Criteria

I. It is the policy of Louisiana Healthcare Connections that proton beam therapy is **medically necessary** for the following indications:
- **A.** Ocular tumors with no distant metastasis. Fiducial markers (tantalum clips) are permitted to allow eye and tumor position verification;
- **B.** 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;
- **C.** Tumors that approach or are located at the base of the skull, including but not limited to: chordoma or chondrosarcoma;
- **D.** Primary hepatocellular cancer ~~treated in a hypofractionated regimen~~;
- **E.** Primary or benign solid tumors in members/enrollees ~~≤ 18~~ <21 years old;
- **F.** Genetic syndromes making total volume of radiation minimization crucial such as but not limited to NF-1 patients and retinoblastoma;
- **G.** Malignant and benign primary CNS tumors;
- **H.** Advanced (eg,T4) and/or unresectable head and neck cancers, when normal tissue constraints cannot be met by photon-based therapy;
- **I.** Cancers of the paranasal sinuses and other accessory sinuses, when normal tissue constraints cannot be met by photon-based therapy;
- **J.** Non-metastatic retroperitoneal sarcomas (i.e., preoperative treatment of resectable disease or primary treatment for those with unresectable disease);
- **K.** Re-irradiation cases where cumulative critical structure dose would exceed tolerance dose;
- **L.** Hodgkin and Non-Hodgkin lymphoma, to spare critical structures when normal tissue constraints cannot be met with photon therapy (including three dimensional and IMRT techniques);
- **M.** Non-Small Cell Lung Cancer, to spare critical structures when critical organ dose constraints cannot be met with photon therapy (including three dimensional and IMRT neutron techniques);

N. Thymomas and Thymic carcinoma, to spare critical structures when critical organ dose constraints cannot be met with photon therapy (including three dimensional and IMRT techniques).

II. It is the policy of Louisiana Healthcare Connections that NBT is **medically necessary** in the treatment of salivary gland tumors considered surgically unresectable, or for a member/enrollee~~patient~~ with salivary gland tumors who is medically inoperable.

III. All other indications for PBT and NBT are considered **not medically necessary** as insufficient evidence exists to recommend proton and/or neutron beam therapy as superior to other treatments available.

Background

Proton beam therapy (PBT) is an important method of treatment used in managing malignant disease with a well-defined target. Unlike x-rays, protons cause little damage to the tissues they pass through to reach their destination. Their energy is released after traveling a specified distance, thus delivering more radiation to the tumor and doing less damage to the nearby normal tissue. Because of this, PBT may be more useful for tumors with distinct edges rather than those whose edges are mixed with normal tissue.

The American Society of Radiation Oncology (ASTRO) evaluated the evidence of use of PBT up until November 2009. The use of PBT was evaluated for CNS tumors, gastrointestinal malignancies, lung, head and neck, prostate, and pediatric tumors. Data evaluated did not provide sufficient evidence to support PBT for lung cancer, head and neck cancer, GI malignancies, and pediatric non-CNS malignancies. For hepatocellular carcinoma and prostate cancers, evidence supports the efficacy of PBT, but there is no support that it is a superior treatment to other external beam radiation therapy approaches. For pediatric CNS malignancies, PBT appears to be superior to other external beam radiation therapy (EBRT) approaches, but more data is needed to determine the most appropriate approach. For large ocular melanomas and chordomas, evidence supports there to be a benefit of PBT over other EBRT approaches. Current evidence is limited for PBT indications and more robust clinical trials are needed to determine the appropriate clinical setting for its use.

Radiation therapy (RT) plays a critical role in the local tumor control of benign and low-grade central nervous system tumors in children but is not without the risk of long-term treatment-related sequelae. PBT is an advanced RT modality with a unique dose-deposition pattern that allows for treatment of a target volume with reduced scatter dose delivered to normal tissues compared with conventional photon RT and is now increasingly utilized in children with the hope of mitigating radiation-induced late effects.[32]

ASTRO's Proton Beam Model Policy, updated from the previous version in 2014, expanded its recommendations for use. Based on medical necessity requirements and published clinical data, in addition to its previous recommendations, additional disease sites that frequently support the use of PBT include the following:

- 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
- Re-irradiation cases (where cumulative critical structure dose would exceed tolerance dose)

