CHAPTER ELEVEN
PROTON BEAM RADIATION
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Particle radiation has weight and mass and usually an electrical charge. X-rays and gamma rays have no weigh or mass. Particle radiation includes parts of atoms such as positively charged protons and neutral neutrons. Massive cyclotrons and linear accelerators use enormous amounts of energy to accelerate these particles. Protons and neutrons have a mass that is 1800 times that of electrons so they cannot be accelerated to the same speed as electrons or beta particles. Since most particles have a charge, they can be aimed and controlled by electronic means. Neutrons do not have a charge so they cannot be controlled as accurately as the charged particles, but they are used because they actually have a higher relative biological effectiveness (RBE) than other particles.

Since x-rays and gamma rays have no weight or mass, they can travel very fast, approaching the speed of visible light, or 186,000 miles per second. Scientists would like to be able to get the same speed from particles, but since they are quite heavy and massive, it is not possible.

Understanding How Protons Work
All matter is made up of atoms. This includes animal, vegetable, mineral and metals. It also includes cancerous tumors. In the center of every atom is a nucleus. Orbiting the nucleus of each atom are negatively charged electrons.

When energized charged particles, such as protons or other forms of radiation, pass near orbiting electrons, the positive charge of the protons attracts the negatively charged electrons, pulling them out of their orbits. This is called ionization; it changes the characteristics of the atom and consequently the character of the molecule within which the atom resides.

This crucial change is the basis for the beneficial aspects of all forms of radiation therapy. Because of ionization, the radiation damages molecules within the cells, particularly the DNA or genetic material. Damaging the DNA destroys specific cell functions, especially the ability to divide or proliferate.

Enzymes within the cells attempt to rebuild the injured area of the DNA; however, if damage from the radiation is too extensive, the enzymes will not be able to repair the injury.

While both normal and cancerous cells go through this repair process, a cancer cell's ability to repair molecular injury is frequently inferior. As a result, cancer cells sustain more permanent damage and subsequent cell death than occurs in the normal cell population. This permits selective destruction of bad cells that may be growing among good cells.

Both conventional x-ray therapy and proton beams work on the principle of selective cell destruction. The major advantage of proton treatment over conventional radiation, however, is that the characteristic energy distribution of protons can be deposited in tissue volumes designated by the physician in a three dimensional pattern. This capability provides greater control and precision and, therefore, superior management of treatment.

Radiation therapy requires that conventional x-rays be delivered into the body in total doses sufficient to assure that enough ionization events occur to damage all the cancer cells. The lack of charge and mass in conventional x-rays-called photons-results in most of the energy being deposited in normal tissues near the body's surface. Undesirable energy may be deposited beyond the target or the cancer volume as the x-rays continue through the tissue.

This undesirable pattern of energy placement can result in unnecessary damage to healthy tissues. This may prevent the use of sufficient radiation to control the cancer. There is a finite limit as to how much radiation the body can withstand.

Protons Energized to Specific Velocities

Protons may be energized to specific velocities. These energies determine how deeply in the body protons will deposit their maximum energy. As the protons move through the body, they slow down, causing increased interaction with orbiting electrons.

Maximum interaction with electrons occurs as the protons approach their targeted stopping point. Thus, maximum energy is released within the designated cancer volume. The surrounding healthy cells receive significantly less injury than the cells in the designated volume. This point, where the high dosage region of energy release occurs, is called the Bragg peak.

The favorable absorption characteristics of protons allows the physician to predict and control their depth of travel within the patient. At the tumor site, the Bragg peak can be enlarged to conform to the thickness of the designated volume of the tumor. The heavy mass also results in minimal deviation and minimal side-scatter. This is a significant factor in reducing unwanted side-effects and maximizing treatment benefit.

Conventional x-rays

Conventional x-rays lose most of their energy near the body's surface and exponentially deposit energy as they travel through tissue. Electrons, because of their low mass, are easily deflected from their initial direction and produce significant secondary lateral scatter. When photons or electrons (x-rays) are used, healthy tissues surrounding the tumor target frequently receive equal doses, given the designated volume. Radiation oncologists attempt to circumvent these problems. They often employ multi-field arrangements to build up the doses, and spare as much of the normal tissue as possible, by restricting the dose in those tissues to a level the patient can tolerate.

Multi-field arrangements can be used with protons also. When they are used, the dose to normal tissues is cut to half or less, thereby minimizing adverse, normal-tissue damage. When multiple proton fields are used, the dose in the overlapped beams is further increased relative to normal tissue. This permits more effective doses to be delivered to the designated volume than can be achieved with x-rays.

