

Review article

Proton Beam Therapy in Head And Neck Cancer

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ABSTRACT

High-energy x-rays, deposit an entrance and an exit dose to healthy vital surrounding organs thus provide greatest challenge to treat cancer ,so the dose which is safely administered is limited. To improve organ sparing and/or safely escalate doses of radiation proton therapy plays a vital role. It is a new emerging and treatment modality ,a highly precise beam is used to target radiation directly at the tumor locating point, thereby minimizes the possible damages to close healthy tissues and substantially reduces the risk of both severe and long-term side and subsequent effects.

Introduction

The well established and accepted therapeutic modality for head and neck cancer is external beam radiation therapy¹. Linear accelerator which produces high energy x-rays are usually used in radiotherapy. Using high doses of external beam radiation it would be possible to treat and cure patients suffering with head and neck cancer². However, it results in acute and late toxicity. Chronic xerostomia, which can affect eating, communication, pain, and emotion, as well as increase the risk of developing dental caries is caused by radiation exposure to salivary glands. Patients with high doses of radiation to the mandible are at risk for mandibular osteoradionecrosis , especially if they require post radiation dental extractions¹, with 0% risk for less than 54 Gy per treatment and 9.8% risk for 54 Gy . In children ,low doses of radiation produce complications such as neurocognitive deficits, hearing loss, pituitary dysfunction, hypothyroidism, cardiac

dysfunction, pulmonary disease, diminished vertebral body growth, scoliosis, gastrointestinal tract dysfunction, infertility, and Secondary metastasis. ⁵. The shortcomes of external beam radiotherapy can be substantially overcome by using hadrons (i.e., protons and light ions such as carbon, helium, oxygen and neon, in particular carbon ions)⁴The marked reduction in dose of proton beam therapy to the body and healthy organs reduce the extent of the harmful low-dose x-ray effect⁵

HISTORY AND STATUS OF PROTON THERAPY

After construction of the cyclotron at Lawrence Berkeley Laboratory, patients were treated for cancer in 1954. In 1990, Loma Linda University opened the first hospital-based proton therapy center with gantry systems³ Today there are 16 proton therapy centers in operation in the United States and 46 centers worldwide³ The PSI or Paul Scherer Institute is the

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only center in the world has the experience of treatment with intensity modulated proton therapy. Paul Scherer Institute, is the first proton therapy center, has the world's only gantry so far using so-called spot-scanning technology. Proton therapy typically takes about a quarter to half an hour each day and is delivered five days a week for nearly four to seven weeks for treatment. Based on each patient, the course of treatment and time duration per treatment each day differs.⁴ Smaller and less expensive proton beam delivery units are under investigation to expand the clinical application of proton beam therapy.⁶

RADIOBIOLOGY AND MECHANISM OF PROTON BEAM RADIATION

Linear Energy Transfer (LET) is the rate of energy deposited or lost per distance travelled. Charged particles generally have higher LET than X and γ rays because of their greater energy deposition along the track. Protons are positively charged subatomic particles.⁵ The LET value for therapeutic proton-beam ranges from 0.2 to 2.0 keV/mM, the protons slow down and deposit most of their energy just before stopping. The region of maximum dose deposition at the end of the proton range is called the Bragg Peak, named after William Henry Bragg who described the phenomenon for α particles in 1903. The location of the Bragg Peak is a function of the proton energy and the electron density of the material through which it passes. By changing the energy of the proton beam and density, the accurate location of maximum dose deposition (the Bragg Peak) can be specified within the tumor. There is no significant radiation dose beyond the Bragg Peak. In contrast, the dose from a photon beam decreases exponentially with depth in the irradiated tissues.⁶

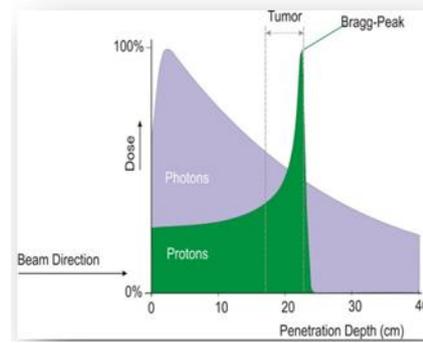


FIG 1 GRAPHIC ILLUSTRATION OF BRAGG PEAK EFFECT¹²

Proton Beam Delivery

Proton delivery techniques can be divided into passive or active. The most commonly used passive technique in the clinical setting, spreads the beam laterally using a combination of gold (or lead) and Lexan foils. The combination of low and high atomic number of these materials, produces a flat beam of constant flux and a constant range. By using a rotating plastic wheel, the beam is changed in depth that effectively allows for the superposition of multiple Bragg peaks of varying energy and intensity. This creates a region of uniform high dose called the spread-out Bragg peak (SOBP). It is followed by collimation of the beam by brass or Cerrobend® apertures and its penetration depth is diversified by means of a wax bolus. This arrangement creates a uniform dose across the treatment volume, as displayed in Fig. 2,

