APPLICATION OF PROTON RADIATION THERAPY*

J.O. Archambeau
Nassau County Medical Center
East Meadow, New York

G.W. Bennett and G.S. Levine
Brookhaven National Laboratory
Upton, New York

Abstract

Assessment of the available data indicates that proton radiation therapy has more to offer the patient than existing x-ray therapy. The physical properties of proton beams which allow the major fraction of the dose to be confined to a designated volume are reviewed. Dose delivery schemes employing protons are discussed and treatment plans including dose distributions are compared for protons and x-rays.

Introduction

Irradiation has an established role in the therapy of cancer. Radiation control of the cancer depends on a relative radiosensitivity existing between the cancer and the normal tissue contained in the irradiated volume. If the cancer is more radioresistant than surrounding normal tissues, a therapy failure results since increasing the dose to a level that controls the cancer causes unacceptable normal tissue damage. Consequently, definition of the volume to be irradiated, specification of the radiation, and selection of the time-dose schedule that will control the cancer while preserving normal tissues become the all important functions of the therapist.

Attempts to improve the therapy results must focus on increasing the dose to the cancer relative to normal tissues. This may be accomplished either by altering the radiosensitivity between the cancer and normal tissues or by changing the dose distribution of the radiation. The accelerator physicist is aware of these requirements and has suggested that protons can be usefully utilized to achieve an improved dose distribution.

Proton Beams

Protons have a fixed range in tissue. The dose distribution along this range is such that most of the dose is deposited over the last few centimeters. Fortunately, this region of increased dose can be arbitrarily widened by suitable variation of the energy and flux intensity of the beam. As a consequence of these properties the major fraction of the absorbed dose of protons can be confined to a designated volume.

Proton beams for radiation therapy are entirely practical.[1] An energy of 200 MeV corresponds to a range of 25 cm of tissue so that every organ in the body is accessible. There is very little contamination due to unwanted secondary particles. Large treatment volumes (e.g. 25 cm diameter field, 10 cm axial length) require less than 1 nanoampere average current for exposure to a dose fraction of 200 rads in 10 minutes treatment duration. Large field sizes are achieved by use of quadrupole magnets in the beam transport, or by multiple coulomb scattering in a thin absorber, or a combination of both. Field shaping is cleanly accomplished with lead collimators 5 cm thick.

Ionization accounts for 94% of the radiation dose deposited by the proton beam; 6% is due to nuclear interactions. This simplifies the dosimetry and beam calibration. One rad thus corresponds to 1.45×10^7 protons per square centimeter of field area, at a beam energy of 200 MeV. The conversion factor for other values of energy or residual range may be deduced from the Bragg curve. An ionization chamber is sufficient for dosimetry if the field size is known and is easily calibrated versus a faraday cup.

Scattering and divergence are not nearly the problems with proton irradiation that they are with conventional x-ray "point" sources. In traversing 25 cm of water the proton beam increases in radius by only 4 mm due to multiple scattering. Proton beams have a maximum transverse phase space emittance of 3-10 centimeter milliradians, resulting in a divergence of $\pm$ 0.5 to 1.5 milliradians for a 10 cm diameter field. (Cobalt teletherapy beams, for example, have a divergence of $\pm$ 50 milliradians for the same field size if the source to tumor distance is 100 cm.)

Therapy

The ability to confine the dose allows the therapist to administer a higher absorbed dose to the cancer without exceeding the tolerance of the normal tissues, or it will permit him to deliver the desired dose to the cancer while reducing the dose to normal tissues. Such a capacity should manifest itself clinically by an increased rate of local control of the cancer, a decreased patient morbidity and by an increase in the number of patients suitable for therapy.

The feasibility and technical competence for performing proton irradiation has been clearly demonstrated in the clinical ablation of the pituitary using protons.[2] Cancer therapy using proton beams continues in Sweden[3] and in Russia[4] but not in the United States. As yet, the data are insufficient to demonstrate whether proton therapy has a clinical usefulness or not.

Treatment Planning

This potential of protons for therapy is best demonstrated by developing proton treatment plans for patients who have already received x-ray therapy. The clinical objectives and precautions suitable for x-ray therapy are presumed to apply for proton treatment planning.

The cancer containing volume is designated using diagnostic x-rays, radio-isotope scans or surgical visualization. The projection of this tumor containing volume is made on the skin of the patient and the radiation beam is then shaped to include the area using collimators and shields. The distance between the projected tumor and the edges of the irradiated field represent a margin of safety that makes up for the lack of precision in defining extent of the cancer on a histologic basis.

