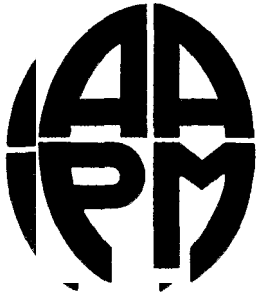
AAPM REPORT NO. 16

PROTOCOL FOR HEAVY CHARGED-PARTICLE THERAPY BEAM DOSIMETRY



Published by the American Institute of Physics
for the American Association of Physicists in Medicine

AAPM REPORT NO. 16

PROTOCOL FOR HEAVY CHARGED-PARTICLE THERAPY BEAM DOSIMETRY

A REPORT OF TASK GROUP 20
RADIATION THERAPY COMMITTEE
AMERICAN ASSOCIATION OF
PHYSICISTS IN MEDICINE

John T. Lyman, *Lawrence Berkeley Laboratory,* Chairman
Miguel Awschalom, *Fermi National Accelerator Laboratory*
Peter Berardo, *Lockheed Software Technology Center, Austin TX*
Hans Bicchsel, *1211 22nd Avenue E., Capitol Hill, Seattle WA*
George T. *Y.* Chen, *University of Chicago/Michael Reese Hospital*
John Dicello, *Clarkson University*
Peter Fessenden, *Stanford University*
Michael Goitein, *Massachusetts General Hospital*
Gabrial Lam, *TRIUMF, Vancouver, British Columbia*
Joseph C. McDonald, *Battelle Northwest Laboratories*
Alfred Ft. Smith, *University of Pennsylvania*
Randall Ten Haken, *University of Michigan Hospital*
Lynn Verhey, *Massachusetts General Hospital*
Sandra Zink, *National Cancer Institute*

April 1986

Published for the
American Association of Physicists in Medicine
by the American Institute of Physics

Further copies of this report may be obtained from

Executive Secretary
American Association of Physicists in Medicine
335 E. 45 Street
New York. NY 10017

Library of Congress Catalog Card Number: 86-71345
International Standard Book Number: 0-88318-500-8
International Standard Serial Number: 0271-7344

Published by the American Institute of Physics, Inc.,
335 East 45 Street, New York, New York 10017

Printed in the United States of America

Contents

Chapter I

Introduction

Beams of negative pions, protons and the nuclei of helium and heavier ions such as carbon and argon, known as heavy charged particles, are of interest in radiation biology and radiation therapy because of several distinct physical properties (Wilson, 1946; Raju, 1980). As these charged particles pass through a medium, their rate of energy loss or specific ionization increases with decreasing particle velocity, giving rise to a sharp maximum in ionization near the end of the range, known as the Bragg peak [1]. The position of the Bragg peak is energy dependent (Raju et al., 1978).

Proton, helium and heavier ion beams have been used for biomedical purposes since the 1950s (Tobias et al., 1952); pions have been used since the 1960s. Clinical trials using these beams are now in progress in several countries.

The rationale for charged-particle radiotherapy lies in either a physical dose distribution advantage (protons) or a combination of physical and biological advantages (heavy ions and pions) (Wilson, 1946; PART II, 1977; PART III, 1982). With these modalities, theoretical considerations suggest the possibility of increasing the local tumor control without increasing normal tissue complications. When testing these possibilities, it is essential that for each particle modality, dose be measured precisely and accurately. Furthermore, among different charged-particle therapy centers, it is highly desirable to define consistent methods of charged-particle dosimetry, which, when coupled with data on relative biological effectiveness, may aid in comparison of results with the different particles.

The need for precise and accurate dosimetry has been recognized in radiotherapy since X-rays were first used therapeutically. Over the years, physicists have developed techniques to measure the quantity and quality of ionizing radiations. Since the dose-response curve for tumors may be steep (Shukovsky and Fletcher, 1973; Battermann et al., 1981), as can be the dose-complication relationship, small changes (» 5 percent) in absorbed

[1] In honor of W. H. Bragg who first observed that monoenergetic alpha particles have a well defined range in air and ionize most heavily near the end of their path (Bragg and Kleeman, 1904).

dose could result in a significant change in the probability of cure and/or complication. In this context, precise dosimetry has an essential role in radiotherapy. Since 1977, members of Task Group No. 20 of the Radiation Therapy Committee of the American Association of Physicists in Medicine (AAPM) have been performing ionometric and calorimetric intercomparisons as well as other dosimetric measurements using heavy charged particles.

This protocol presents guidelines for the dosimetry of therapeutic beams of heavy charged particles based on the experience of this task group. There are insufficient basic data to allow the desired accuracy in dosimetry in all situations; however, the protocol is intended to serve as a resource for standardization of the dosimetry. Considerations of both a technical and clinical nature are discussed insofar as they influence dosimetry practices. This protocol will be updated as additional basic physical data and relevant heavy charged-particle dosimetry information become available.

Chapter 2

Heavy Charged-Particle Beams

2.1 Particle Types

The particles whose dosimetry is addressed by this protocol have masses many times greater than that of an electron. These particles are negative pions, protons, helium and ions of heavier elements such as carbon, neon, argon, and others. Heavy charged-particle beams are obtained from particle accelerators (such as cyclotrons, linear accelerators, or synchrotrons) either by acceleration of the particles of interest (primary beam) or by a nuclear interaction between an accelerated particle and some target material from which the desired particles (e.g., pion or carbon-11) can be obtained as a secondary beam.

2.2 Beam Characteristics

The depth dose distributions of these beams are characterized by a relatively low dose in the entrance region (plateau) followed by a narrow region of elevated dose in the stopping region (peak) (Bragg and Kleeman, 1904; Wilson, 1946; Bakker and Segre, 1951; Lyman and Howard, 1977). The Bragg peak makes possible the irradiation of a very small localized region within the body with an entrance dose lower than that in the peak region (Tobias et al., 1952). When the energy of the particles entering the body is modulated in order to produce an extended Bragg peak, the ratio of peak-to-plateau doses decreases (Koehler et al., 1975); however, the biologically effective dose at depth can still be greater than the entrance dose (Lyman, 1983).

When charged particles interact with matter, the most important energy loss mechanism is by the interactions with atomic electrons (NAS, 1964). In addition, charged particles also will undergo elastic and non-elastic interactions with the atomic nuclei of the medium. The fundamental differences between electron beams and heavy charged-particle beams occur because the electron rest mass, m, is very small in comparison with heavy charged-

particle masses. Incident electrons interacting with atomic electrons of the irradiated material can lose a large fraction of their energy in a single interaction. Heavy charged particles colliding with electrons will lose only a small fraction of their energy per collision (usually about 25 eV, but on the average 100 eV and at most $\approx 4mE/M$). In traversing a medium, charged particles undergo many deflections and the totality of these deflections is referred to as multiple Coulomb scattering. Nuclear scattering is the main contributor to the multiple Coulomb scattering. When compared to electron beams, the heavy charged-particle beams have a smaller scattering angle and therefore have much sharper lateral distributions as they transverse a dense medium (Carlsson and Rosander, 1973; Bichsel et al., 1982; Lyman et al., 1985).

2.3 Beam Quality

It is well known (Lea, 1962) that biological effects in tissue depend not only on the dose, but also on the detailed distribution of the energy loss along the particle tracks. LET is one measure of this distribution. The need for determining the biological effects as a function of beam quality has long been recognized (Appendix E).

A monoenergetic charged-particle beam will have a single value of LET. As the beam slows down in a medium a distribution in LET will result due to straggling' and the mean LET of the primary beam will increase because of the change in energy loss.

Heavy ions may have interactions with nuclei while slowing down in the medium. These interactions may result in fragmentation of the incident ion. The fragmentation depends upon the nature of the medium, ion type and its energy (Goldhaber and Heckman, 1978). Generally, the fragments will initially have a velocity approximately the same as the primary ions, a smaller nuclear charge and, therefore, a lower rate of energy loss than the primary ion because the rate of energy loss varies as the square of the nuclear charge (Bichsel, 1972; Janni, 1982). This will result in a large variation in the energy loss and ranges of the different particles (Lyman, 1984). The importance of the fragmentation of the primary beam ions depends upon how it affects the absorbed dose distribution in LET. Inelastic interactions can also include fragmentation of an absorber nucleus. The charged fragments from a target nucleus fragmentation will have lower energies than the fragments from a projectile and therefore the dose due to the target fragments will generally be locally deposited.

Pions and protons do not fragment. A fraction of these particles undergo collisions with absorber nuclei resulting in fragmentation of the latter. Some pions are lost from the beam by decay into a muon and a neutrino. Among the particles considered here the negative pion has the unique property of being captured by nuclei of the medium when it comes to rest. Nuclear

'Due to the statistical variation in the number of interactions of the beam particles.

spallation occurs and the rest mass of the pion (140 MeV), except for approximately 40 MeV used in overcoming the nuclear binding energy, appears in the form of kinetic energy of nuclear fragments. The disintegration products include photons, neutrons, protons, deuterons, tritons, alpha particles as well as heavy nuclear fragments such as lithium, beryllium or carbon nuclei (Shortt, 1979). This nuclear spallation process is commonly called a "star" because of its characteristic appearance in nuclear emulsion or cloud chamber photographs.

A pion beam can have a narrow LET distribution when it enters the stopping medium. This distribution will then increase in mean value and broaden due to the energy loss and straggling of the pions as they slow down. In the stopping region the LET distribution will be broadened by the contribution of the short-range charged fragments and the neutrons. The number and type of fragments produced following the pion capture varies depending upon the nature of the capturing nucleus (Richman, 1981).

These properties of the charged-particle beams need to receive special consideration when measuring characteristics of the beam since they will lead to different dosimetry problems in different regions of the beam.

2.4 Shaping of High-Dose Volume

Beam shaping in three dimensions is required for therapeutic applications. The manner in which large diameter beams are generated and shaped will affect beam uniformity, radiation-quality, dose rate and treatment times.

2.4.1 Longitudinal Distribution

The stopping region of the heavy charged-particle beams must be extended over the treatment volume for most therapeutic applications. Beam shaping along the axis of penetration of the beam is done in a variety of ways as is deemed most appropriate for each particle beam. The technique used most often has been the modulation of the amount of material in the beamline in order to vary the range of the beam in the treatment volume as a function of time. Hydraulic devices (Larsson, 1961; Amols et al., 1977 and Lyman and Howard, 1977), metallic composite filters or ridge filters (Karlsson, 1964 and Lyman and Howard, 1977), and non-metallic devices, such as acrylic propellers (Koehler et al., 1975; Lam, 1982) have been used. The distribution of absorbed dose in the extended peak region is designed in most cases to achieve a uniform biological effect across the peak. In general, the high LET component will be larger in the distal part of the spread peak than in the proximal region. For dose measurements in the peak, the LET dependence of dosimeters must be known.

