Establishing Proton Technology Equipment for Cancer treatment- Is this treatment cost-effective: A Rapid Health technology Assessment

Health Technology Assessment in India (HTAIn)
Postgraduate Institute of Medical Education & Research, Chandigarh

Policy Brief

Evidence Summary:

- Limited evidence to suggest that PBT is a clinically effective technology in comparison to current clinical practice.
- Less than half of published clinical trials of PBT are prospective. Only 10% of prospective studies of PBT are randomized.
- Most of the studies reporting clinical effectiveness of PBT are single armed observational studies.
- Current indication for proton therapy in a few international clinical guidelines for PBT is only for a small number of cancers such as skull, spine, ocular soft tissue cancers and few pediatric cancers.
- No international agency has strongly appraised the effectiveness of PBT in comparison to IMRT, CRT, SBRT.
- Indian literature suggests that even IMRT and 3D-CRT are not cost-effective at current threshold.

Image source: Internet

Proton beam therapy in comparison to existing current clinical practice including CRT, SBRT, IMRT, Carbon-ion therapy, Photon radiotherapy, Enucleation and plaque brachytherapy is recommended as cost-ineffective technology.

Policy Recommendations:

- Limited evidence to suggest that PBT is a clinically effective technology in comparison to current clinical practice.
- Less than half of published clinical trials of PBT are prospective. Only 10% of prospective studies of PBT are randomized.
- Current indication for proton therapy in a few international clinical guidelines for PBT is only for a small number of cancers such as skull, spine, ocular soft tissue cancers and few pediatric cancers.
- No international agency has strongly appraised the effectiveness of PBT in comparison to IMRT, CRT, SBRT.
- Indian literature suggests that even IMRT and 3D-CRT are not cost-effective at current threshold.

Background and Gap in Literature:

Radiation therapy is a vital speciality in cancer management as it is effective in treating malignancies as radical or palliative treatment. It is based on high energy beams/radioactive substances to halt the growth and division of tumour cells. Nearly two-third of cancer patients require radiation therapy as a unique treatment or as part of more complex therapeutic protocol. Earliest form of radiation was based on single large exposure. Various modalities were established in order to minimize the side effects and maximize the tumor dose. The establishment of cobalt units was a notable discovery. There is growing interest in the use of proton beam therapy (PBT) for the treatment of cancer. Proton therapy is a form of radiation treatment used to destroy tumor cells. Unlike x-rays (regular radiation treatment), it uses protons to sends beams of high energy that can target tumors more precisely than X-ray radiation. However, given the limited capacity and higher costs, decisions on which radiation therapy should be used to treat cancer patients should be based on comparisons of proton therapy against current best practice.

Research Question:

Is establishing Proton Technology Equipment for cancer treatment cost-effective for India?

Population:

Adult or pediatric population suffering from any type of cancer irrespective of stage

Intervention:

Proton Beam Therapy (PBT)

Comparators:

Conventional radiotherapy (CRT) Stereotactic body therapy (SBRT) Intensity Modulated Radiation therapy (IMRT) Carbonion therapy Photon radiotherapy Enucleation and plaque brachytherapy

Outcomes of Interest:

Local recurrence-free survival, overall survival, toxicity, relapse-free survival including local recurrence, loco-regional recurrence, distant metastasis and death, quality of life and economic costs.

Policy Brief

Methods and Approach

We have attempted a review of existing literature on clinical effectiveness of PBT relative to other available modalities for radiation therapy. Furthermore, existing literature on health economic evidence and recommendations of various international guidelines was being reviewed using methods for rapid health technology assessment.

Health Economic Evidence

Study and year	Country	Cancer type	Interventions assessed	Stated Perspective	Reported main result
Grutters et al 2010	The Netherlands	Inoperable stage I nonsmall cell lung cancer	PBT, carbonion therapy, CRT, and SBRT	Dutch health Care perspective	PBT and CRT dominated by carbon-ion therapy and SBRT
Parthan et al 2012	USA	Localized prostate cancer	PBT, IMRT, and SBRT	Health care payer and societal	PBT and IMRT dominated by SBRT in both perspectives
Ramaekers et al 2013 Dutch	The Netherlands	Locally advanced (stage 3–4) head and neck cancer	PBT for all patient, IMRT for all patients, and PBT if efficient	health Care perspective	ICER for PBT if efficient versus IMRT for all: €60,278 ICER for PBT for all versus IMPT if efficient: €127,946
Moriaty et al 2015	USA	Intraocular melanoma	PBT, enucleation, and plaque brachytherapy	Provider perspective	ICER for PBT versus enucleation: $106,100 ICER for plaque brachytherapy versus enucleation: $77,500 ICER for PBT versus plaque brachytherapy not reported
Mailhot Vega et al 2016.	USA	Breast cancer	PBT and photon radiotherapy	Societal perspective	In base case analysis with $50,000 threshold: Women with no CRFs: PBT not cost-effective for all ages and for all photon MHD tested (up to 10 Gy).
Leung et al 2017	Taiwan	Inoperable advanced hepatocellular carcinoma (large tumours)	PBT and SBRT	Single payer healthcare system	ICER for PBT versus SBRT: NT$ 213,354 (equivalent to US $14,180 in 2016 prices)
Sher et al 2018	USA	Oropharyngeal squamous cell carcinoma	PBT and IMRT	Payer perspective and societal perspective	HPV-positive patients: ICERs for PBT versus IMRT: $288,000 and $390,000 in the payer and societal perspectives respectively. HPV-negative patients: ICERs for PBT versus IMRT: $516,000 and $695,000 in the payer and societal perspectives respectively

Clinical Guidelines on PBT:

NICE	PBT for the treatment of malignant brain tumors and prostate cancer is currently being monitored
ILROG	Adults with mediastinal lymphomas and for young women. Heavily pretreated patients who are at elevated risk for radiation-related toxicity to the heart, lungs, and/or bone marrow.
NCCN	Chondosarcomas of the skull base and axial skeleton, cancer of the nasopharynx, nasal cavity, or paranasal sinuses, cranio-spinal irradiation. No clear evidence supports a benefit or decrement to proton therapy over IMRT for either treatment efficacy or long-term toxicity.
ASTRO	• Ocular tumors, including intraocular melanomas, Tumors that approach or are located at the base of skull, including but not limited to Chordoma, 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 when at least one of the four criteria noted above apply
ESMO	No recommendation on PBT due to lack of clear evidence on benefits associated with PBT

Results:

- Particle therapy results in higher survival rates than CRT in stage I inoperable NSCLC patients.
- No firm conclusions can be drawn on the reduction of side effects after particle therapy.
- Particle therapy may be more beneficial in stage III NSCLC, where 2-year survival is only 26–36% with concurrent chemo-radiation with photons, and severe adverse events occur more frequently.
- However, more evidence is needed on whether particle therapy is actually beneficial in advanced stage NSCLC.

Impact of Proton beam therapy on quality of life among cancer patients

Quality of life (QoI) did not deteriorate during PBT in case skull base cancers and after PBT in brain tumors. PRO higher for PBT than photon therapy in case of head and neck and lung cancers. Patient reported breast cosmesis was appropriate after PBT and comparable to photon modalities.