

Molina Clinical Policy
Neutron and Proton Beam Radiation Therapy
Policy No. 464

Last Approval: 12/11/2024
 Next Review Due By: December 2025



Disclaimer

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. Policies are not a supplementation or recommendation for treatment; Providers are solely responsible for the diagnosis, treatment, and clinical recommendations for the Member. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (e.g., will be paid for by Molina) for a particular Member. The Member's benefit plan determines coverage – each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their Providers will need to consult the Member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a Member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid Members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this MCP and provide the directive for all Medicare members. References included were accurate at the time of policy approval and publication.

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STATEMENT

General Information

It is an expectation that all patients receive care/services from a licensed clinician. All appropriate supporting documentation, including recent pertinent office visit notes, laboratory data, and results of any special testing must be provided. If applicable: All prior relevant imaging results and the reason that alternative imaging cannot be performed must be included in the documentation submitted.

Where a specific clinical indication is not directly addressed in this guideline, medical necessity determination will be made based on widely accepted standard of care criteria. These criteria are supported by evidence-based or peer-reviewed sources such as medical literature, societal guidelines and state/national recommendations.

Purpose

Proton Beam Therapy

Proton beam therapy (PBRT) is a type of highly precise external beam radiotherapy that uses charged particles (i.e., protons) to treat various cancers. Protons are unique since they only travel a certain distance into the body before they stop and deliver their highest dose of radiation at the end of the beam's pathway. This targeted burst of energy, which gives PBRT its high degree of precision, is called the Bragg peak.

Over the years, PBRT has been used to treat cancers with the goal of improving patient outcomes such as improved overall survival, decreased rates of long-term (chronic) toxicity, and decreased rates of second cancers due to radiotherapy treatments. Although PBRT has been in use for many years, there have been only a limited number clinical trials that provide adequate evidence that PBRT is superior to other types of standard state-of-the-art radiation treatment modalities in terms of clinically significant results.

Much of the PBRT research has involved the comparison of the radiation doses delivered to organs at risk with PBRT versus the doses delivered with Intensity Modulated Radiation Therapy (IMRT).

Dosimetric advantages with PBRT do not always translate into clinical benefits. ⁽¹⁾ This may be due to the greater uncertainty in the delivered biologically effective dose distributions with PBRT due to such factors as:

- Inter-fractional and intra-fractional organ motion, which is particularly difficult to account for with protons
- Setup variability
- Approximations made in dose computations methods due to the entrance dose and neutron dose in the tissues around the target which can be higher than they are for photons with uncertainties in the range in complex tissues (especially around metallic implants) and the lateral penumbra
- The assumption of a constant RBE of 1.1 AND

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- The deposition of a higher linear energy transfer beyond the target
- Even though more than 170,000 patients have been treated with PBRT to date, the clinical evidence for protons so far has not been unequivocally clear and broad enough to alleviate concerns
- Current research involving PBRT is ongoing. Multiple multicenter phase 3 randomized controlled trials (RCTs) are currently in progress

Neutron Beam Therapy

Neutron beam radiation therapy (NBRT) is a specialized type of external beam radiotherapy that uses high-energy neutrons (neutral subatomic particles). The neutrons are targeted toward tissue masses that are characterized by lower tumor oxygen levels and a slower cell cycle, since neutrons require less oxygen and are less dependent on the cell's position in the cell division cycle. Neutrons produce 20 to 100 times more energy than conventional photon radiation and may be more damaging to surrounding tissues.

NBRT has been employed mainly in the treatment of the salivary gland cancers. Nevertheless, NBRT has not gained wide acceptance because of the practical difficulty in generating neutron particles for use in a cancer center and also due to limited amount of evidence published in peer reviewed medical journals.^(2,3)

Evidence Based Medicine (EBM)

EBM and Evolent Guidelines

Evidence-based medicine (EBM) uses the scientific method to organize and apply current medical data to determine which treatments are medically necessary.

The ASTRO Model Policy for Proton Beam Therapy also states that "there is a need for continued clinical evidence development and comparative effectiveness analyses for the appropriate use of PBT for various disease sites."⁽⁴⁾

Evolent is committed to creating guidelines that follow an EBM approach. Evolent Radiation Oncology guidelines apply the **same standard** of clinical evidence for medical policy benefit coverage decisions. This guideline will be updated periodically. New and significant medical evidence will be included in these updates.