2.4.2 Transverse Distribution

Initially the primary charged-particle beams are usually small in diameter compared to large tumors. Various methods, such as multiple scattering techniques and scanning techniques, have been employed to enlarge the beam diameter. The multiple scattering methods involve a thin (relative to the range of the particles) absorber placed a long distance from the point where the beam enters the patient. The beam diverges in the long drift space. To achieve acceptable beam uniformity, a large fraction of the particles must lie outside the useful therapy beam area and must be stopped in a collimator. Greater beam utilization can be achieved with a scattering system which includes devices that totally absorb portions of the primary beam in regions where the dose is higher than desired (Schneider et al., 1974; Crowe et al., 1975; and Koehler et al., 1977).

Magnetic methods of enlarging the beam diameter may be used alone or in conjunction with multiple scattering techniques. Either radial defocusing or overfocusing the beam are the simplest magnetic methods. These are similar to the simple scattering method in that most of the particles will be outside the field of interest resulting in a low efficiency of particle utilization. An advantage of this method is that it does not introduce extra beam energy degrading material into the beamline, however, it can be sensitive to variations in beam tuning or to beam motion. A small beam can be scanned over a larger area in a Lissajou figure to obtain a larger uniform field (Larsson, 1961). The entire radiation field is uniformly covered by sweeping the beam over the field in a time that is short compared to the total irradiation time.

Raster scan methods are under development (Lehman et al., 1979; Kanai et al., 1980). Raster scanning is the rapid sweeping of a small pencil beam over the desired treatment field. The field being completely covered in a time which is short compared to the treatment time. It may be possible to scan the treatment volume with a pencil beam which can be modulated in energy and intensity in order to accurately shape the beam to the target volume. This type of treatment is expected to lead to high instantaneous dose rates which may complicate the dosimetry with ionization chambers (Boag, 1982) as well as the pattern of the biological effectiveness of the radiations.

The major appeal of the magnetic methods is that the beam enlargement is accomplished with a minimum of material in the beamline. With the heavier, less easily-scattered particles, this is a distinct advantage because lower-energy beams can be used to achieve the same depth of penetration. In addition, fewer secondary particles will be present.

In the plane perpendicular to the beam axis, the desired shape is usually achieved by collimation of the beam. Low melting temperature alloys are often used to produce the irregularly shaped collimators (Powers et al., 1973).

"Scanning" of the patient or of the beam is also used in some applications such as the pion channels at Los Alamos and TRIUMF (Amols et al., 1980; Lam and Skarsgard, 1983); in proton beams in both Japan (Kanai et al.,

1980) and Russia. With the multichannel pion applicator used at SIN (von Essen et al., 1982), the size of the treatment volume is controlled by the pion energy, the choice of which channels are used and by the manner in which the patient is scanned in three dimensions within the applicator.

2.5 Time Structure

The pulse structures of some accelerators can create problems in dose measurements (ICRU, 1982). For some accelerators, the length of a beam pulse is long compared to the ion collection time for an ionization chamber, for other accelerators, the time is short. The beam pulses may be variable in pulse width and instantaneous intensity. Short pulsed, high intensity beams may be found in raster scan methods of field shaping. The time structure of the beam being measured must be known as it can effect both the choice and the efficiency of the dosimetry system.

Chapter 3

Dosimetric Principles

3.1 Introduction

For heavy charged-particle beams it is useful to consider the determination of absorbed dose from a knowledge of the types of charged particles, their fluence spectra and the stopping power, *S*, of the absorber material at the point of interest. If the energy of the particles is denoted by E and if delta ray equilibrium is established, the dose in a small mass m inside a homogeneous medium is given by (Rubach and Bichsel, 1982

$$D_m = \sum_{i=1}^{n} \int_0^{\infty} \Phi_i(E)(S(E)/\rho)_i \mathrm{d}E \qquad (3.1)$$

where *i* is an index to sum over the different types of contributing particles, (the mass stopping power is the Kerma factor for charged particles). It is assumed that the energy loss in the material is small compared to E (i.e., all particles are "crossers") and that no nuclear reactions take place in m.

If the spread in energy is small (which is usually not the case for therapy beams), the mean value theorem can be used to simplify the equation to

$$D_m = \sum_{i=1}^{n} (\Phi_i)(S(\overline{E}_i)/\rho)_i \qquad (3.2)$$

where $\Phi_i = \int \Phi_i(E)\mathrm{d}E$, , is the total number of particles per unit area of type *i* passing through the absorber, and $\overline{E}_i = \int E\Phi_i(E)\mathrm{d}E) / \int (\Phi_i(E)\mathrm{d}E$. Equation 3.1 provides the theoretically soundest approach to determining the absorbed dose in a patient. Measurements of deposited energy or ionization with instruments such as calorimeters or ionization chambers allow the determination of dose in the materials used in the construction of the instrument. Equation 3.3 (below) must then be invoked to convert the results to an estimate of the absorbed dose in tissue. For this reason it is desirable to use tissue-equivalent (TE) materials in the construction of the instruments whenever possible, so that corrections and, most importantly, the uncertainties in the corrections will be small and may be energy independent. For

some charged-particle beams, the direct measurement of fluence, e.g., with a Faraday cup, can be used to predict dose in tissue (see Chapter 5).

Any measurement of absorbed dose in a particle beam is related to the particle fluence by Equation 3.1 and the energy transfer across the interfaces of the instrument (in particular, the transmission of delta rays) must be identified in order to determine the dose experimentally. The methods used to achieve these measurements are discussed in Chapter 6.

If the dose in the dosimeter, D_d, has been measured, the dose in the patient (tissue), D_t, can be calculated as:

$$D_t = D_d \sum_{i=1}^{n} \int_0^\infty (\Phi_i(E)(S(E)/\rho)_i)_t \mathrm{d}E \Big/ \sum_{i=1}^{n} \int_0^\infty (\Phi_i(E)(S(E)/\rho)_i)_d \mathrm{d}E \tag{3.3}$$

where the fluences in the patient and the dosimeter may be different. A measurement of D_d therefore is not sufficient to determine D_t if the fluence spectra $\Phi_i(E)$ are not known for all the particles. If the fluences are not well known, it is recommended that several estimates of the integrals in Equation 3.3 be made with various possible values of $\Phi_i(E)$ so that the uncertainty of the ratio can be estimated.

3.2 General Considerations for Dose Measurements

The dose described by Equation 3.1 may not be proportional to the effect observed in a dosimeter. Examples of effects that must be taken into account in the types of dosimeters that are routinely used in particle therapy are:

1. In a calorimeter, the heat defect may depend on the type of particle and its energy.

2. In an ionization chamber, $\overline{w}$, the average energy required to produce an ion pair in the gas, will depend both on particle type and particle energy.

3. The yield of ferric ions from ferrous ions in chemical dosimetry depends strongly on the stopping power of the particles.

4. If the composition of the dosimeter is heterogeneous it is important to consider carefully the transmission delta rays and secondary charged particles across the interfaces.

5. Recombination in the ionization chamber will make the measured charge different than the initially released charge.

For all instruments used, the relation between energy deposition and observed effect must be studied and carefully documented.

For ionization chambers, some of the problems are considered in Appendix C. The problems differ for nearly parallel high energy beams and for beams that are highly convergent or divergent (where particles may be incident on the dosimeter from many different directions). It is useful to consider two regions for the determination of the conversion factors:

1. the plateau, where all the primary particles have approximately the same velocity;

2. the region in the vicinity of the Bragg peak.

3.3 Uncertainties and Errors in Dosimetry

In any determination of dose in a patient, it is very important to explore fully the assumptions used in the calculations. It is important to evaluate the performance of a measuring system carefully. In particular, the stochastic uncertainties as well as the uncertainties in the parameters and correction factors needed to relate the detector response to a statement of absorbed dose in repeated measurements under presumably identical conditions should be determined. The magnitude of the uncertainties in the methods recommended by this protocol are discussed in Chapter 8. A discussion of the distinction between random and non-random uncertainties, and how these may be combined has been given by Müller (1979).

Chapter 4

Calorimetry

4.1 Introduction

The absorbed dose calorimeter is a good instrument upon which to base an absolute dosimetric calibration. It can be considered a primary standard since it does not rely upon the use of a radiation source for calibration. The energy deposited per unit mass of the calorimeter's central absorber, or core, is determined by measuring a response associated with heat dissipated by the radiation, and then by measuring a response when a known amount of heat is dissipated from an electrical calibration heater mounted in the core.

The quantity of heat produced in the calorimeter core is proportional to the absorbed energy. However for different materials it is possible to have either endothermic or exothermic radiochemical reactions which may necessitate a correction to relate the measured temperature rise to the energy absorbed.

The production of heat from the absorption of radiation is a multi-step process consisting of ionization, excitation, and thermal agitation. There is virtually no known dependence of the quantity of heat per unit dose upon dose rate, or upon ionization density for solid elements. Finally, it is necessary to convert the absorbed dose measured in the calorimeter to absorbed dose in tissue.

Because there is no national or international standard for absorbed dose in charged-particle beams, the ionization chambers currently in use for charged-particle radiation therapy dosimetry are calibrated with respect to a cobalt standard. A TE-plastic calorimeter is used for intercomparison of dosimetry. The calorimeter is also used to reduce the uncertainty in the determination of the absorbed dose by the A-150 ionization chambers (Mcdonald et al., 1981a and 1981b).

4.2 Material and Methods

A-150 tissue equivalent plastic (Shonka et al, 1958) has been employed for many years in the construction of dosimeters which have been used in a wide variety of radiation fields. A-150 has a number of features which are useful for this application (Goodman, 1978; Laughlin, 1974; Domen, 1980). The mass energy absorption coefficient ratio for A-150 plastic relative to ICRU-defined tissue or water is close to unity for a wide range of photon energies. The same is true of the stopping power ratio for charged particles and the kerma ratio for neutrons (Awschalom et al., 1983 ; Rubach and Bichsel, 1982b). The elemental composition for the plastic matches nearly exactly in terms of the hydrogen content for ICRU defined tissue (ICRU, 1964). However, the carbon and oxygen content in the two media are nearly interchanged. This necessitates a correction for the calculation of dose in ICRU tissue based on a measurement using an A-150 dosimeter.

Phantoms constructed for the purpose of carrying out calibrations and comparisons are best made from A-150, which provides a homogeneous medium for irradiation.

A calorimeter constructed specifically for use in charged-particle beams has been described by McDonald and Domen (1986). This device minimizes the use of high *Z* materials in, or near, the core. The electrical calibration heater in the core (Domen, 1980) comprises less than 0.1 percent of the core mass. The calorimeter is capable of being calibrated in either the quasi-adiabatic (Laughlin and Genna, 1966) or in the heat-loss-compensated mode (Domen and Lamperti, 1974).

4.3 Thermal Defect Corrections

When certain materials such as A-150 plastic are irradiated a small quantity of the energy deposited does not appear as heat. Endothermic radiochemical reactions in the polymer constituents of A-150, including such reactions as hydrogen bond breakage and hydrogen gas evolution, are responsible for the consumption of about 4 percent of the incident energy (McDonald et al., 1976; McDonald and Goodman, 1982). Although there are a wide variety of secondary charged particles set into motion by primary charged-particle beams, it is recommended that the correction factor for the thermal defect in A-150 be taken as 1.040 ± .015 for all particles.