Because of the dose-distribution characteristic of protons, the radiation oncologist can increase the dose to the tumor while reducing the dose to surrounding normal tissues. This allows the dose to be increased beyond that which less-conformal radiation would allow. The overall affects lead to the potential for fewer harmful side effects, more direct impact on the tumor, and increased tumor control.

The patient feels nothing during treatment. The minimized normal-tissue injury results in the potential for fewer effects following treatment such as nausea, vomiting, or diarrhea. The patient experiences a better quality of life during and after proton treatment. Proton's provide a vast new potential for non-invasive treatment of all cancer patients when the tumor is localized.

For conformal proton beam planning purposes the patients are immobilized in a custom-fitting plastic cylinder. A balloon is placed in the rectum and inflated with 120 cc of water so as to exclude the majority of the rectal volume from the prostate treatment fields. A thin slice Computed Tomography (CT) scan of the pelvis is performed with the patient in his immobilization cylinder. The prostate, bladder, and rectum are outlined by a physician on LLUMC’s 3D conformal planning system which utilizes beam’s eye view planning and dose-volume histograms to optimize individual treatment plans.

In virtually all instances a simple two field (right and left lateral beams) plan provides for the best coverage of the gland while sparing the majority of the bladder and rectum. All individual cerrobend apertures and wax tissue compensators are produced on automated milling machines controlled by the 3D planning system. Patient position is verified daily before each conformal proton beam treatment by obtaining orthogonal radiographs of the patient’s pelvis in the treatment position via a coaxially mounted x-ray tube. Measurements are made from various bony landmarks to the isocenter and compared with optimal measurements obtained from a computer-generated digitally reconstructed radiograph (generated from the CT planning scan). The treatment table is moved to match the various measurements. Fig. 11-1 shows a patient receiving proton beam radiation.

Typically, the time required for each patient's set-up and treatment is 20-30 minutes per day.

Between January ,1992 and December, 1995 260 patients with early stage prostate cancer (defined as stages T1-T2B, PSA <15 NO or Nx, no prior hormonal therapy or surgery) were treated. The radiation dose to the prostate was 74-75CGE (Cobalt Gray Equivalent, utilizing a proton RBE of 1.1) given at a dose rate of 1.8-2.0 Gy per day. Two hundred and nine patients were treated with conformal protons alone while fifty one were treated with a combination of 30 CGE protons to the prostate and seminal vesicles plus 45 GY conformal photons to the pelvis.

By 1998 the number of patients treated had risen to 319. Their study was published in Urology 53: 978-984 1999.
Three hundred nineteen patients with T1 -T2b prostate cancer and initial prostate-specific antigen (PSA) levels of 15.0 ng/mL or less received conformal radiation doses of 74 to 75 cobalt gray equivalent with protons alone or combined with photons. No patient had pre- or post-treatment hormonal therapy until disease progression was documented. Patients were evaluated for biochemical disease-free survival, PSA nadir, and toxicity; the mean and median follow-up period was 43 months.

Overall 5-year clinical and biochemical disease-free survival rates were 97% and 88%, respectively. Initial PSA level, stage, and post-treatment PSA nadir were independent prognostic variables for biochemical disease-free survival: a PSA nadir 0.5 ng/mL or less was associated with a 5-year biochemical disease-free survival rate of 98%, versus 88% and 42% for nadirs 0.51 to 1.0 and greater than 1.0 ng/mL, respectively. No severe treatment-related morbidity was seen.

It appears that patients treated with conformal protons have 5-year biochemical disease-free survival rates comparable to those who undergo radical prostatectomy, and display no significant toxicity.

Protons are a superior particle for clinical use because:
They have favorable physical dose absorption characteristics in tissues which allow exact energy deposition, thereby sparing normal tissues and organs;
Their radiobiologic characteristics are similar to photons (x-rays), and thus, are well known.

As of November 1999, 4,666 patients have been treated at Loma Linda for several different types of cancer. Proton Beam therapy seems to have similar results as that attained from Conformal 3D radiation.

If you are considering proton treatment at Loma Linda, you or your physician should contact the patient referral office:

Phone: (909) 558-4288 or (800) PROTONS (USA only)
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E-mail: Referral@dominion.llumc.edu -- referral and information service
For more information, visit their web site at: http://www.llu.edu/llu/ci/

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