ASTRO states there is a need for continued clinical evidence development and comparative effectiveness analyses for the appropriate use of PBT for various disease sites and as such all other indications are suitable for Coverage with Evidence Development (CED). They note that radiation therapy for patients treated under the CED paradigm should be covered by the insurance carrier as long as the patient is enrolled either in an IRB-approved clinical trial or in a multi-institutional patient registry adhering to Medicare requirements for CED.[21]

Head and Neck Cancer

Guidelines from National Comprehensive Cancer Network (NCCN) regarding PBT in the treatment of head and neck cancer state the following. "Achieving high conformal dose distributions is especially important for patients whose primary tumors are periocular in location and/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. Non-randomized single institution clinical reports and systematic comparisons demonstrate safety and efficacy of PBT in the above-mentioned specific clinical scenarios. Either intensity-modulated radiation therapy (IMRT) or 3D conformal RT is recommended. Proton therapy can be considered when normal tissue constraints cannot be met by photon-based therapies."[12]

Central Nervous System Cancers

NCCN guidelines note that it is reasonable to consider proton beam thearpy for craniospinal irradiation where available, as it is associated with less toxicity.[18]

Uveal Melanoma

Per NCCN guidelines on uveal melanoma, "Tumor localization for PBT may be performed using indirect ophthalmoscopy, transillumination, and/or ultrasound (intraoperative or postoperative but before proton beamand/or preoperative), MRI and or/CT. For intraocular tumors, fiducial markers (tantalum clips) are encouraged to permit eye and tumor position verification for image-guided radiotherapy delivery."[19]

A practice parameter on PBT from the American College of Radiology/ASTRO also notes that "in the most common systems, the ophthalmologist will guide patient selection with tumor/target definition through techniques such as funduscopic examination, fluorescein angiogram, ultrasound, and direct tumor measurements intraoperatively. Most commonly but not imperatively, radio-opaque fiducial markers are sutured to the sclera and used as references for tumor definition. Treatment planning for ocular tumors has been most frequently performed with a treatment planning algorithm and software system developed specifically for treatment of ocular tumors. This requires multiple measurements that are obtained by the ophthalmologist, both from clinical examination and from surgical evaluation at the time of fiducial clip placement."[20]

Non-metastatic Retroperitoneal Sarcomas

Per NCCN guidelines on soft tissue sarcoma (STS), surgical resection of a localized tumor with negative margins is the standard, potentially curative treatment for patients with retroperitoneal/intra-abdominal STS. Radiation therapy (RT) can be administered as preoperative treatment for patients with resectable disease or as a primary treatment for those with unresectable disease. Post-operative RT is discouraged, but may be considered in rare instances. Newer RT techniques such as IMRT and 3D conformal RT using protons or photons may allow tumor target coverage and acceptable clinical outcomes within normal tissue dose constraints to adjacent organs at risk. When EBRT is used, sophisticated treatment planning with IMRT, tomotherapy and/or proton therapy can be used to improve therapeutic effect. However, the safety and efficacy of adjuvant RT techniques have yet to be evaluated in a multicenter RCT. RT is not a substitute to definitive surgical resection with negative margins, and re-resection to negative margins is preferable.[22]

HepatocellularHepatobiliary Cancer

Per NCCN guidelines on hepatocellular carcinoma (HCC), EBRT is a treatment option for patients with unresectable disease, or for those who are medically inoperable due to comorbidity. All tumors irrespective of the location may be amenable to RT [3D conformal RT, IMRT, and stereotactic Body Radiation therapy (SBRT)]. Image-guided radiotherapy is strongly recommended when using EBRT, IMRT, and SBRT to improve treatment accuracy and reduce treatment-related toxicity. Hypofractionation with photons or protons is an acceptable option for intrahepatic tumors, though treatment at centers with experience is recommended. PBT may be appropriate in specific situations.[17] In a phase II study, 94.8% of patients with unresectable HCC who received high-dose hypofractionated PBT demonstrated >80% local control after 2 years, as defined by RECIST criteria.[23] Several ongoing studies are continuing to investigate the impact of hypofractionated PBT on HCC outcomes, including randomized trials comparing PBT to radiofrequency ablation. (RFA). Data has demonstrated that local control is exceptional regardless of the fractionation used.[35] In a phase III study using the Child-Pugh classification, an evaluation of clinical outcomes of PBT versus RFA demonstrated PBT could be applied safely in patients with small recurrent hepatocellular carcinoma. The 2-year local progression-free survival (LPFS) rate was 94.8% versus 83.2% respectively, demonstrating that PBT is not inferior to RFA treatment.[33]