Chapter 5

Faraday Cup Dosimetry

5.1 Introduction

As described in Chapter 3, dosimetry can be based on a fluence measurement made in a charged-particle beam. The total fluence can be measured with a Faraday cup (Brown and Tautfest, 1956) which is a well insulated, conductive absorber thick enough to stop all the primaries and charged secondaries in a particle beam, allowing a measurement of the beam current.

5.2 Materials and Methods

The required elements for a dose determination with the fluence method using a Faraday cup include:

1. a beam transport system which limits the beam to near-mono-energetic primary particles;

2. a large parallel plate transmission ionization chamber which remains in the beam at all times and gives a signal proportional to ionization; and

3. one or more small thimble ionization chambers or diodes whose dimensions are considerably smaller than the dimension of the beam whose purpose is:

   (a) to scan the beam to provide a measure of its effective area; and

   (b) to provide a secondary monitor to which the beam calibration can be transfered.

Both the parallel plate transmission ionization chamber and the Faraday cup must be large enough to accept the entire beam transmitted by the collimation system. The parallel plate chamber is used as a relative monitor of beam intensity during the calibration process. Other monitors such as toroidal transformers and secondary emission monitors (SEM) may also be

used. The Faraday cup is used to determine the number, N, of primary particles of known energy per monitor unit (charge collected on the transmission ionization chamber). The Faraday cup can subsequently be replaced by a small ionization chamber which will then collect a charge Q per monitor unit at the point of interest. The final parameters required for dose calculation are the stopping powers of the charged particles of this energy in muscle tissue as well as the effective area of the beam. The procedure for the dose determination, in Gy, is outlined in Equation 5.1:

$$D_t = \frac{N}{a}(S/\rho)(1.602 \times 10^{-10}), \qquad (5.1)$$

where (S/p) is the mass stopping power of charged particles of this energy in muscle tissue in units of MeV $cm^2 g^{-1}$ and a is the effective area of beam (cm^2).

5.3 Procedures

The success of a Faraday cup dose determination depends on the accuracy of the determination of the fluence and the effective area, the evaluation of the effects of secondary particles in the beam, and the knowledge of the mass stopping power, S/p.

The efficiency of the Faraday cup is affected by secondary charged particles produced by primary interactions in the front window and residual gas, or by the escape of charged secondaries from the collector. By increasing the magnetic field to a high value under good vacuum, one can usually produce a detection efficiency independent of electric field of nearly 100 percent (Verhey et al., 1979).

The effective area of the beam needs to be determined. If the beam is assumed to be either uniform with a small penumbra or with a Gaussian beam intensity distribution, the effective area of the beam can be determined from scans along orthogonal axes. The ionization as a function of distance from the beam center line is plotted and integrated to large distances in order to include any tails in the beam.

The use of Equations 3.2 and 5.1 implies a single energy and single primary particle type in the beam. In situations where a known flux of secondary particles exists it would be possible to evaluate dose independently from each of the beam constituents. It is necessary to estimate the fraction of deposited charge which is due to each of these secondary particles. In practice the use of Faraday cups for charged-particle dosimetry has been limited to the calibration of proton beams.

The use of Equations 3.2 and 5.1 assumes that all energy loss is produced by interactions with electrons. For all heavy particles there is a component of energy loss due to nuclear interactions which must be estimated through calculations based on cross-section data and then factored into the stopping powers which is required for a dose determination.

The evaluation of all the above factors will permit a determination of dose in tissue in a monoenergetic beam. In the case of a monoenergetic proton beam, the dose may be determined to a accuracy of ±5 percent (Verhey et al., 1979).

Chapter 6

Ionization Chambers

6.1 Introduction

The ionization chamber occupies a central and complex role in charged-particle dosimetry. Chambers of well-defined geometry, such as parallel plate ionization chambers, may serve as absolute dosimeters (although often the quantities with which such a calibration is achieved turn out to be derived from intercomparison of ionization chambers with other absolute devices). Alternatively, a chamber of ill-defined geometry, such as a thimble chamber, may serve as a quasi-absolute dosimeter either through a calibration in a very different beam (such as a ^{60}Co beam) and the use of calculated conversion factors or through calibration in a very similar beam with an absolute dosimeter and the use of a measured calibration factor. Finally, ionization chambers very often serve as secondary and tertiary dosimeters which are calibrated against an absolute device such as a calorimeter and used to determine dose in routine daily measurements.

The measurement precision of ionization chambers can be very great, perhaps the best of all instruments used in dosimetry. Their primary disadvantage is that recombination effects can be very substantial in beams of high instantaneous intensity even to the point of making them impractical at the average dose rates needed for routine operation.

The observed effect is the ionization in a gas caused by energy deposited in the gas by the charged particles and their delta rays. The factor needed to convert the observed ionization into absorbed energy in the gas (the mean energy, $\overline{w}$, needed to produce one ion pair) is not known with sufficient accuracy to give the absolute dose in the gas with sufficiently small uncertainty. The dose conversion factor needed to derive dose in the wall material from dose in the gas is also not well known. It is therefore recommended that, when possible, the ionization chamber be calibrated with a calorimeter or other absolute dosimeter.

6.2 Ionization Chambers of Known Geometry

In a parallel plate ionization chamber, with the beam incident perpendicular to the walls, the charge produced per unit mass of gas, J_g, is given by

$$J_g = Q/m_g = \sum_{i=1}^{n} \int_0^\infty \frac{\Phi_i(E)(S(E)/\rho)_i}{\overline{w}_i(E)/e} \mathrm{d}E, \tag{6.1}$$

where $\overline{w}_i(E)$ is the mean value of the energy necessary to produce an ion pair for the *ith* particle species (ICRU, 1979b) and delta ray effects are neglected for the moment.

Since only a single quantity, J_g, is measured, it is necessary that a large amount of additional information be known to derive the dose in the chamber wall, D_d, from J_g. Only if $\overline{w}(E)$ is constant for all particles and energies, can we write

$$J_g \overline{w}/e = \sum_{i=1}^{n} \int_0^\infty \Phi_i(E)(S(E)/\rho)_i \mathrm{d}E, \tag{6.2}$$

and that the dose in the chamber wall is given by:

$$D_d = J_g \overline{w}/e \sum_{i=1}^{n} \int_0^\infty (\Phi_i(E)(S(E)/\rho)_i)_d \mathrm{d}E \Big/ \sum_{i=1}^{n} \int_0^\infty (\Phi_i(E)(S(E)/\rho)_i)_g \mathrm{d}E\,, \tag{6.3}$$

in analogy to Equation 3.3.

If no secondary heavy particles are produced in the gas (there will always be delta rays) and if $(S(E)/p)_d$ and $(S(E)/p)_g$, do not differ very much, it will not be necessary to know $\Phi_i(E)$ very accurately in order to obtain the quotient of the two integrals with a small uncertainty.

If n is 1 and if $\Phi(E)$ can be approximated with a Dirac delta function, we get

$$D_d = J_g \overline{w}/e \frac{(S(E)/\rho)_d}{(S(E)/\rho)_g} = J_g(\overline{w}/e)(S/\rho)_g^d, \tag{6.4}$$

If this approximation is valid, the uncertainty of the dose D_d is determined by the uncertainty of $\overline{w}$ and of the stopping powers (assuming that J_g can be determined with negligible uncertainty).

There are a large number of corrections which affect the accuracy with which a practical dosimetry can be based on equation 6.4 and some of these are discussed in Appendix C.

6.3 The Ionization Chambers of Indeterminate Geometry

The mass of gas within an ionization chamber may be deduced by measuring its response in a calibrated beam such as a ^{60}Co beam. The mass is

given by:

$$m_g = \frac{(\overline{W}/e)}{N_g} \tag{6.5}$$

where N_g(AAPM, 1983) is defined as

$$N_g = \frac{N_x K(\overline{W}/e) A_{ion} A_d \beta_d}{(\overline{L}/\rho)_g^d (\overline{\mu}_{en}/\rho)_d^g} \tag{6.6}$$

N_x is the cobalt-60 exposure calibration factor (R/C); K is the charge produced in air per unit mass per unit exposure; A_d is the attenuation and scattering correction factor for the chamber wall when exposed to cobalt-60 radiation; A_{ion} is the correction factor for incomplete ion collection; β_d is the quotient of absorbed dose to the collision fraction of kerma for the wall of the ionization chamber; $(L/\rho)_g^d$ is the ratio of the mean, restricted collision mass stopping power of the wall material to that of the gas (air) in the chamber for the secondary electrons released by ^{60}Co gamma rays; $(\mu_{en}/\rho)_d^g$ is the ratio of the mean energy-absorption coefficient for air to that of the wall for ^{60}Co gamma rays.

The conversion factors of Equation 6.6 either have well-known values for cobalt-60 or are chamber specific and calculable. Table D.1 gives values to use for these factors for a few common chamber/gas combinations. It is recommended that N_x or M_g be determined at regular intervals as a constancy check on the performance of the chamber and electrometer.

Once m_g has been derived from the ^{60}CO calibration factor, its value may be substituted in equation 6.4 $(J_g = Q/m_g)$ allowing dose determination in a charged-particle beam provided the product of $(\overline{w}/e)$ and $(S/r)_g^d$ and the appropriate correction factors (Appendix D) are known.

An ionization chamber which carries a ^{60}Co beam calibration factor, such as from an NBS calibration or through intercomparison with a chamber which does carry an NBS calibration, can be used to determine dose in a charged-particle beam through application of equations 6.4, 6.5 and 6.6. This requires that several parameters, including the product of the parameters $(\overline{w}/e)$ and $(S/r)_g^d$, be known.

However, the uncertainties in $\overline{w}$ for the particular spectrum of primary and secondary charged particles in the beam of interest are typically 5 to 10 percent (ICRU, 1979b) and there are lesser but still significant uncertainties in the value of $(S/r)_g^d$. One may, on the other hand, use an intercomparison of an ionization chamber with an absolute dosimeter such as a calorimeter as a determination of the product of these parameters. This is done by defining a conversion factor C_p, which converts the charge per unit mass collected by the ionization chamber to dose in the chamber wall.

$$C_p = (\overline{w}/e)(S/\rho)_g^d, \tag{6.7}$$

By using the chamber in conjunction with a TE calorimeter, the conversion factor, C_p, can be determined directly. Combining Equation 6.4 and 6.7 we

have

$$C_p = \frac{D_d m_g}{Q}, \tag{6.8}$$

where D_d is determined by the TE calorimeter (McDonald and Domen, 1986), m_g, is determined by equations 6.5 and 6.6 and Q is the charge measured by the ionization chamber and corrected for electrometer calibration, polarity effects, displacement factor, ion collection efficiency and for the mass of gas present at 22°C and 760 torr.

