IEHP UM Subcommittee Approved Authorization Guidelines
Proton Beam Radiation Therapy for Prostate Cancer

Policy:
The use of Proton Beam Therapy (PBT) in Prostate cancer has not been established as more effective than other forms of External Beam Radiation Therapies (EBRT’s), such as Intensity Modulated Radiation Therapy (IMRT). PBT has more gastrointestinal morbidity than IMRT (1, 3) and IMRT is more cost-effective than PBT for patients with prostate cancer (2, 6).

IEHP considers Proton Beam Therapy for localized Prostate cancer to be not medically necessary as it has not been established to be more effective in increasing overall survival, and reducing gastrointestinal morbidities when compared to IMRT. Thus IEHP adopts IMRT as it treatment of choice for localized prostate cancer.

Analysis of the medical literature does not demonstrate proton beam therapy to clinically superior to other forms of EBRT (4, 5). Alternative forms of EBRT are more readily available and more cost-effective (2, 6).

Medically Necessary/Medical Necessity includes in part that the services is "not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that individual's illness, injury or disease.

Medi-Cal
Proton Beam Treatment Policy Update
Effective for dates of service on or after February 1, 2013, CPT-4 codes 77520 – 77525 are not reimbursable when claimed with ICD-9-CM code 185 (malignant neoplasm of prostate) or 233.4 (carcinoma in situ, prostate).

Neither the National Cancer Institute nor the National Institute of Health recommends Proton Beam Treatment (PBT) for prostate cancer treatment since clinical trials are still being done to prove its efficacy and safety.

Additionally, the California Code of Regulations (CCR), Title 22, Section 51303, excludes experimental and investigational therapies as benefits in the scope of services provided by the Department of Health Care Services (DHCS).
Medical Review Criteria Guidelines for Managing Care (Apollo):

Indications/Coverage examples:
Proton Beam Radiotherapy is covered on the basis of medical necessity for any of the following radiosensitive tumors:

1. Uveal melanomas confined to the globe (iris, choroid or ciliary body) without evidence of metastases or extrascleral extension, and tumors up to 24 mm in diameter. (the uvea is comprised of the iris, ciliary body, and choroid - the vascular middle coat of the eye)
2. Chordomas or chondrosarcomas arising at the base of the skull or along the axial skeleton without metastases.
3. Pituitary adenoma when conventional stereotactic radiation is not an option.
4. Other central nervous system tumors located near vital structures.
5. Intracranial arteriovenous malformations (AVMs) not amenable to surgical excision or other conventional forms of treatment.
6. CNS lesions (primary or metastatic malignancies or AVMs) measuring ≤ 3 cm in diameter that are adjacent to critical structures such as the optic nerve, base of skull, brain stem or spinal cord.
7. Prostate cancer (as an option in addition to IMRT or conformal radiation therapy).

Limitations/exclusions - verify coverage with each health plan – covered indications vary:

1. Proton Beam Therapy is significantly more expensive therapy than other options, but not clinically superior; therefore, some health plans will not cover proton beam therapy for prostate cancer.
2. Proton Beam Radiotherapy does not have substantial evidence for clinical efficacy and may be considered experimental for age-related macular degeneration, non-uveal melanomas, hepatocellular carcinomas and choroidal hemangiomas.

ECRI’s Health Technology Assessment Information Service:

<table>
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<th>Table 2. Systematic Reviews and Technology Assessments Reference</th>
<th>Purpose of Systematic Review Technology Assessment</th>
<th>Resources Searched and Inclusion Criteria</th>
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To compare the effects of proton beam therapy, with or without external beam radiotherapy, against alternative radiotherapy modalities and other treatments of prostate cancer.

MEDLINE (via PubMed) search was performed from January 1966 through March 2011 and was limited to English-language articles on human subjects. 234 citations were identified. Bibliographies from recent review articles and clinical studies were also reviewed. Inclusion criteria included full-length English language publications, comparative trials of any size or single-arm studies of at least 10 patients per arm with prostate cancer; reporting on one or more relevant outcomes.

This review did not identify any clinical trials evaluating the use of intensity-modulated radiation therapy (IMRT) compared to proton beam therapy (PBT) to treat prostate cancer.

“There is inadequate evidence from comparative studies to permit conclusions for any of the 4 comparisons considered here.”

To appraise the comparative clinical effectiveness and comparative value of brachytherapy, IMRT, and PBT for men with clinically-localized, low-risk prostate cancer.

MEDLINE, EMBASE, and The Cochrane Library (including the Database of Abstracts of Reviews of Effects) plus reference lists of all eligible studies published during the period January 1995 – August 2008; for IMRT, publications between January 2007 and August 2008 were added to studies from the previous ICER appraisal.

Of the 387 articles identified for inclusion, no comparison studies of interest were identified; only 15 single arm studies (6 PBT, 9 IMRT).