This guideline provides coverage for Proton Beam and Neutron Beam Radiation Treatment (PBRT) for different types of cancer based on medical necessity criteria and does not apply a higher standard of clinical evidence for the coverage of proton beam therapy than for any other form of radiation therapy treatment.

PRINCIPLES OF EBM APPLIED TO ALL TREATMENT MODALITIES (INCLUDING PROTON & NEUTRON BEAM RADIATION THERAPY)

Definition

Prevalence of a type of cancer is defined as the number of cases of that type of cancer, both new and existing, in the population in a given period of time.

It is necessary for all unproven and potentially harmful types of radiation treatment to be validated for use through data generated from clinical research and medical evidence. Due to different degrees of prevalence (i.e., high vs low) for each type of cancer, different levels of medical evidence will be available and required to prove the efficacy of a given radiation treatment for a given type of cancer. This applies equally to ALL radiation treatments including - brachytherapy, intraoperative radiation therapy, photon, electron, neutron, and proton beam radiation treatments.

Evidence Requirements for Highly Prevalent Types of Cancers

Definition

Highly Prevalent Types of Cancer include cancers with $\geq 60,000$ cases per year in the USA - including Breast, Prostate, Lung, Melanoma of the Skin, Colon, Adult Lymphoma, Bladder, Kidney, Head and Neck, Uterus, and Pancreatic cancers.

Since **Highly Prevalent Types of Cancer** occur frequently in the population, historically it has been feasible and beneficial to enroll these cancer patients in clinical research trials that produce the highest degree of medical evidence. The type of clinical research trials that produce the highest degree of medical evidence are Phase 3 randomized controlled trials (RCTs).

Due to the relative abundance of **Highly Prevalent Types of Cancer**, the validation of a specific treatment modality requires that a significant, superior, and clinically meaningful benefit be demonstrated in a phase 3 RCT using that specific treatment modality. Historical examples of new radiation treatment modalities and technologies include:

- LDR Brachytherapy
- HDR Brachytherapy
- Electronic Brachytherapy
- Gamma beam Cobalt-60 LINAC technology
- Photon beam treatments with 2D/3D LINAC technology
- Photon beam treatment with IMRT LINAC technology
- Intraoperative LINAC technology

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- Neutron beam LINAC technology
- Proton beam with 3D/IMPT/Flash LINAC technology

Evidence based validation has historically been required prior to the full acceptance and approval of previously unproven and potentially harmful types of radiation treatment.

As in the case of other radiation treatment modalities, in order for Proton/Neutron beam treatment to be validated for use with a **Highly Prevalent Type of Cancer**, it must first demonstrate a significant, superior, and clinically meaningful benefit when compared to a standard type of radiation treatment in a published Phase 3 RCT for a specific type of cancer.

Evidence Requirements for Less Prevalent Types of Cancer

Definition

Less Prevalent Type of Cancer includes all other cancers with <60,000 cases per year in the USA. The medical evidence required to support the acceptance of PBRT for **Less Prevalent Types of Cancer** will be described below. ⁽⁵⁾

Less Prevalent Cancer Types

Due to their low numbers in the population, enrollment of **Less Prevalent Types of Cancers** in Phase 3 RCTs is extremely difficult and may be impossible.

Indications for PBRT in **Less Prevalent Types of Cancers** may include cancers that are supported by clinical research under the following conditions:

- PBRT trials cited in peer-reviewed medical literature that appear in scientific, medical, and publications in which original manuscripts are published, only after having been critically reviewed for scientific accuracy, validity, and reliability by unbiased, independent experts prior to publication. In-house publications of entities whose business relates to the manufacture, sale, or distribution of proton beam treatment equipment are excluded from consideration.
- In determining whether approval of PBRT is supported for **Less Prevalent Types of Cancers**, the evidence in published, peer-reviewed medical literature listed below will be reviewed. The following will be considered:
 - Whether the clinical characteristics of the beneficiary and the cancer are adequately represented in the published evidence.
 - Whether the administered PBRT regimen is adequately represented in the published evidence.
 - Whether the reported study outcomes demonstrate a significant, superior, and clinically meaningful benefit for the patients receiving PBRT. A significant, clinically meaningful benefit consists of:

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- A survival benefit OR A benefit in decreased chronic/long term toxicity (not a decrease in acute toxicity) AND
- A significance value of $p < 0.05$
- In determining whether approval of PBRT is supported for **Less Prevalent Types of Cancers**, the following will also be considered:
 - whether the experimental design, in light of the PBRT treatment and conditions under investigation, is appropriate to address the investigative question. (*For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover.*)
 - That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of PBRT.