The dose to the chamber wall when the ionization chamber is subsequently used for dosimetry is obtained by

$$D_d = \frac{Q}{m_g} C_p, \tag{6.9}$$

The final conversion from dose in the chamber wall to that in tissue is made by

$$D_t = D_d (S/\rho)^t_d, \tag{6.10}$$

where $(S/r)^t_d$ is the wall-to-tissue conversion factor consisting of the ratio of the mass stopping powers of tissue to wall.

The conversion factor C_p must be evaluated at a range of experimental conditions which spans that range of values which could obtain under therapy conditions. For example one could determine C_p in the entrance region of an unmodulated beam and near the end of a spread Bragg peak. This would approximate both the highest and lowest energy spectrum. If a significant change in C_p is noted between these two points, then further measurements would be required including measurements elsewhere in a spread peak. In a pion or heavy ion beam where the particle spectrum may change with depth or tune, it may be necessary to measure C_p for a large number of therapy conditions.

In the absence of a calorimeter, the quantities on the right side of Equation 6.7 must be evaluated separately. Recommended values are given in Appendix D.

Chapter 7

Methods of Relative Dosimetry

7.1 Introduction

In daily dosimetry secondary and tertiary instruments are needed to transfer the primary calibration, and for specialized applications such as *in vivo* dosimetry, symmetry assessment, and large area or volume measurement. Ionization chambers, discussed in Chapter 6, are often used in such applications. However other active detectors, such as silicon diodes have advantages such as a smaller sensitive volume, and passive detectors may be particularly valuable for verification of dynamic treatments or in pulsed beams. It is occasionally an advantage that these detectors only minimally perturb the radiation field. In addition, some of the techniques allow accumulation of data relating to radiation quality.

7.2 Thermoluminescent Dosimetry (TLD)

A standard for photon and electron dosimetry is LiF, available in powder, small extruded chip or ribbon, and thin teflon-impregnanted disc forms (Gooden and Bricker, 1972). With careful attention to handling, annealing and calibration, a precision of ±3 percent can be achieved. This technique can be extended directly to proton beams because of their low-LET nature.

For heavy-ion beams (including helium) TLD materials require special care in their use because of their sensitivity to LET (Tochilin et al., 1968; Hoffmann et al., 1980 and 1986; Chu et al. 1986). Pion beams present the same high-LET problem, and in addition, are accompanied by varying amounts of neutrons to which ^{6}Li is quite sensitive via its high cross-section for capture of thermal neutrons (Cooke and Hogstrom, 1980). Much work has been done with pion beams (Hogstrom and Amols, 1980; Hogstrom and Irifune, 1980; Salzmann, 1979), resulting in the following two promising methods:

1. The first method employs ^{7}LiF (TLD 700, available from the Harshaw Chemical Company, Solon, Ohio, U.S.A.) in conjunction with irradia-

tion of Al foils or pellets. The irradiation of ^{27}Al results in ^{24}Na production via the (p^-,t) and (n, a) reactions. (The ^{24}Na is produced mainly by the capture of stopped negative pions in ^{27}Al, and occasionally by a nuclear interaction between star neutrons and ^{27}Al.) Detection of the ^{24}Na via counting of decay γ's or betas allows an assessment of the pion star distribution. A knowledge of the pion star distribution allows a correction to be made for the reduction of sensitivity of ^{7}Li thermoluminescence at high-LET. Aluminum foils allow information on radiation quality (pion star production) to be obtained over large areas with excellent spatial resolution if a magnet is used in conjunction with the detection of betas from ^{24}Na decay (Seiler et al., 1982). Pellets, on the other hand, can be located precisely *in vivo* with radiographs.

2. For CaF_2(Tm) the ratio of the high and low temperature peaks in the glow curve can be analyzed to give an indication of the pion beam quality (Hoffmann et al., 1980). This in turn can be used to correct the integrated thermoluminescent output for loss of sensitivity at high-LET. A feature of this technique is that a single dosimeter gives both absorbed dose and radiation quality information. In addition, the high sensitivty of CaF_2(Tm) allows the use of small amounts of the dosimeter. This material holds promise for use in a similar fashion in heavy-ion beams (Hoffman et al., 1986).

   Since ^{7}Li is much less sensitive to thermal neutrons than is ^{6}Li, irradiation of ^{6}LiF and ^{7}LiF simultaneously can give information on the neutron component of a beam. In addition, recent work of phototransferred thermoluminescence inddicates a second readout of LiF (and possibly other materials), when the second readout is proceeded by ultraviolet irradiation, may give quality and dose information (Hoffman et al., 1984).

7.3 Photographic Film Emulsion

Film has long played a role in charged-particle beam alignment and, with care, has been useful in limited situations in conventional photon and electron radiotherapy dosimetry. However, because the sensitivity of film increases markedly at low photon energy (below about 30 keV due to photoelectric interactions with the Ag in the film), in a manner that does not mimic tissue, quantitative film dosimetry is difficult or impossible even for conventional radiations where low kV (primary or scatter) is involved.

With heavy charged-particle beams where the radiation quality is fairly constant, such as for protons, or in the plateau regions of heavy ion beams, film studies accompanied by careful calibration techniques should prove of value. The excellent spatial resolution is of particular interest. With pions in general and heavy ions in the regions where ion fragmentation is signif-

icant, the film sensitivity most likely does not follow that of tissue, or air, well enough to be useful in a simple manner for many situations. Special procedures are worth exploring, however, because data can be accumulated readily over large areas with film, offering much potential value for treatment plan verification. For pions, a method employing fluorescent screens in contact with the film (Blattmann et al., 1981) analogous to diagnostic radiology techniques is being explored, and there seems to be some promise that, with the proper screen material, the resultant film exposure can be used as indicative of relative tissue dose. Alternatively, thin sheets of aluminum foil irradiated in contact with the film may lead to sufficiently accurate correction to the film sensitivity via analysis of the aluminum activation (Blattmann et al., 1981). In any case, film dosimetry is a means to rapidly assessing which regions require further dosimetric investigation.

7.4 Silicon Diode Detectors

Silicon *pn* junction diode detectors are excellent charged-particle detectors, because they are stable, linear in their energy response to all charged particles, and can be made small and/or very thin (less than 0.01 mm).

Some of the earliest published pion dosimetry (Richman et al., 1966) was done with silicon detectors, and they have continued to play a role in clinical pion dosimetry (Richman, 1981). However, care must be exercised in interpreting the results obtained with silicon detectors, because (Dicello et al., 1980),

1. the detector material is not tissue equivalent and
2. the geometry of the detectors is generally planar with a surrounding annular holder. For charged particles with ill-defined direction, such as for secondaries associated with (non-plateau) pions, the proper geometric corrections are difficult.

Perhaps the main benefit of silicon diode detectors in clinical dosimetry is for estimation of beam quality *in vivo* situations (Richman, 1981). In these cases very thin "totally depleted" detectors are used to give particle-by-particle dE/dx values, from which estimates of LET in tissue can be made.

7.5 Activation

Heavy charged particles produce radioactive isotopes by inelastic nuclear interactions. With knowledge of the cross-sections for the interactions of interest, the particle fluence or the fluence density can be determined (depending on the isotope half-life relative to the duration of the exposure) from the induced activity. For pulsed beams, where saturation effects in ionization chambers may make their use impractical, activation of material placed

in the beam can be used for absolute dosimetry. Activation is also used in conjunction with some film dosimetry (see Section 7.3) in order to correct for changes in film response with changes in LET.

7.6 Other Relative Dose and Radiation Quality Estimates

Relative dose and quality estimates will certainly play a role in aiding valid comparisons among different radiation modalities if such determinations can be done easily (therefore routinely) and accurately. To date, it cannot be said this can be accomplished. The subject should be considered under development, and new materials and novel techniques with old materials must be encouraged. Included in this category is the use of lyoluminescence (Ettinger, 1980) just beginning to be explored seriously. Other possibilities are explained in the review article by Thomas and Perez-Mendez (1989).

Chapter 8

Practical Considerations

8.1 Introduction

The accurate calibration of a particle beam and the transfer of that calibration to a secondary standard are complex tasks fraught with pitfalls. The necessary experimental procedures will depend on details of the beam being calibrated and the instruments being used. The following sections outline some general procedures which should help assure accuracy.

8.2 Experimental Methods

The charged-particle beam intensity should be monitored continuously. For the modalities that use secondary beams the primary beam should also be monitored. The beam should be monitored by more than one independent transmission monitor device. Generally the monitoring is done with some combination of ionization chambers and/or secondary electron emission monitors (SEM) (Lyman and Howard, 1977). The suitability of the monitor device is in part determined by the pulse structure, duty factor and dose rate of the beam. Transmission ionization chambers can be either sealed or open to the atmosphere. If the chamber is not sealed, a convenient procedure for correction for ambient conditions should be established. The filling gas for the monitor chambers is usually dry air, nitrogen or argon. It is essential that linearity and dose-rate independence be established as well as the relationship between monitor response and absorbed dose. The temporal variation of background reading in the monitor chamber should be established and corrections applied where appropriate. The effects of recombination on the measured current should be determined. The pulse structure of some accelerators can make the verification of the saturation very difficult. If the number of particles per pulse or if the shape of the spill changes from pulse to pulse a more complicated analysis than a voltage versus charge collected curve is needed.

Once the beam monitoring is established the beam should be calibrated

with an absolute (primary) dosimeter such as a calorimeter or Faraday cup. This will provide a statement of the absorbed dose in the dosimeter material (or to a selected material such as the wall of the secondary instrument to be used in the next step of the procedure) per unit response of the beam monitor(s). This calibration may be performed in a relatively "clean" beam -- that is, one in which the fluence spectrum $\Phi_i(E)$ (see Chapter 3 and 6) is well known and, perhaps, corresponds to the plateau region of either a monoenergetic beam or the plateau of an energy (range) modulated beam - it will not usually be possible to make an absolute calibration in the region of the Bragg peak of a monoenergetic beam since the rapid variation of dose with position leads to substantial uncertainties.

Once the dose to a material such as the TE plastic of a calorimeter has been established, the dose to muscle is deduced by application of the relationship:

$$D_t = D_d(S/\rho)_d^t \tag{8.1}$$

where $(S/r)_d^t$ is equal to the ratio of the mass stopping powers of ICRU muscle to TE plastic weighted by the relative abundances and energies of the each type of ionizing particle in the charged-particle beam. The use of TE plastic makes this final conversion factor close to unity. Appendix D gives recommended values for this factor.

Once the beam calibration is established it should be transfered to a secondary standard such as an ionization chamber. This device should be placed in the region of the beam calibrated by the primary dosimeter and its response per unit of response of the beam monitor(s) determined-and corrected for open ionization chambers, for example, to standard contitions of temperature (22°C) and pressure (760 torr). This gives the calibration of the secondary detector in units of dose to the dosimeter wall per unit detector response. This may be converted through equation 8.1 to dose to muscle per unit detector response.