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Single Field

A single irradiation field is used when the lesion lies close to the skin surface and when the dose required is not maximal. This approach is outlined in Fig. 1 for a patient with a cancer of the breast that involves the lymph nodes in the shoulder region which lie 3 to 5 cm below the skin surface.

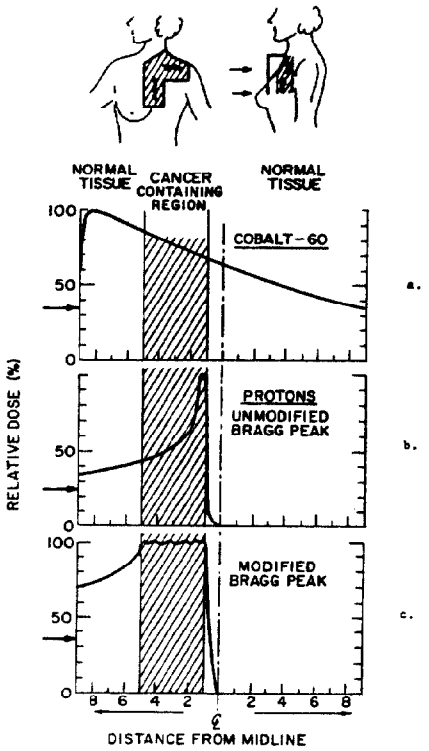

Fig. 1. Single Field Dose Distributions
a. Depth dose curve for Cobalt-60 gamma rays
b. Depth dose curve for mono-energetic proton beam
c. Multiple proton beam depth dose distribution. The energy and intensity of each beam pulse is adjusted to obtain uniform dose throughout the cancer containing volume.

When a patient is irradiated with a single x-ray field, the dose falls off exponentially across the irradiated volume as shown in Fig. 1a. As a consequence, tissues overlying the cancer containing region receive a higher dose than does the cancer. In addition, the dose across the cancer is not uniform and tissues distal to the cancer containing volume are irradiated albeit with a lower dose.

The proton dose distribution is different. With appropriate use of absorbers the depth of penetration of the Bragg peak can be adjusted to conform to the far edge of the cancer, as shown for a 200 MeV proton beam in Fig. 1b. In this instance the area of increased dose is narrower than the tumor containing region. However, by combining beams of different energies and appropriate flux densities the region of increased dose can be made sufficiently wide to encompass the cancer containing volume. (Fig. 1c) If a patient were to be treated with a beam modified as described, the surface tissues receive a dose 20% lower than the tissues in the cancer containing region. (Fig. 2) Because of the sharp cutoff of the beam, the tissues beyond the cancer volume would not be irradiated, while the dose across the cancer containing region is uniform.

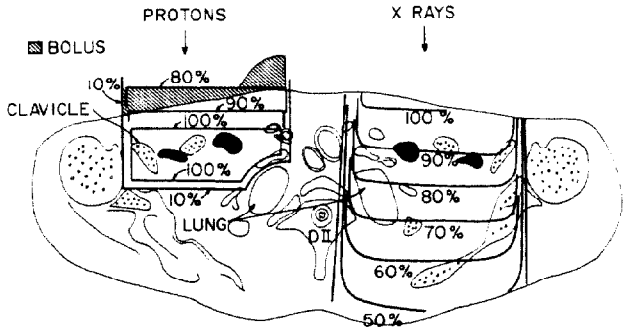

Fig. 2. Single Field Dose Distribution for Protons and X rays from Fig. 1 superimposed on the anatomical cross section of the patient with breast cancer. Solid lines indicate contours of equal dose, irregular solid areas are involved lymph nodes.

Opposed Fields

When the cancer is in the central third of the body the use of a single field of x-ray is inappropriate because of the extreme fall off of the dose across the field. In these instances a second field is employed (usually directed opposite the first field). This permits a summation of the dose across the field. If tissue sensitivity is restrictive, other fields can be utilized or the beam or patient can be rotated.

The approach utilizing two opposed fields is illustrated in Fig. 3. In this instance a patient having a bronchogenic carcinoma involving the root of the lung was treated with x-rays. Again, the

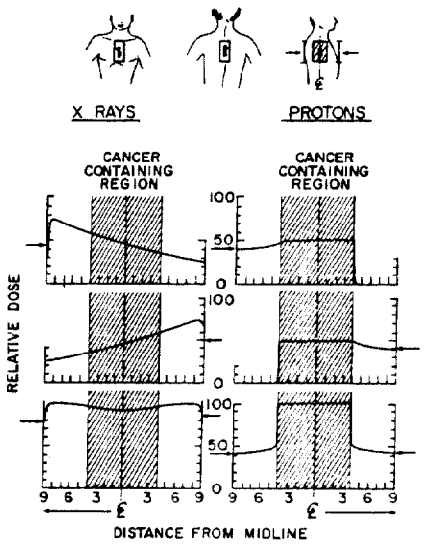

Fig. 3. Parallel opposed overlapped field dose distributions for x rays and protons. Curves show dose vs. depth for beams entering anterior and posterior surfaces; lowest curves show the result.