Prostate Cancer

ASTRO recommends coverage of PBT for the treatment of non-metastatic prostate cancer when enrolled in an institutional review board (IRB)–approved study or a multi-institutional registry that adheres to Medicare requirements for Coverage with Evidence Development (CED).[21] NCCN guidelines note that there lacks clear evidence to support a benefit or decrement to proton therapy over IMRT for either treatment efficacy or long-term toxicity. Firm conclusions regarding differences in toxicity or effectiveness of proton and photon therapy cannot be drawn because of the limitations of the available studies.[24]

Thymomas and Thymic Carcinomas

Per NCCN, PBT has been shown to improve dosimetry compared to IMRT allowing better sparing of the normal organs (lungs, heart, and esophagus). Additionally, favorable results in

terms of both local control and toxicity have been obtained with PBT. Based on these data, PBT ~~may be~~is considered an appropriate treatment option~~in certain circumstances~~.[29]

Hodgkin Lymphoma

Per NCCN, "Treatment with photons, electrons or protons may all be appropriate, depending on the clinical circumstances. Advanced RT technologies such as IMRT/volumetric modulated arc therapy (VMAT), breath hold or respiratory gating, and/or image-guided RT (IGRT), or proton therapy may offer significant and clinically relevant advantages in specific instances to spare important organs at risk (OAR) such as the heart (including coronary arteries, valves, and left ventricle), lungs, kidneys, spinal cord, esophagus, carotid artery, bone marrow, breasts, stomach, muscle/soft tissue, and salivary glands and decrease the risk for late, normal tissue damage while still achieving the primary goal of local tumor control. For optimal mediastinal treatment planning, organs/tissues to be contoured should include the lungs, heart, coronary arteries, and left ventricle."[28]

Esophageal and Esophagogastric Junction Cancers

NCCN guidelines indicate this emerging technique may offer protection of normal tissue by limiting exposure of adjacent organs to radiation in addition to lowering the rates of post-operative pulmonary, cardiac, gastrointestinal, and wound complications. The guidelines recommend that patients with esophageal cancer be treated with PBT within a clinical trial, noting that data is early and evolving.[26] An overall low-quality body of evidence suggests that PBT has possible benefit for the treatment of esophageal adenocarcinoma (EAC). PBT may have similar effectiveness to both IMRT and 3DCRT and results in significantly reduced radiation exposure to adjacent organs at risk. PBT could possibly result in fewer complications than IMRT (intensity-modulated radiation therapy) and 3DCRT (3-dimensional conformal radiation therapy) among patients undergoing esophagectomy, however the statistical significance of these findings was mixed. The rate of nonoperative complications was comparable between PBT and IMRT.[36]
~~NCCN guidelines recommend that patients with esophageal cancer be treated with PBT within a clinical trial, noting that data is early and evolving.~~

Neutron Beam Therapy

NBT utilizes neutrons, rather than photons, to destroy tumor cells. Neutrons are much heavier than photons and appear to be more effective at causing damage to very dense tumors. It is however more clinically difficult to generate neutron particles, so it has not gained wide acceptance for treatment. It has most commonly been studied in salivary gland tumors which are either unable to be removed completely or for recurrent disease.

NCCN states NBT was historically considered a promising solution for unresectable salivary gland cancer, however, they no longer recommend NBT as a general solution for salivary gland cancers due to the diminishing demand, high rates of long-term toxicity over time, concerns regarding the methodologic robustness of available randomized trial data, and closure of all but one center in the U.S. The panel recognizes the potential clinical value of neutron therapy for select patients, particularly those with unresectable disease meeting the RTOG-MRC clinical trial criteria. The NCCN guidelines note that PBT can be considered when normal tissue constraints cannot be met by photon-based therapy.[12]

Coding Implications

This clinical policy references Current Procedural Terminology (CPT®). CPT® is a registered trademark of the American Medical Association. All CPT codes and descriptions are copyrighted 2020 American Medical Association. All rights reserved. CPT codes and CPT descriptions are from the current manuals and those included herein are not intended to be all-inclusive and are included for informational purposes only. Codes referenced in this clinical policy are for informational purposes only and may not support medical necessity. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