There are two reasons to transfer the calibration to a secondary detector. The first is to simplify subsequent measurements of dose since the primary devices tend to be cumbersome and time-consuming to operate. The second reason is to carry the calibration into other beam conditions in which the beam quality may be uncertain or at least the flux spectrum $\Phi_i(E)$ more complex than the calibration beam. Implicitly, at least, one is invoking a relationship derived from equation (6.1) to relate the response per unit dose in the complex situation to that in the "cleaner" calibration beam:

$$\frac{R_{complex}}{R_{calibration}} = \frac{\sum_{i=1}^{n} \int_0^\infty \left[\frac{\Phi_i(E)(S(E)/\rho)_i}{\overline{w}_i(E)/e}\right]_d dE}{\overline{w}_c/e(S_c/\rho)_g^d \sum_{i=1}^{n} \int_0^\infty \left[\frac{\Phi_i(E)(S(E)/\rho)_i}{\overline{W}_i(E)/e}\right]_g dE} \tag{8.2}$$

Where subscript *c* refers to the single, monoenergetic particle used for calibration and where the complex beam is assumed to be made up of *n* different

particles, each with a spectrum of energies. R represents the ratio of dose to the dosimeter wall divided by the detected charge per unit mass.

In practice, calibration and measurement often support the proposition that the correction factor is close to unity. This is confirmed for example when absolute measurements are made in the plateau region of an unmodulated proton or heavy ion beam, and both in the plateau and throughout the region of a spread out Bragg peak.

For most situations the secondary dosimeter recommended is the combination of an ionization chamber and electrometer (calibrated with a calorimeter). This may be an inappropriate system for use at an accelerator with a low duty factor. There are a variety of materials and sizes available for ionization chambers. This protocol recommends a relatively small chamber (≈ 0.1 cm^3) made of A-150 plastic (Shonka et al., 1958). It is also recommended the chamber be filled with air. Air is the first choice over TE gas because air does not have to be flowed through the chamber, the ionic recombination is less and the composition is less variable. It is acceptable to use methane-based TE gas (ICRU, 1977) if it can be established that the properties of the TE gas are the same as the TE gas that was used to determine the mass of the gas in the collection volume. If TE gas is used, it must be flowed through the chamber during the intercomparison procedures at a flow rate consistent with that used for the determination of the mass. In beams with high instantaneous dose rates (in excess of 1 Gy/sec) general recombination can create inefficiencies in ion collection. Thus care must be taken to either decrease the dose rate or to evaluate the magnitude of the charge collection efficiency (Boag, 1982).

8.3 Uncertainties

It is important that an analysis of the uncertainty of each of the factors present in equation 6.4 be carried out. Absolute dose determinations in photon beams are routinely made at the 4 to 5 percent level, corresponding to the 95% confidence limit (ICRU, 1976).

If equation 6.4 is used to determine the dose D_d, the uncertainty will be considerably larger due to the large error in $\overline{w}/e$ (page 14 and ICRU, 1979b). Instead, the procedures outlined in this section of the protocol are designed to minimize the reliance of the dose calibration on poorly measured experimental values and in its place rely, on calorimetry. Table 8.1 gives typical uncertainties involved in the determination of C_p using Equation 6.8 under optimal conditions. The uncertainty in the dose D_d is derived from the determination of absorbed dose in a carbon (rather than A-150) calorimeter transferred to a point in water (ICRU, 1984).

Table 8.1: Percent Uncertainties, Random and Non-random, Corresponding to 95% Confidence Limit (ICRU, 1984)

Factor	Source	Percent Uncertainty
m_g	Exposure Calibration, N_x	2.0
	Constants, W/e, $(S/\rho)_g$	2.7
Q	Ionization Charge	0.5
	Corrections (t-p, Saturation)	0.3
D_d	Calorimetry	1.7
C_p	Overall:	3.8

8.4 Dosimetry Intercomparisons

Institutions engaged in heavy charged-particle therapy should periodically carry out dosimetry intercomparisons. The purpose of these intercomparisons is to verify the institution's conformity to dosimetry standards, procedures, and techniques as outlined in this protocol and to compare the institution's statement of absorbed dose to that measured by the other participants in the intercomparison.

The intercomparisons should take place during the initial "start-up" phase of the institution's therapy program and at such times that the institutions make changes in its standards, procedures, or techniques which may affect the institution's absorbed dose standard. Intercomparisons may also serve as an educational process for physicists from institutions where a charged-particle therapy program is being planned or implemented.

The intercomparison measurements should include as a minimum the total absorbed dose in the proximal (maximum ionization) region of a peak spread to the average treatment dimension using the dosimeter which is the institution's secondary standard. The use of a calibrated tissue-equivalent ionization chamber is recommended for this purpose. Other participants should likewise use a secondary standard dosimeter or one whose calibration is traceable to their secondary standard. Measurements should also be made in the central and distal peak regions and in the plateau region of the beam. Calorimetry should be compared with the ionization chamber technique whenever possible. Specific parameters that should be compared are:

1. calibration of the charge measurement of the electrometer employed (a calibrated current source can be used for this purpose), with a voltage source with calibration traceable to NBS and a capacitor either

calibrated by NBS or with a calibration traceable to NBS;

2. measurement of the photon calibration of the ionization chamber with a gamma-ray source whose calibration is traceable to the NBS;

3. measurement of the ionization chamber's response in the charged-particle beam (This measurement should be made in the same phantom as that used for beam output determinations);

4. measurement of the absorbed dose in the spread peak and plateau (a measurement near proximal peak as a minimum requirement; measurements in the central and near distal peak are desirable).

For ionization chamber measurements a common set of physical parameters appropriate to the charged-particle beam being intercompared should be used.

Chapter 9

Recommendations

It is the recommendation of the task group that:

- Dosimeters be calibrated by a comparison with a calorimeter. At present we recommend one made of TE plastic (Bewley, et al., 1974; Greene and Major, 1975; McDonald et al., 1976; Caumes et al., 1984).

- In the event that a calorimeter is unavailable, it is the recommendation that proton beams be calibrated with a Faraday cup.

- In the event that neither a calorimeter nor a Faraday cup (for protons) is available, it is the recommendation of the task group that an ionization chamber bearing a ^{60}Co calibration be used and its calibration corrected by application of equations 6.4, 6.5 and 6.6 using the recommended factors listed in Appendix D.

- That the calibration be carried out in the center of a spread out Bragg peak, the extent in depth of which is substantially larger than the dimensions of the sensitive volume of the dosimeter. In the absence of measurements to the contrary, that the calibration be assumed to be constant both in the plateau and throughout the spread out Bragg peak.

- A difference of 5 percent or less between the dose determinations based on the calorimeter and that based on other dosimeters discussed in this protocol is presently considered to be within experimental uncertainties. Any difference greater than 5 percent should be examined carefully to evaluate the reason of the difference. For reproducible differences of less than 5 percent it is recommended that, for the sake of internal consistency, the local dose standard continue to be used.

- In an attempt to make the distribution of biological dose inside a target volume constant with depth, it is necessary with some charged-particle beams to produce a physical dose distribution which decreases with depth through the target volume. The recommendation of the task

group is that the dose be specified at a point near maximum physical dose, namely, that point near the proximal end of the spread out Bragg peak at which the physical dose is almost a maximum. In the case of a low LET charged-particle beam such as protons, the physical dose distribution is flat throughout the target volume; the use of the proximal peak dose is consistent with this recommendation.

Appendix A

Definitions

AAPM: The American Association of Physicists in Medicine.

Absorbed Dose: The quotient of $d\bar{e}$ by dm where $d\bar{e}$ is the mean energy imparted by ionizing radiation to matter of mass dm.

Biologically Effective Dose: Absorbed Dose x RBE where RBE is the relative biological efficiency of the radiation beam, determined for the particular biological system at the specified dose level and fractionation scheme under consideration and for a particular endpoint.

Bragg Peak The region of increased ionization observed near the end of range of a heavy charged particle beam

Collimator: An arrangement of shielding material designed to define the lateral dimensions of a beam of radiation.

Delta Rays Secondary electrons, of sufficient energy to produce ionization, which have been ejected from the track of an ionizing particle.

Displacement factor: A correction factor needed to convert the ionization measured by a dosimeter in a phantom to the ionization which would be observed at the same point in the phantom in the absence of the dosimeter cavity. It is necessary to correct for the attenuation in and scatter out from the material displaced by the dosimeter.

Dose: Absorbed dose unless otherwise qualified.

Elastic Scattering: Interactions is which the total kinetic energy is conserved.

Fluence: The quotient of dN by da, where dN is the number of particles or photons incident on a sphere of cross-sectional area da.

Heat Defect: The proportion of energy deposited by ionizing radiation which does not go into the production of heat.

Heavy charged particles: Those atomic and subatomic charged particles with masses substantially heavier than that of an electron.

Heavy ions: Nuclei of elements with charge $Z \geq 2$.

Inelastic Scattering: Interactions in which there is a change in the total kinetic energy of the system.

Lineal energy (y): The quotient of e by $\bar{l}$, where e is the energy imparted to the matter in a volume of interest by an energy deposition event, and $\bar{l}$ is

the mean chord length in the volume.

Linear energy transfer (LET): (L_{Δ}). The quotient of dE by dl, where dl is the distance traversed by a particle and dE is the mean energy loss in dl due to collisions with energy transfers less than some specified value Δ.

Linear Stopping Power: The quotient of dE by dl, where dl is the distance traversed by a particle and dE is the mean energy loss in dl due to collisions of all possible particles.

Mass Stopping Power The quotient of the linear stopping power and r, the density of the stopping material.

Muons: A μ lepton with mass equal to 106 MeV. Formerly classified as a meson. Important for this protocol because muons are contaminants of pion beams.

Pions: Pi mesons are singly-charged particles with mass equal to 140 MeV. In this protocol a pion is considered to be a heavy charged particle. In most instances the negative pion undergoes an interaction with an atomic nucleus near the end of its range with resulting nuclear disintegration and liberation of mixed low and high-LET radiations.

Plateau: The region of the depth-dose curve of a heavy charged-particle beam, at smaller depths than the Bragg peak, in which the dose is almost constant.

RBE: A ratio of the absorbed dose of a reference radiation to the absorbed dose of a test radiation to produce the same level of biological effect, other conditions being equal.

Radiation quality: Those characteristics of the radiation that describe the spatial distribution of energy transfers by charged particles, and which influence the effectiveness of any radiation when other physical factors such as absorbed dose, absorbed dose rate and fractionation are kept constant. Linear energy transfer is one parameter for describing quality.

Recombination (Initial and general): The process whereby ions formed by the passage of an ionizing particle through a gas recombine with oppositely charged ions. If the combining ions were produced by the same ionizing particle it is refer to as initial recombination; if produced by different ionizing particles it is called general recombination.

Specific Energy: The quotient of e by m, where e is the energy imparted to matter of mass m.

Task Group 20: A task group of the American Association of Physicists in Medicine (AAPM) Radiation Therapy Committee which was formed to work on problems of heavy charged particle beam dosimetry.