INDICATIONS FOR PROTON BEAM RADIATION THERAPY (PBRT)

PBRT Indications for Specific Cancer Types

Based on the medical evidence criteria described above, the following adult cancer types are indicated for treatment with PBRT:

- Liver (Hepatocellular Carcinoma) and intrahepatic bile duct cancers ^(6,7,8,9,10,11,12,13,14)
- Paranasal Sinus, Nasopharynx, Maxillary Sinus, Ethmoid Sinus, Cavernous Sinus cancers ^(15,16,17,18,19)
- Chordomas and Chondrosarcomas Spine and Base of Skull ^(21,22,23,24,25,26)
- Meningioma ^(27,28)
- Arteriovenous Malformations (AVM) ^(29,30)
- Acoustic Neuroma ^(31,32,33,34)
- Pituitary Adenoma ^(35,36,37,38,39)
- Intraocular (Uveal) Melanoma ^(40,41,42,43,44)
- Other brain or spinal tumors that are adjacent critical structures such as an optic nerve, optic chiasm, brain stem, or spinal cord AND cannot be sufficiently spared using IMRT or SRS treatment.

PBRT Indications for Pediatric Cancers

PBRT will be approved for ALL pediatric patients (≤ 18 years old). ^(45,46) Patients > 18 years old with cancers displaying the same histology as common pediatric cancers, will be evaluated and may be approved for PBRT as an adolescent or young adult (AYA) on a case-by-case basis. ⁽⁴⁷⁾

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Pediatric cancer patients, who require PBRT, should be treated by Radiation Oncologists with access to clinical research trials who have considerable clinical experience treating pediatric patients.

Consider multidisciplinary consultation, which includes a radiation oncologist for the optimal method to reduce radiation-induced late effects.

Radiation Oncologists who specialize in this patient population will have the discretion to choose the appropriate number of fractions and dose that are needed to treat these patients.

(48)

PBRT Indications for Cases of Re-Irradiation

Definitions

Re-irradiation is defined as the use of additional radiation treatment to treat an area of the body that has already received prior radiation to that same area.

The term "re-irradiation" does NOT apply to situations where a patient has received radiation treatment to one area of the body (i.e., the lung) and now requires radiation to a completely separate area of the body (i.e. the brain).

PBRT will be approved for ALL patients who have received any previous radiation to an anatomic location and who now require an additional course of radiation to that same anatomic area.

The radiation dose and the number of fractionations prescribed for each patient receiving re-irradiation will be different and based on that patient's prior treatment history. The dose and the number of fractionations will be left to the discretion on the treating physician and when possible, based on peer reviewed literature. (49,50,51,52,53,54,55,56)

INDICATIONS FOR NEUTRON BEAM RADIATION THERAPY (NBRT)

NBRT Indications

- Neutron beam therapy is considered medically necessary for salivary gland cancers that are unresectable or for patients with recurrent salivary cancers. (2,57,58,59,60,61,62)

Exclusions for PBRT & NBRT

The following scenarios are excluded from coverage with PBRT & NBRT:

- Where the medical evidence for PBRT for a particular type of cancer is an Abstract, Meeting Abstract, or is a published Case Study (*since these published sources only contain anecdotal information or incomplete study details*).
- Where there is insufficient medical evidence to deem PBRT medically necessary for a specific type of cancer even though the patient is enrolled in a clinical trial for PBRT

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(Enrollment in a clinical trial is NOT considered a valid criterion for coverage for PBRT. Nonetheless, a patient may appeal for PBRT coverage to the Health Plan).

- Where there is insufficient medical evidence to deem PBRT medically necessary and the only published studies are “physics” or “dosimetry” studies. These studies make theoretical predictions and are not considered adequate medical evidence.
- Treatment of other tumors with NBRT that are not mentioned in the **Indications for NBRT** section.

CODING AND STANDARDS

Coding

CPT Codes

32701, 61796, 61797, 61798, 61799, 61800, 63620, 63621, 77014, 77261, 77262, 77263, 77280, 77285, 77290, 77293, 77295, 77299, 77300, 77301, 77321, 77331, 77332, 77333, 77334, 77336, 77338, 77370, 77372, 77373, 77387, 77399, 77423, 77427, 77432, 77435, 77470, 77499, 77520, 77522, 77523, 77525, G0339, G0340, G6001, G6002, G6017

POLICY HISTORY

12/11/24 New Policy.

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