EVOLENT CLINICAL GUIDELINE 7001 FOR PROTON BEAM RADIATION THERAPY AND NEUTRON BEAM RADIATION THERAPY SERVICES

Guideline or Policy Number: Evolent_CG_7001	**Applicable Codes**	
"Evolent" refers to Evolent Health LLC and Evolent Specialty Services, Inc. 		
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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 clinicals 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*
- 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.

Special Note

See **Legislative Requirements** for specific mandates for Illinois, Oklahoma, Oregon, Virginia, and Washington.

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 ≥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
- 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:
  - 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]
- Oropharynx Cancer (stage III/IV) [20]
- 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]

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 (*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.

LEGISLATIVE REQUIREMENTS

State of Illinois [63]

HB 2799

HB2799 Enrolled

Section 5. The Illinois Insurance Code is amended by adding Section 356z.61 as follows: (215 ILCS 5/356z.61 new)

(b) A group or individual policy of accident and health insurance or managed care plan that is amended, delivered, issued, or renewed on or after January 1, 2025 that provides coverage for the treatment of cancer shall not apply a higher standard of clinical evidence for the coverage of proton beam therapy than the insurer applies for the coverage of any other form of radiation therapy treatment.

(c) A group or individual policy of accident and health insurance or managed care plan that is amended, delivered, issued, or renewed on or after January 1, 2025 that provides coverage

or benefits to any resident of this State for radiation oncology shall include coverage or benefits for medically necessary proton beam therapy for the treatment of cancer.
Section 99. Effective date. This Act takes effect January 1, 2024.

State of Oklahoma [64]

HB 1515

ENROLLED HOUSE BILL NO. 1515

SECTION 1. NEW LAW A new section of law to be codified in the Oklahoma Statutes as Section 6060.9b of Title 36, unless there is created a duplication in numbering, reads as follows:

A. A health benefit plan, as defined in subsection C of Section 6060.4 of Title 36 of the Oklahoma Statutes, that provides coverage for cancer therapy shall be prohibited from holding proton radiation therapy to a higher standard of clinical evidence for medical policy benefit coverage decisions than the health plan requires for coverage of any other radiation therapy treatment.

B. Nothing in this section shall be construed to mandate the coverage of proton radiation therapy by a health benefit plan.

SECTION 2. This act shall become effective November 1, 2015.

State of Oregon [65]

ORS 743A.130

ORS 743A.130
Proton beam therapy

(1) A health benefit plan, as defined in ORS 7438.005 (Definitions), that provides coverage of radiation therapy for the treatment of prostate cancer must provide coverage for proton beam therapy for the treatment of prostate cancer on a basis no less favorable than the coverage of radiation therapy.

(2) The coverage of proton beam therapy under subsection (1) of this section may be subject to prior authorization, as defined in ORS 7438.001 (Definitions), or other utilization review, as defined in ORS 7438.001 (Definitions), if the prior authorization or utilization review applied to proton beam therapy is no more restrictive than the prior authorization or utilization review applied to radiation therapy.

(3) This section is exempt from ORS 743A.001 (Automatic repeal of certain statutes on individual and group health insurance). [2019 c.466 §2; 2021 c.384 §1]

Note: 743A.130 (Proton beam therapy) was added to and made a part of the Insurance Code by legislative action but was not added to ORS chapter 743A or any series therein.

See Preface to Oregon Revised Statutes for further explanation.

Commonwealth of Virginia [66]

Section §38.2-3407.14:1 of the Code of Virginia

Be it enacted by the General Assembly of Virginia:

1. That §38.2-3407.14:1 of the Code of Virginia is amended and reenacted as follows: §38.2-3407 .14: 1. Standard of clinical evidence for decisions on coverage for proton radiation therapy.

B. Notwithstanding the provisions of §38.2-3419, each policy, contract, or plan issued or provided by a carrier that provides coverage for cancer therapy shall not hold proton radiation therapy to a higher standard of clinical evidence for decisions regarding coverage under the policy, contract, or plan than is applied for decisions regarding coverage of other types of radiation therapy treatment, and each carrier may consider at least one of the following a sufficient standard of clinical evidence to justify coverage of proton radiation therapy:

1. That a proton radiation therapy treatment is covered by Medicare, Medicaid, or any other governmental health care coverage for any type of cancer.

2. That a patient's treating physician or radiation oncologist recommends proton radiation therapy for such patient's cancer treatment.

C. Nothing in this section shall be construed to mandate the coverage of proton radiation therapy under any policy, contract, or plan issued or provided by a carrier.

D. The requirements of this section shall apply to all insurance policies, subscription contracts, and health care plans delivered, issued for delivery, reissued, or extended in the Commonwealth on and after January 1, 2018, or at any time thereafter when any term of the policy, contract, or plan is changed or any premium adjustment is made.

E. This section shall not apply to policies or contracts designed for issuance to persons eligible for coverage under Title XVIII of the Social Security Act, known as Medicare, or any other similar coverage under state or federal governmental plans.

2. That the requirements of this act shall apply to all insurance policies, subscription contracts, and health care plans delivered, issued for delivery, reissued, or extended in the Commonwealth on and after January 1, 2025, or at any time thereafter when any term of the policy, contract, or plan is changed or any premium adjustment is made.

State of Washington [67]

HTCC Coverage Determination 20190517A

Number and coverage topic:
20190517A – Proton beam therapy – re-review

HTCC coverage determination:

Proton beam therapy is a covered benefit for children/adolescents less than 21 years old.

Proton beam therapy is a covered benefit with conditions for individuals 21 years old and older, consistent with the criteria identified in the reimbursement determination.

HTCC reimbursement determination:

Limitations of coverage:
For individuals 21 years old and older proton beam therapy is a covered benefit with conditions for the following primary cancers:

- Esophageal
- Head/neck
- Skull-based
- Hepatocellular carcinoma
- Brain/ spinal
- Ocular
- Other primary cancers where all other treatment options are contraindicated after review by a multidisciplinary tumor board.

Non-covered indicators:
Proton beam therapy is not covered for all other conditions.

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

Applicable Lines of Business

☒	CHIP (Children's Health Insurance Program)
☒	Commercial
☒	Exchange/Marketplace
☒	Medicaid
☒	Medicare Advantage

Policy History

Summary

Date	Summary
August 2024	• This guideline replaces Evolent Clinical Guideline 229 for Neutron Beam Therapy (NBT) • This guideline replaces Evolent Clinical Guideline 221 for Proton Beam Radiation Therapy • This guideline replaces Evolent Utilization Management External Radiation Therapy Policy 2010 for Neutron Beam and Proton Beam Radiation Therapy

LEGAL AND COMPLIANCE

Guideline Approval

Committee

Reviewed / Approved by Evolent Specialty Clinical Guideline Review Committee

Disclaimer

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