Tissue-equivalent material: A material, the absorption and scattering properties of which, for a given radiation, simulate those of a given biological material, such as soft tissue, muscle, bone or fat.

Appendix B

List of Symbols

a sectional area (m^2)

A atomic weight (kg/mol)

A_d attenuation and scattering factor for the ionization chamber wall when exposed to ^{60}Co radiation.

c speed of light in vacuum m s^{-1}

C_p conversion factor for absorbed dose in A-150 plastic from ionization in the chamber gas for a particle beam.

D absorbed dose (Gy)

D_d absorbed dose in dosimeter wall (Gy)

D_g absorbed dose in dosimeter gas (Gy)

D_t absorbed dose in muscle tissue (Gy)

e electronic charge (C)

E kinetic energy of particle (MeV)

E_s heat defect in calorimeter

J_g ionization charge per unit mass of gas (C kg^{-1})

K charge produced in air per unit mass per unit exposure (C kg^{-1})

k correction factors for ionization chambers

L_Δ restricted linear stopping power $(dE/dl)_\Delta$ (J m^{-1})

m mass (kg)

m_e electron mass (kg)

m_g mass of gas in an ionization chambers sensitive volume (kg)

N number of particles, photons, etc.

N_g cavity gas calibration factor (Gy C^{-1})

N_x exposure calibration factor (R C^{-1})

Q charge (C)

S linear stopping power (J m^{-1})

S/r mass stopping power (J $m^2 kg^{-1}$)

$(S/r)_i^j$ mass stopping power ratio for two materials, j over i

T temperature (°C)

u atomic mass unit

U electrical potential difference (V)

v velocity (m s^{-1})

V chamber collecting volume (m^3)

$\overline{w}$ mean energy expended in gas per ion pair formed when the initial ionizing particles are not completely stopped in the gas volume (J)

$\overline{W}$ mean energy expended in gas per ion pair formed when the initial ionizing particles are stopped in the volume (J)

x depth in absorber in beam direction (m)

ze charge of a heavy particle (C)

Z atomic number

b velocity relative to the speed of light (v/c)

e energy deposited in a small mass (MeV)

μ_{en}/r mass energy absorption coefficient ($m^2 kg^{-1}$)

$(\mu_{en}/r)_i^j$ ratio mass energy absorption coefficients for two materials, (j over i)

Φ fluence (dN/da) (m^{-2})

r density kg m^{-3})

Appendix C

Limitations on the Use of Ionization Chambers

C.1 Introduction

With our current knowledge, the ionization chamber method can yield absolute dose in heavy charged-particle beams with uncertainties of about 10 percent. For comparative dose measurements with charged particles of approximately equal velocities, a relative uncertainty of a few percent can be assumed. If detailed calculations are made of the ionization and energy loss processes, a relative uncertainty of the dose of about 2 percent can be achieved in principle (Rubach and Bichsel, 1982b).

If there are many different particles in the beam (such as in the Bragg peak of the negative pions), with a wide spread energy, it is necessary to know the particle spectra well in order to calculate the integrals in Equation 3.3.

A particular problem for pion dosimetry is that the carbon and oxygen content of the A-150 plastic and the TE gas are quite different (Table C.1). Because the kerma value for a carbon star is about twice as big as for an oxygen star (Shortt, 1979), there could be quite a difference in the energy deposition in the gas and in the solid (it would be less for the gas). To solve this problem we must know:

1. The number of pions stopping in the gas.

2. The energy deposition by the fragments in the gas.

For all heavy particles there is a component of energy loss due to nuclear interactions which must be estimated through the use of cross-sections and then factored into the stopping power which is required for a dose determination. It is therefore necessary to be fully aware of this uncertainty in the values of $\overline{w}$ and $(S/\rho)^{d}_{g}$. If the approximation is not valid, the errors in the calculation of the conversion factors must be included. The delta ray problem is one of the major difficulties in the interpretation of ionization measurements in small cavities (i.e., small compared to the range of the

Table C.1: Percent Elemental Composition, by Weight, of A-150 Tissue-Equivalent Plastic Compared to ICRU Muscle Tissue and TE gas

Element	ICRU Muscle[a]	A-150 Plastic[b]	TE gas[c]
H	10.2	10.2 ± 0.1	10.2
C	12.3	76.8 ± .5	45.6
O	72.9	5.9 ± .2	40.7
N	3.5	3.6 ± .2	3.5
Ca	0.007	1.8 ± .1	
F	not listed	1.7 ± .1	
Other (P, S, K, Na, Cl, Mg)	1.1		
Total	100.0	100.0 ± .5	100.0

(a) ICRU (1964)

(b) Smathers et al. (1977)

(c) Rossi and Failla (1956)

charged particles, but comparable to the range of the delta rays (Brenner et al., 1981)).

The uncertainty introduced by the lack of knowledge about $\overline{w}$ is also important, and probably amounts to several percent (section 3.2). In the peak region the $\overline{w}$ problems for the crossing particles are the same as for the plateau region, but for the secondaries, the $\overline{w}$ and $\overline{W}$ ($\overline{W}$ is the mean energy expended in a gas per ion pair formed by a particle whose energy is completely dissipated in the ionization chamber gas, (ICRU, 1979b)) values may not be very well known. In addition, many of the secondaries may be stoppers or starters (e.g., many of the star products from negative pions) or fragment secondaries in heavy ion beams.

C.2 Ion Pair Production in the Gas

A review of $\overline{w}$ and $\overline{W}$ has been presented in ICRU Report 31 (197913). It was pointed out that there is no practical theory for $\overline{w}$. In particular, there is no method of predicting the dependence of $\overline{w}$ on the energy of the charged particles. However $\overline{w}$ is insensitive to radiation characteristics such as charge, mass and energy of the incident particle, provided it is much faster than the valence electrons in the gaseous material. Most of the measurements have been made at energies below 10 MeV. It is below this energy where the major variations in $\overline{w}$ are observed. This is of concern to the heavy charged-particle

dosimetry whenever a significant fraction of the dose is from the contribution of low velocity particles. Measurements by Nuton et al. (1981) show a very unexpected energy dependence for 0.4-l MeV protons in a mixture of Ar and CH_4

The only high energy measurements that have been made were by Bakker and Segre (1951), by Schimmerling et al. (1976 and 1983), and by Thomas et al. (1980). For these experiments, the problem of delta ray production was not discussed. A theory of $\overline{w}$ would require that the energy loss spectra or the delta ray spectra be known quite well. This would appear to be more difficult than to measure $\overline{w}$ directly with adequate accuracy (but in the measurements the passage of delta rays across interfaces must be considered very carefully.

C.3 Stopping Powers

In order to calculate the stopping power, the mean excitation energy, *I,* of the atoms in the stopping material must be known. From the evaluation of experimental data with theoretical I-values, Bichsel and Porter (1982) believe that the Bethe-Bloch theory with a z^3 correction permits calculations of stopping power for protons and alpha particles for energies above 0.3 and 1.5 MeV, respectively, with an uncertainty of no more than 2 percent in hydrogen, nitrogen, oxygen, methane, air and CO_2 (Bichsel and Hilko, 1980) at 2 MeV, and less than 1 percent at several hundred MeV. This assumes that no further corrections are needed in the theory (Ahlen, 1980). It must be noted, that no measurements have been made over an extended energy range at one accelerator with one given method. For TE plastic and other organic solids (Bichsel, 1982), the situation is less satisfactory. The major problem is that there are vast fluctuations in the *I* value of polyethylene determined in experiments.

C.4 Ionization Recombination

Ionic recombination is an effect which needs to be evaluated when using ionization chambers. There are theories for the ion collection efficiency under conditions of continous and pulsed irradiations. The theory for pulsed irradiation applies in the situation where the length of the pulse is short compared to the ion collection time. The situation encountered at a heavy particle accelerator generally falls between the two theories. The general condition is a pulse which is long compared to the transit time of an ion across the chamber, The pulse comes at the repetition rate of the accelerator and the size and shape of the pulses can be quite variable. This pulse is composed of a series of smaller pulses characteristic of the radio-frequency of the accelerator. The width and interval between the pulses of this microstructure are both short compared to the transit time. Recombination is described as being either columnar (initial) or volume (general). Columnar recombination describes

the recombination of the positive and negative charge carriers which were formed along the track of a single charged particle. Since the probability of the recombination depends upon the ion density along a single track, columnar recombination will be independent of the dose rate, and will be more important for the densely ionizing particles (high LET radiations). Volume recombination will be dependent on dose rate. These two types of recombination can be distinguished experimentally by plotting the reciprocal of the observed ionization current against an appropriate function of the collecting field strength, U (Boag, 1966). For initial recombination one should find

$$1 / i = 1 / i_{sat} + constant / U$$

while for general recombination

$$1 / i = 1 / i_{sat} + constant / U^2$$

The effects due to recombination, particularly columnar recombination, for the heavier ions should be explored, e.g. by placing the electric field in a parallel plate ionization chamber at different angles with respect to the beam direction (see also Rubach et al., 1983). Boag (1982) has discussed recombination correction for pulsed radiation in a swept beam technique.

C.5 Stability of the Ionization Chamber

The following problems should be considered in the stability of the ionization chamber performance:

1. the response of an ionization chamber may be sensitive to the humidity (Kristensen and Sundbom, 1981: Mijnheer et al., 1983) as well as the temperature and pressure;
2. the position and stability of the collecting electrode;
3. the composition of the gas (Williams, 1980);
4. changes in the sensitivity and calibration of the electrometers, digital voltmeters etc.

At a given institution, the most desirable check on the stability of an ionization chamber would be by intercomparison with another ionization chamber in a cobalt therapy beam or other photon standard.

C.6 Calibration of the Ionization Chamber

Because the uncertainty of the energy per ion pair for gases may be as much as 10 percent and the uncertainty of the stopping powers for the wall materials as much as 4 to 10 percent (depending on particle energy), it is recommended that the ionization chamber be calibrated with a calorimeter (see Chapter 6).

Appendix D

Heavy Charged Particle Dosimetry Factors

As shown in Equations 6.4 and 6.10, absolute dosimetry with a TE ionization chamber in a charged particle beam requires the evaluation of $\overline{w}$, the mean energy required to form an ion pair in the gas of the chamber, and two stopping power ratios - one from gas to TE plastic and the second from TE plastic to tissue.

The value of $\overline{w}$ has been measured for electrons and for low energy protons and alpha particles in various gases. At higher energies the assumption that $\overline{w}$ will approach the electron value asymptotically (ICRU, 1979b) has not been corroborated by experimental or theoretical work. Since there is typically a 10 percent difference between the low energy measurements and the electron values, it is believed that experimental values should lie between these limits.

Stopping power values for individual mono-energetic particles in various materials can be calculated if the ionization potentials of the elements are well-known (Bichsel and Porter, 1982). Bragg additivity assumes that for compounds, stopping power can be calculated by weighting the stopping power of each constituent by its fractional composition. This technique has been used to produce the values in Table D.1. The energy distribution of the primary beam as well as the distribution of particle types must be folded into this calculation. Fortunately, the stopping power ratios are not strongly dependent on energy (see Bichsel, 1982).