CPT Codes	Description
77423	High energy neutron radiation treatment delivery; 1 or more isocenter(s) with coplanar or non-coplanar geometry with blocking and/or wedge, and/or compensator(s)
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	Description
S8030	Scleral application of tantalum ring(s) for localization of lesions for proton beam therapy

~~ICD-10-CM diagnosis codes that support coverage criteria for proton beam therapy~~
~~+ Indicates a code requiring an additional character~~

~~ICD-10-CM Code~~	~~Description~~
~~C06.9~~	~~Malignant neoplasm of mouth, unspecified site (minor salivary gland, unspecified site)~~
~~C08.0-C08.9~~	~~Malignant neoplasm of other and unspecified major salivary glands~~
~~C11.0-C11.9~~	~~Malignant neoplasm of nasopharynx~~
~~C16.0~~	~~Malignant neoplasm of cardia~~
~~C22.0 – C22.8~~	~~Malignant neoplasm of liver and intrahepatic ducts~~
~~C31.0-C31.9~~	~~Malignant neoplasm of accessory sinuses~~
~~C34.0-C34.92~~	~~Malignant neoplasm of bronchus and lung~~
~~C37~~	~~Malignant neoplasm of thymus~~
~~C41.0~~	~~Malignant neoplasm of bones of skull and face~~
~~C41.2~~	~~Malignant neoplasm of vertebral column~~
~~C48.0~~	~~Malignant neoplasm of retroperitoneum~~
~~C69.00 – C69.92~~	~~Malignant neoplasm of eye and adnexa~~
~~C70.0 – C70.9~~	~~Malignant neoplasm of meninges~~

~~ICD-10-CM Code~~	~~Description~~
~~C71.0 – C71.9~~	~~Malignant neoplasm of brain~~
~~C72.0 – C72.9~~	~~Malignant neoplasm of spinal cord, cranial nerves and other parts of central nervous system~~
~~C75.1 – C75.3~~	~~Malignant neoplasm of pituitary, craniopharyngeal duct, and pineal gland~~
~~C78.00-C78.2~~	~~Secondary malignant neoplasm of lung~~
~~C78.89~~	~~Secondary malignant neoplasm of other digestive organs~~
~~C79.31~~	~~Secondary malignant neoplasm of brain~~
~~C79.40 – C79.49~~	~~Secondary malignant neoplasm of other and unspecified parts of nervous system~~
~~C81.00-C96.9~~	~~Malignant neoplasm of lymphoid, hematopoietic and related tissue~~
~~D09.20-D09.22~~	~~Carcinoma in situ of eye~~
~~D31.00-D31.92~~	~~Benign neoplasm of eye and adnexa~~
~~D32.0 – D32.9~~	~~Benign neoplasm of meninges~~
~~D33.0 – D33.9~~	~~Benign neoplasm of brain and other parts of central nervous system~~
~~D35.2~~	~~Benign neoplasm of pituitary gland~~
~~D42.1~~	~~Neoplasm of uncertain behavior of spinal meninges~~
~~D43.4~~	~~Neoplasm of uncertain behavior of spinal cord~~
~~D44.3~~	~~Neoplasm of uncertain behavior of pituitary gland~~
~~D44.4~~	~~Neoplasm of uncertain behavior of craniopharyngeal duct~~

Reviews, Revisions, and Approvals	Revision Date	Approval Date
Converted corporate to local policy.	11/2020	
Annual review. References reviewed and updated. Reviewed by specialist. Changed "Last Review Date" in the header to "Date of Last Review" and "Date" in revision log to "Revision Date". Added “may not support medical necessity” in coding implications. Replaced ICD-10 code C78.82 with C78.2. Updated background regarding PBT for benign and low-grade central nervous system tumors in children	2/22	2/22
Changed policy name to Therapies instead of Therapy. Removed “treated in a hypofractionated regimen” from I. D. Changed age to <21 in I. F. Added “and/or neutron” to criteria III. for clarity. Background updated and minor rewording with no clinical significance. Removed ICD-10 diagnosis code table. References reviewed, reformatted and updated.	1/23	

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Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. LHCC makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable LHCC administrative policies and procedures.

This clinical policy is effective as of the date determined by LHCC. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. LHCC retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom LHCC has no control or right of control. Providers are not agents or employees of LHCC.

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