“No evidence has been presented to date on the effects of either PBT or IMRT on overall or disease-specific survival, limiting the

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### Table 3: Comparative Clinical Trials Reference

<table>
<thead>
<tr>
<th>Number of Patients</th>
<th>Treatment</th>
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<th>Conclusions Presented in the Abstract</th>
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<tbody>
<tr>
<td><strong>Nonrandomized Controlled/Comparison Studies</strong></td>
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<tr>
<td>Sheets et al. 2012 (1)</td>
<td>1368 patients with localized prostate cancer</td>
<td>Intensity modulated radiation therapy (IMRT) vs. proton therapy</td>
<td>Based on Surveillance, Epidemiology, and End Results-Medicare linked data from 2000 to 2009, a propensity score-matched comparison of IMRT and proton therapy indicated that IMRT patients had a lower rate of gastrointestinal morbidity (absolute risk, 12.2 vs. 17.8 per 100 person-years; relative</td>
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<td></td>
<td></td>
<td></td>
<td>“Among patients with nonmetastatic prostate cancer… [the use of] IMRT compared with proton therapy was associated with less gastrointestinal morbidity.”</td>
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</table>
Yoon et al. 2010 (8) | 5 prostate cancer patients | IMRT vs. proton therapy | Secondary cancer risk was assessed by ion chamber and CR-39 detectors during IMRT and proton therapy, respectively. The average secondary dose of IMRT was approximately one order of magnitude higher than proton therapy (range 3 mSv/Gy [millisievert/Gray] to 1 mSv/Gy (IMRT) vs. 0.4 mSv/Gy to 0.1 mSv/Gy (proton therapy). “Comparisons of organ-specific organ equivalent dose showed that the estimated secondary cancer risk using scattering mode in proton therapy is either significantly lower than the cases in IMRT treatment or, at least, does not exceed the risk induced by conventional IMRT treatment.”

**National Comprehensive Cancer Network Guideline on Prostate Cancer:**
Proton Therapy is not recommended for routine use at this time, since clinical trials have not yet yielded data to demonstrate superiority to, or equivalence of, Proton Beam and conventional beam for treatment of prostate cancer. (4)

**AHRQ's Technology Assessment (March 2010):**
For comparative effectiveness between different forms of radiation treatments (BT, EBRT, SBRT), available data also could not determine if one form of radiation therapy is superior to another form in terms of overall or disease-specific survival. Available data suggest that higher EBRT dose is associated with increased rates of long-term biochemical control compared with lower EBRT dose. Available data also suggest BT is associated with more genitourinary toxicity and less gastrointestinal toxicity compared with EBRT. Whether EBRT is administered as a standard fractionation or moderate hypofractionation seems to make little difference in terms of biochemical control and late genitourinary and gastrointestinal toxicities. (5)

**American College of Radiology (2006):**
For stage T1 and T2 prostate cancer, the American College of Radiology (ACR) (2006) indicates that “dose escalation using IMRT has an improved therapeutic ratio with improved PSA relapse free survival rates and reduced gastrointestinal and genitourinary toxicity.” Due to limited data comparing Proton Beam Therapy to other methods of irradiation or to radical Prostatectomy, however, the ACR indicates that further studies are needed to clearly define its role to treat stage T1, and T2 prostate cancer. (7)
National Cancer Institute (NCI):  
The NCI (2011) lists PBT as a treatment option under clinical evaluation due to a lack of supporting data. NCI states “although Proton Therapy could theoretically improve the therapeutic ratio of prostate radiation, allowing for an increase in dose to the tumor without a substantial increase in side effects, no randomized controlled trials have been conducted to compare its efficacy and toxicity with those of other forms of radiation therapy.

American Society of Radiation Oncology (ASTRO):  
In a technology evaluation of PBT, ASTRO (2010) concluded that outcomes for patients treated with PBT were similar to those treated with Intensity Modulated Radiation Therapy (IMRT). Based on the clinical data, there was no clear benefit from PBT over IMRT including disease control or prevention of late toxicity. ASTRO stated that “further head to head clinical trials may be needed to determine the role of PBT in treating prostate cancer.”

Cigna Medical Coverage Policy for Proton Beam Therapy in Prostate Cancer:  
Cigna covers Proton Beam Therapy (PBT) as medically necessary for the treatment of localized cancer of the prostate (i.e., cancer that is confined to the prostate). Cigna considers proton beam therapy to be clinically equivalent, but not clinically superior, to conventional external beam radiation therapy (i.e., three-dimensional conformal radiotherapy [3D-CRT], intensity modulated radiation therapy [IMRT] or image-guided radiation therapy [IGRT]) for the treatment of localized cancer of the prostate.

Coverage for Proton Beam Therapy for the treatment of localized prostate cancer may depend upon the applicable health benefit plan definition of medical necessity. Many health benefit plans administered by Cigna contain definitions of medical necessity which include a cost comparison component. Because Proton Beam Therapy for the treatment of localized prostate cancer is significantly more expensive than conventional External Beam Radiation Therapy (i.e., three-dimensional Conformal Radiotherapy [3D-CRT], Intensity Modulated Radiation Therapy [IMRT] or Image-Guided Radiation Therapy [IGRT]) but is not clinically superior, it is considered not medically necessary under those plans. For health benefit plans which contain definitions of medical necessity that do not include a cost comparison component, proton beam therapy may be covered as medically necessary for the treatment of localized prostate cancer (i.e., cancer that is confined to the prostate).

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Bibliography:


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