In cases where $\overline{w}$ and S / r^{d}_{g} are not well known separately but the product has been determined by calorimetry, the quantity C_p (see equation 6.8) is to be used. Recommended values are given in Table D.l.

Table D.1: Recommended Dosimetry Factors When Using Methane-based TE gas or Air, A-150 plastic and ICRU Muscle Tissue

Particle Beam	$\bar{w}/e$	$(S/\rho)^d_g$	$(S/\rho)^t_a$	C_p	Comments
Proton	30.2[a]	0.991[b]	0.984[c]	30.0	Plateau-TE gas
	30.2[a]	0.97[b]	0.975[c]	29.3	Peak-TE gas
	34.3[d]				Air
Heavy Ion	33.7	1.145		38.6	Plateau-Air
	33.7	1.158		39.0	Peak-Air
Pion			0.98[e]	29.5[e]	Plateau-TE gas
			0.92[e]	30.1[e]	Peak-TE gas

(a) ICRU, 1979b

(b) Bichsel, 1983; Berger and Seltzer, 1982

(c) Janni, 1982

(d) Verhey et al., 1979

(e) Private Communication (A. R. Smith, 1983)

Appendix E

Radiation Quality

E.1 Introduction

It is well-established that the absorbed dose is insufficient to uniquely define the response of biological systems exposed to high LET radiations (Lea, 1962; Raju, 1980). The term, radiation quality, is frequently employed to encompass many of the physical characteristics relevant to biological and clinical studies and is discussed in ICRU Report 30 (1979a). For the purposes of this protocol, radiation quality simply refers to those physical characteristics other than the dose, dose rate, and fractionation schedule which are relevant to radiological studies.

E.2 Phase Space

It is necessary to specify the phase space of the incident beam in order to ensure reproducibility of biological results. The specification of accelerating voltage of the machine and its half value layer (for photons) are examples which are used routinely in this respect; the complexity of heavy charged-particle beams require more sophisticated approaches (Paciotti et al., 1981; Alonso et al., 1980). Beams of heavy charged particles are rarely composed of mono-energetic particles of a single type. The variation in energy and the presence of contaminants can alter both dose distribution and the biological response. Therefore, it is desirable that the distribution in particle type, and momentum vector be known at the surface of the patient for treatment planning.

E.3 Cross Sections

As energetic heavy charged particles pass through tissue, they are capable of producing long range electrons (delta rays) from atomic interactions and secondary neutrons and heavy charged particles from nuclear interactions. There are even weak interactions, such as muon decays in a pion beam,

which play a significant role in dosimetry. The probabilities of producing secondary particles as a function of energy and angle either from the primary beam or from collisions with target nuclei are fundamental information for calculations or analyses of experimental results. Such data are required as input for dosimetric calculations (Dicello et al., 1980; Schimmerling, 1980), microdosimetric calculations (Brenner et al., 1981) and treatment planning (Chen, 1980).

E.4 Theory and Calculations

In principle, the data described in the previous two subsections are sufficient for the calculation of all physical information used to define radiation quality. However, there are two practical limitations to this approach. First, cross sections needed for such calculations are not generally available. Furthermore, the uncertainties associated with the cross-sectional and phase-space data often are too large for clinical applications. Second, the theories needed in the calculations introduce significant errors of their own. In addition, calculations may require large amounts of manpower and computer time. For these reasons, such calculations are strongly dependent on experimental testing to verify and improve the calculations and to reduce calculation time. However, recent advances, particularly in track structure (see Paretzke, 1980), have resulted in simpler calculations which reproduce experimental data at the nanometer and micrometer level, as well as the absolute dose (Brenner et al., 1981).

Because of the high costs associated with accelerator machine time and experimentation on accelerators for energetic heavy charged particles, it is recommended that any program directed toward an evaluation of radiation quality be balanced with respect to experiments and calculations.

E.5 LET

The parameter, linear energy transfer (LET), introduced by Zirkle (1940) has proven to be a useful, although limited, concept for correlating the radiation field with biological effects. As originally conceived, LET was simply the energy lost by a charged particle as it traverses a specified distance. LET is now defined (ICRU, 1980) as follows: The linear energy transfer or restricted linear collision stopping power, L_{Δ} of a material for charged particles is the quotient of dE by dl where dE is the energy lost by a charged particle in traversing a distance dl due to those collisions with electrons in which the energy loss is less than A. Only for large energy transfers (A) does the LET (L_{Δ}) approach the value of the stopping power (S).

With the introduction of the concept of LET, it was hoped that a simple relationship could be developed between the energy lost by a particle and the energy deposited in a specific site. Kellerer and Chmelevsky (1975) evaluated

the range in proton energy and site size (for spherical volumes) over which LET was an acceptable parameter. These data can be useful in evaluating the accuracy and reliability of physics experiments and calculations. However, the application of such results to biological interpretations should be done with caution where the volume and shape of the sensitive site is uncertain.

The usefulness of LET in the interpretation of radiobiological data lies primarily in its simplicity; therefore, it is unlikely that individuals involved in high-LET studies will be dissuaded from its use. However, it is recommended that extreme care be exercised in the use of LET for the evaluation of clinical studies.

E.6 Microdosimetry

A variety of approaches have been pursued in order to develop a method for evaluating the relationship between the physics and biology which was not subject to the limitations of LET. One of the most successful was the approach initiated by Rossi and Rosenzweig (1955) which ultimately expanded into the field of microdosimetry (Rossi, 1971). It was proposed that the macroscopic average quantity, LET, be replaced by a new quantity, lineal energy (y), which is the energy deposited by an event in a specified volume divided by the mean path length through the volume. One can then investigate the characteristics of the probability distribution of energy deposited by an event as a function of lineal energy and site size. These distributions were relatively easily obtained experimentally for effective tissue equivalent volumes down to a fraction of a μm^3. The linear distributions may be converted to distributions as a function of energy per unit mass, defined as specific energy, *z*. The specific energy then, is analogous to the macroscopic absorbed dose.

$$D = \lim_{m \to 0} \bar{z}$$

Perhaps the greatest significance of this approach is that it describes the influence of stochastic processes in biologically relevant sites.

Today, microdosimetry includes the study of the spectral and spatial distributions of energy deposition in biological structures and the relationship between these distributions and subsequent chemical and biological processes (e.g., see Booz et al., 1981). The experimental technique developed by Rossi and Rosensweig (1955) has become a standard method for the measurement of microdosimetric distributions. This technique uses a proportional counter, usually spherical in shape, constructed of tissue-equivalent materials and filled with a tissue-equivalent gas. The pressure of the gas is chosen to simulate a microscopic sphere of unit density tissue (Rossi, 1971). Because this approach is relatively simple and sensitive to variations in radiation quality, it has received extensive use.

The limitations of this approach are twofold. Firstly, because the method analyzes the pulse-height (number of ion pairs) of individual events, it is lim-

ited to low beam intensities which are not easily obtained at many biomedical facilities for heavy charged particles without altering the phase space. Secondly, the use of proportional counters limits the method to volumes with equivalent diameters greater than about 0.lμm. This is because at smaller volumes, the region of proportionality in the gas represents a significant fraction of the total volume and this distorts the spectrum.

It was hoped that the latter limitation would not be a severe one, because there was evidence that at least some sites of biological interest were above this limiting size (Kellerer and Rossi, 1972). Recent results suggest that this may be too simplistic an assumption (e.g., Goodhead and Thacker, 1977; Kellerer and Rossi, 1978). Nevertheless, these types of data have served several significant purposes. For example, such measurements provide quantitative data of many of the physical processes affecting biological response and provide a means for the quantitative comparison of radiation qualities. Secondly, microdosimetric results impose severe restrictions on dosimetric calculations and measurements. Finally, such data have been found to be useful, in certain (semi-empirical) biological models such as the alpha-beta (quadratic) model for survival (see Rossi, 1971; Kellerer and Rossi, 1972; Zaider and Dicello, 1978).

As was stated earlier, two of the limitations of measurements with proportional counters are that they are dose-rate limited and they cannot be performed for equivalent diameters below the micrometer level. The variance method, developed by Bengtsson and Lindborg (1974) is not limited by these restrictions. By measuring the variation in charge collected in an ion chamber operated at the appropriate pressure, one can determine the dose mean lineal energy (y_D) for equivalent diameters into the nanometer range. However, only this mean parameter is obtained, not the distribution itself. Furthermore, at the smaller diameters, there is no direct relationship between ion pairs produced and energy deposited (the W value is not constant, (Brenner et al. 1981), which will frequently make the experimental data difficult to analyze.

It should be realized that there is no single detector or technique which will satisfy all requirements for all radiations. Therefore, each group must design its system to achieve its specific objectives.

E.7 Indirect Techniques

Those methods for evaluating radiation quality discussed previously are all capable of directly determining the macroscopic absorbed dose as well as more detailed information. There are innumerable calculations and measurements which contribute to a better understanding of the radiation quality, although they do not directly deal with dose. Included in these are the use of photographic emulsions, track detectors, capacitive chambers, solid state detectors, and activation techniques. The use of such techniques is encour-

aged. For details, consult Thomas and Perez-Mendez (1980) and references therein.

E.8 Radiation Quality and Biological Response

One objective of any clinical program is to evaluate sufficiently the physical characteristics associated with patient treatments so that at least the average response can be specified prior to treatment. For experimental programs, data are needed also to develop the most effective techniques. Although a proper determination of radiation quality may uniquely define the biological response, it does not predict responses per se. There is a great deal of chemistry which transpires after the initial physical events which profoundly influences the ultimate biological endpoint. Although this is an exciting area of research, so far the incorporation of chemical processes in treatment planning for high LET radiations has only been achieved indirectly through empirical methods or biological modeling. One can either

1. invoke a model which is based on assumptions concerning the nature of the chemical processes or

2. interpolate from experimental results.

Interpolation requires an n-dimensional array of data, where n is the number of significant physical and biological parameters being varied. Interpolation alone is seldom practical; therefore, models are almost invariably invoked albeit implicitly. It must be recognized by the clinicians that many data supplied concerning radiation quality immediately implies a model and any interpretations or conclusion based on the biological data are dependent on that model. In this respect, specification of radiation quality involves a certain subjectiveness not present, for example, in the specification of dose.

REFERENCES

AAPM (1980). Protocol for Neutron Beam Dosimetry. Task Group No. 18, Physics Radiation Therapy Committee, American Association of Physicists in Medicine, AAPM Report No. 7.

AAPM (1983). A Protocol for the determination of absorbed dose from high-energy photon and electron beams. Task Group No. 21, Radiation Therapy Committee, American Association of Physicists in Medicine, Med. Phys. 10:741-771.

Ahlen, S.P. (1980). Theoretical and experimental aspects of the energy loss of relativistic heavily ionizing particles. Rev. Mod. Phys. 52:121-173.