Active techniques apply a magnetically guided proton pencil beam in combination with dynamic changes of beam energy and beam intensity during treatment. One advantage of the active system is that it minimizes the production of secondary particles by decreasing the interaction between the primary beam and beam modifying devices. Further, it has the ability to treat complex tumor volumes with greater precision and improved normal tissue sparing. However, the dosimetry and beam delivery is more complex and

difficult; errors in this regard can lead to high and low dose regions and an incomplete treatment of the tumor volume. Organ motion during treatment is another complicating factor that also needs to be considered for effective and accurate treatment of the tumor volume.⁷

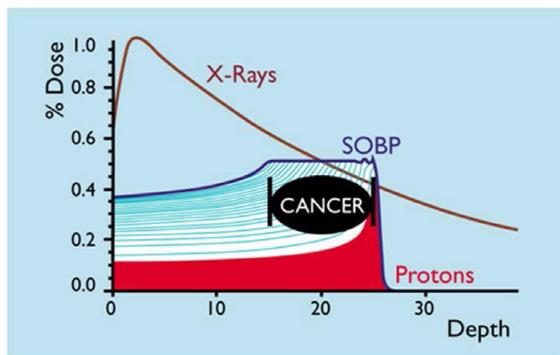


Fig 2 Comparison of the X-ray depth dose curve with the SOBP used in passive proton beam delivery for clinical treatment⁷

SYNCHOTRON

A particular type of cyclic particle accelerator, called synchrotron descended from the cyclotron, in which the guiding magnetic field (bending the particles into a closed path) is time-dependent, being *synchronized* to a particle beam of increasing kinetic energy. Accelerators used for proton therapy typically produce protons with energies in the range of 70 to 250 MeV (mega electron volts; million electron volts). When the beam arrives at the proton room it must be delivered to the target site. A gantry allows for beam delivery 360 degrees around the patient. Patients using lasers and X-rays images accurately aligned relative to the beam delivery system (isocenter). The combination of gantry proton delivery with six-degree-of-freedom robotic patient positioners (Fig. 3) allows clinicians the greatest flexibility in proton beam delivery in treating the target volume while sparing critical structures. Treatment times per beam is of the order of 1-2 minutes, during which time the patient feels

nothing and is under constant audio and visual monitoring by the therapy team⁷

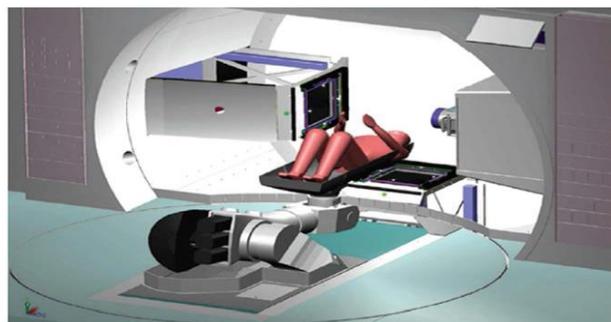


FIG 3 SCHEMATIC ILLUSTRATION OF ROBOTIC PATIENT POSITIONER AND GANTRY BEAM DELIVERY SYSTEM⁷

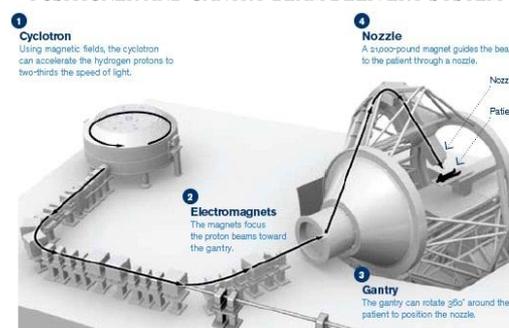


FIG 4 SCHEMATIC ILLUSTRATION OF PARTS¹⁴

TREATMENT PLANNING

Creation of custom immobilization devices, including a thermoplastic face mask, alpha cradle body mold, and acquisition of a noncontrast treatment planning CT scan with 1-mm slice thickness. Preoperative and postoperative imaging was coregistered to delineate the initial extent of tumor, areas of residual disease, and postoperative anatomy. Proton treatment planning was 3-dimensional (3D) conformal radiotherapy using uniform scanning beam delivery, which delivers a uniform spread of Bragg peak across each field. The choice of beam angles and number of beams varied by the extent and complexity of each individual patient's tumor. Brass apertures were fabricated to define the shape of each field and conform to the lateral extent of the target, with Lucite range compensators milled to shape the distal end of the proton beam, achieving

distal conformality to the target. Treatment optimization involved multiple iterative adjustments in individual field shape and design to achieve the desired target coverage and normal tissue sparing⁸