projection of the tumor on the chest wall was made and encompassed by the radiation field. The dose distribution for the opposed fields and their summation are illustrated on the left. The use of modified proton beams and their summation are shown on the right side of the Figure. In x-ray therapy the

dose to normal tissues outside the cancer containing volume is the same as that given the cancer. In proton therapy the dose to the normal tissues outside the cancer containing volume is about one-third that received by the cancer. (Fig. 4) If a single proton field were to be employed the dose to the normal tissues would have been 80% that received by the cancer and tissues beyond the cancer containing volume would not have been irradiated.

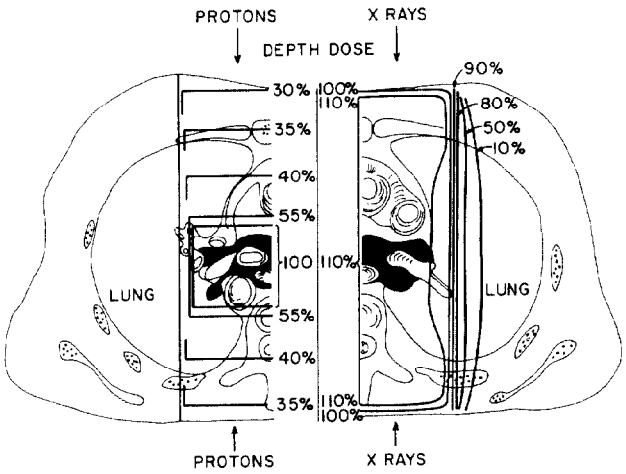

Fig. 4. Isodose Contours for Fig. 3.

In the first example the integral dose to tissues outside the cancer containing volume, the normal tissue dose, is about five times greater for x-rays than for protons. In the second example the normal tissue dose for x-rays was approximately two times that delivered by protons. If multiple fields or beam rotation were employed, the dose to the normal tissues would have been decreased even more. Even using the simple straight-forward approach of the single and overlapped fields of proton irradiation the normal tissues receive a lower dose than they would using beam rotation or wedged fields of x-rays.

Discussion

These two examples demonstrate that the major fraction of the proton dose can be confined to a designated volume. The net result is a reduction in dose delivered to tissues outside this volume. Whether this advantage will improve treatment or not must be tested by prospective, controlled clinical trials. Since the tissue changes produced by protons are equivalent to those produced by a similar x-ray exposure, it is anticipated that the results will at worst be the same. When persistance or recurrence of the disease is a function of the dose delivered an increase in the fraction of local control is expected. In general patients will experience fewer side effects such as weight loss, nausea, vomiting, diarrhea, pain, lethargy and loss of appetite because of the decreased normal tissue dose. Skin reactions and bone marrow damage can be eliminated. In addition, the clinician can expect to realize some technical advantages for improving treatment planning and dose delivery. Treatment will be easier in the sense that single field irradiation can be used more frequently. Sensitive organs as the rectum, bone marrow, intestine can be spared or the dose to these organs can be reduced. The dose to the center of the cancer can be increased. Some cancers will be able to be re-treated or at least the central portions of the lesion can be.

By reducing the volume of normal tissues (e.g. intestine) receiving a high dose, extended or multiple field irradiation can be used. This will permit the irradiation of some patients who are currently excluded from treatment because of the extent of the disease process. Children requiring radiation should benefit from the capacity of localizing the dose in that growing organs, such as bone, can be spared.

Future Development

Developments in proton therapy will benefit all modalities of charged particle therapy. The sharply defined range of protons requires better knowledge of the location of the tumor to be treated. Techniques suggested for this include ultrasonic scanning, surgical staging and radioisotope scanning. Methods must be developed to define the beam interaction region in situ so the beam is properly directed to the target volume. One mechanism for this is utilization of high spacial resolution detection of the radiation from carbon-eleven and oxygen-fifteen generated in tissue by the beam.[5] Using a large aperture dynamic dipole magnet in the beam transport individual beam pulses of variable energy and fixed size can be scanned throughout the tumor volume. This allows uniform irradiation of complex target geometries and increased sparing of skin and normal tissue overlying the tumor.

Conclusion

This paper presents the conviction that the ability to confine the major fraction of the absorbed dose in a designated volume makes protons superior to x-rays and offers radiation therapy a degree of precision and flexibility not available with conventional therapy.

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