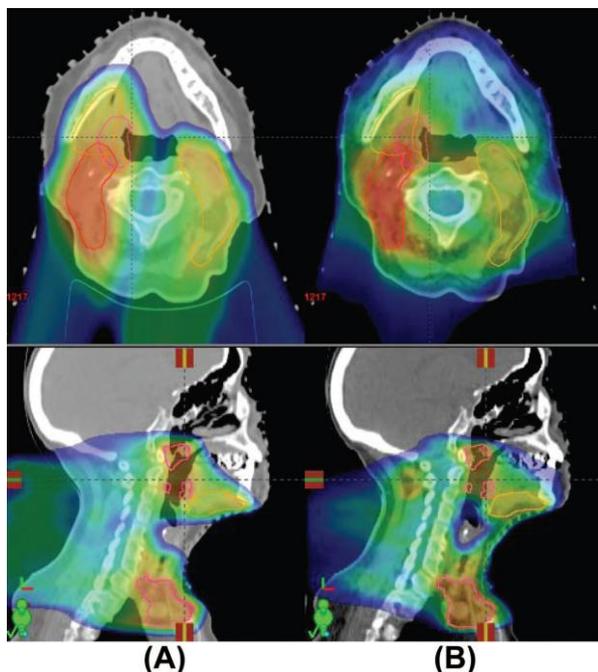


Fig 5 Comparison of (A) a pencil-beam proton plan and (B) intensity-modulated radiation therapy. Both plans obtained similar target coverage. Compared with intensity-modulated radiation therapy, the pencil-beam scanning plan delivered lower doses to the oral cavity (3 versus 16 Gy) as well as to the contralateral (B) parotid gland (20 versus 25Gy)¹¹

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ADVANCEMENTS

Pencil beam scanning, first described by Kanai et al. of Chiba, Japan⁶ used magnets to steer the positively charged proton beam. It was developed for medical use at the Paul Scherer Institute (PSI) in Switzerland. The technology required for beam scanning is more sophisticated and more sensitive to tissue inhomogeneity and organ motion^{9,10} than passive scattering systems. The objectives will be to optimize time history evolution of the 3 manipulated variables (beam current, scanning magnet currents (X & Y)) along a pre-determined beam path in order to reach the prescribed dose in a very conformal way and within the minimum amount of time.¹⁴ For pencil beam scanning, there is no patient-specific hardware needed to shape the beam which also results in less neutron contamination to the patient. Intensity-modulated proton therapy (IMPT) is enabled with beam scanning technology, and a steeper lateral dose gradient can be achieved. Despite the advantages of active pencil beam scanning compared with passive scattering systems, most facilities in existence and in construction use passive scattering system

Intensity-Modulated Radiation Therapy Versus Intensity-Modulated Proton Therapy

Intensity-modulated radiation therapy (IMRT) is a technique where the intensity of photon (X-ray) radiation varies throughout the treatment field create a sharp dose gradient between the target and surrounding nontarget tissue. IMRT is increasingly used for the treatment of head and neck cancers in

effort to decrease morbidity and improve tumor control. The dose is frequently spread among many beams, enters the patient from different angles, results in a “dose bath” in which normal tissue receives a low-to-medium dose of unnecessary irradiation, which may result in unwanted acute and late side effects. The intensity of the proton radiation can also be modulated to produce IMPT. This is achieved by a pencil beam scanning technique in which a small circular beam is scanned across the defined treatment field with the energy and intensity varying so that the dose in each voxel can be optimized.⁶

USES

1. Hodgkin lymphoma in children, adolescents, and young adults

Though x-ray therapy may improve results in HL, it significantly increases the risk of SM, particularly breast, lung, and thyroid cancers and hematogenous cancers. The risk of radiation-induced cancers is proportional to the dose delivered. Using a proton beam treatment planning system, the distribution of proton dose to x-ray dose was compared in patients and found that the integral dose of exposure radiation to the patient was reduced by at least 50% with the use of scattered or scanned proton beams compared with 3-D or intensity modulated x-ray beams. This reduction predicts that the risk of radiation-induced cancers would be reduced by at least 50%.⁵

2. Skull base Chordomas and chondrosarcomas since, vital structures such as optic pathways, brainstem, and spinal cord can be spared⁴

3. Oro pharyngeal carcinoma, by reducing dose to normal structures, including the spinal cord, salivary glands, mandible, and pharyngeal muscles⁴

CONCLUSION

The advantages inherent to protons, with rapid dose fall off, can yield improvements in the ability to escalate radiation dose, or to better spare organs at risk. Although emerging clinical data are promising, new techniques, such as pencil beam scanning and IMPT need to be developed further, and to potentially expand the indications under which proton therapy should be considered.

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