Alonso, J.K., Benton, E.V., Chu, W., Llacer, J., Richier, J. and Tobias, C.A. (1980). "Instrumentation for Measuring Heavy-Ion Fields". In: Biological and Medical Research with Accelerated Heavy Ions at the Bevalac, 1977-1980, pp. 21-34, M.C. Pirruccello and C.A. Tobias, eds., Lawrence Berkeley Laboratory Report LBL-11220.

Amols, H.I., Liska, D.J. and Halbig, J. (1977). The use of a dynamic range shifter for modifying the depth dose distributions of negative pions. Med. Phys. 4:404-407.

AmoIs, H.I., Kittell, R., Paciotti, M.A., Hollend, J.A., Hogstrom, K.R., Collier, M. and Heller, P. (1980). Preclinical studies of dynamic treatment modes in pion therapy. Med. Phys. 7:621-626.

Awschalom, M. and Attix, F.H. (1982). A-150 plastic equivalent gas. Phys. Med. Biol. 25:567-569.

Awschalom, M., Rosenberg, I., Mravca, A. (1983). Kermas for various substances averaged over the energy spectra of fast neutron therapy beams: A study in uncertainties. Med. Phys. 10:395-409.

Bakker, C.J. and Segre, E. (1951). Stopping power and energy loss for ion pair production for 340-MeV protons. Phys. Rev. 81:489-492.

Battermann, J.J., Hart, A.A.M. and Breur, K. (1981). Dose-effect relations of tumor control and complication rate after fast neutron therapy for pelvic tumors. Br. J. Radiol. 54:899-904.

Bengtsson, L.G. and Lindborg, L. (1974). "Comparison of Pulse Height Analysis and Variance Measurement for the Determination of Dose Mean Specific Energy". In: Proceedings of the Fourth Symposium on Microdosimetry, pp. 823, J. Booz, H.G. Ebert, R. Eickel, and A. Waker, eds. EUR 5122 d-e-f, Commission of European Communities, Luxenbourg, 1974.

Berger, M.J. and Seltzer, S.M. (1969). Tables of energy losses and ranges of electrons and protons. National Aeronautics and Space Administration

Report NASA SP-3012. (Available from National Technical Information Service, Springfield, VA 22161).

Berger, M.J. and Seltzer, S.M. (1982). Stopping powers and ranges of electrons and positrons (2nd ed.). National Bureau of Standards Report NBSIR 82-2550-A.

Bewley, D.K., McCullough, E.C., Page, B.C. and Sakata, S. (1974). Neutron dosimetry with a calorimeter. Phys. Med. Biol. 19:831-842.

Bichsel, H. (1968). "Charged Particle Interactions". In: Radiation Dosimetry, (Attix, Roesch and Tochilin, ed.), Academic Press, New York.

Bichsel, H. (1972). Section 8d of American Institute of Physics Handbook. McGraw Hill.

Bichsel, H. (1982). The stopping power of a solid and of a gas of the same composition. Phys. Med. Biol. 27:449-450.

Bichsel, H. and Hilko, R.H. (1980). Measurements of the energy loss of alpha particles in carbon dioxide. Helv. Phys. Acta. 53:655 (abstract).

Bichsel, H. and Porter, L. (1982). Stopping power of protons and alpha particles in H_2, He, N_2, O_2, CH_4 and air. Phys. Rev. A 25:2499-2510.

Bichsel, H. and Rubach, A. (1982). Neutron dosimetry with spherical ionization chambers II. Basic physical data. Phys. Med. Biol. 27:1003

Bichsel, H., Eenmaa, J., Weaver, K. and Wootten, P. (1975). "Attainable accuracy in fast neutron dosimetry system". In: Proceedings of an International Workshop on Particle Radiation Therapy (Key Biscayne, October 1-3, 1975).

Bichsel, H., Hanson, K.M. and Schillaci, M.E. (1982). Lateral displacement in small angle multiple scattering. Phys. Med. Biol. 27:959-961.

Blattman, H., Salzmann, M., Cordt-Richie, I., Crawford, J., Hoffmann, W., Pedroni, E., Shortt, K. and Tremp, J. (1981). Integrating Dosimetry Systems for Dose Mapping of Pion Beams. IAEA Int. Symp. on Biomedical Dosimetry: Physical Aspects, Instrumentation, Calibration, IAEA-SM-249/35.

Boag, J.W. (1966). "Ionization Chambers". In: Radiation Dosimetry, Vol. 2,2nd ed. pp. l-72. F.H. Attix and W.C. Roesch, eds., Academic Press, New York.

Boag, J.W. (1982). The recombination correction for an ionization chamber exposed to pulsed radiation in a "swept beam" technique. I. Theory. Phys. Med. Biol. 27:201-211.

Booz, J., Ebert, H.G. and Hartfiel, H.D. (1981). Eds., Seventh Symposium on Microdosimetry, Harwood Academic Publishers, Chur, Switzerland, 1981.

Bragg, W.H. and Kleeman, R.D. (1904). On the ionization curves of radium. Philosoph. Mag. 8:726-738.

Brenner, D.J. (1982). Calculation of ionization distributions in a tissue-equivalent cloud chamber gas mixture. Radiat. Res. 89:194-202.

Brenner, D.J., Zaider, M., Dicello, J.F. and Bichsel, H. (1981). "Theoretical Approaches to Energy Deposition in Small Sites". In: Proceedings of the Seventh Symposium on Microdosimetry, J. Booz, H.G. Ebert and H.D. Hartfiel, eds. pp. 677-688. Harwood Academic Publishers Ltd., Chur, Switzerland, 1981. [EUR-7147]

Brown, K.L. and Tautfest, G.W. (1956). Faraday-cup monitors for high-energy electron beams. Rev. Sci. Instrum. 27:696-702.

Carlsson, J. and Rosander, K. (1973). Effects of multiple scattering on proton beams in radiotherapy. Phys. Med. Biol. 18:633-640.

Caumes, J., et al. (1984) Direst calibration of ionization chambers with a TE calorimeter at the Orleans Cyclotron. Strahlentherapie 160:127-128.

Chen, G.T.Y. (1980). "Treatment Planning for Charged Particle Radiotherapy". In: Advances in Radiation Protection and Dosimetry in Medicine, Vol. 2, pp. 529-556, R.H. Thomas and V. Perez-Mendez, eds. Plenum Press, New York.

Chu, C.L., Hogstrom, K.R., Chen, G.T.Y. and Hilko, R.A. (1986). Thermoluminescence of ^{7}LiF in therapeutic high-linear-energy-transfer (LET) charged particle beams. Phys. Med. Biol. (in press).

Cooke, D.W. and Hogstrom, K.R. (1980). Thermoluminescent response of LiF and $Li_2B_4O_7$:Mn to pions. Phys. Med. Biol. 25:657-666.

Crowe, K., Kanstein, L., Lyman, J. and Yeater, F. (1975). A large-field medical beam at the 184-inch synchrocyclotron. Lawrence Berkeley Laboratory Report, LBL-4235.

Dicello, J.F., Zaider, M. and Brenner, D.J. (1980). "Dosimetry of pions". In: Advances in Radiation Protection and Dosimetry in Medicine, Vol. 2, R.H. Thomas and V. Perez-Mendez, eds. Plenum Press, New York.

Domen, S.R. (1980). Thermal Diffusivity, Specific Heat and Thermal Conductivity of A-150 Plastic. Phys. Med. Biol. 25:93-102.

Domen, S.R. and Lamperti, P.J. (1974). A Heat-Loss-Compensated Calorimeter: Theory, Design, and Performance. J. Res. NBS 78A:595-610.

Ettinger, K.V., Fairchild, R.G., Anunuso, C.I., Srirath, S. and Vigna Filho, E.D. (1980). Lyoluminescent dosimetric materials and their response to ionizing radiation. Nucl. Instr. Methods 175:119-121.

Fano, U. (1964). "Studies in penetration of charged particles in matter". Nat. Acad. Sci. Nat. Res. Council. Publ. 1133.

Goldhaber, A.S. and Heckman, H.H. (1978). High energy interactions of nuclei. Ann. Rev. Nucl. Part. Sci. 28:161-205.

Gooden, D.S. and Brickner, T.J. (1972). The routine of thermoluminescence dosimetry for radiation therapy. Radiology 102:685-689.

Goodhead, D.T. and Thacker, J. (1977). Inactivation and mutation of cultured mammalian cells by aluminum characteristic ultrasoft x-rays. I. Properties of Aluminum X-Rays and Preliminary Experiments with Chinese Hamster Cells. Int. J. Radiat. Biol. 31:541-559.

Goodman, L.J. (1978). Density and Composition Uniformity of A-150 Tissue-Plastic. Phys. Med. Biol. 23:753-758.

Greene, D. and Major, D. (1975). The use of a calorimeter for neutron dosimetry. Phys. Med. Biol. 20:244-254.

Hoffmann, W., Möller, G., Blattmann, H. and M. Salzmann (1980). Pion dosimetry with thermoluminescent materials. Phys. Med. Biol. 25:913-921.

Hoffmann, W., Lakshmanan A.R. and Spallek, R. (1984). Phototransferred thermoluminescence in LiF for high LET radiation dosimetry. Radiat. Prot. Dosim. 8:225-230.

Hoffmann, W., Prediger, B., Fessenden, P. and Chen, G.T.Y. (1986). Response of CaF_2:Tm thermoluminescence material to heavy ion fields. (to be published)

Hogstrom, K.R. and Amols, H.I. (1980). Pion *in vivo* dosimetry using aluminum activation. Med. Phys. 7:55-60.

Hogstrom, K.R. and Irifune, T. (1980). Depth dose and off-axis characteristics of TLD in therapeutic pion beams. Phys. Med. Biol. 25:667-676.

ICRU (1964). Physical Aspects of Irradiation. ICRU Report 10b, International Commission on Radiation Units and Measurements, Washington, D. C.

ICRU (1970). Linear Energy Transfer. ICRU Report 16, International Commission on Radiation Units and Measurements, Washington, D.C.

ICRU (1976). Determination of absorbed dose in a patient irradiated by beams of X or gamma rays in radiotherapy procedures. ICRU Report 24, International Commission on Radiation Units and Measurements, Washington, D.C.

ICRU (1977). Neutron Dosimetry for Biology and Medicine. ICRU Report 26, International Commission on Radiation Units and Measurements,

Washington, D.C.

ICRU (1979a). Quantitative Concepts and Dosimetry in Radiobiology. ICRU Report 30, International Commission on Radiation Units and Measurements, Washington, D.C.

ICRU (1979b). Average Energy Required to Produce an Ion Pair. ICRU Report 31, International Commission on Radiation Units and Measurements, Washington, D.C.

ICRU (1980). Radiation quantities and unit. ICRU Report 33, International Commission on Radiation Units and Measurements, Washington, D.C.

ICRU (1982). The dosimetry of pulsed radiation. ICRU Report 34, International Commission on Radiation Units and Measurements, Washington, D.C.

ICRU (1984). Radiation Dosimetry: Electron beams with energies between 1 and 50 MeV. ICRU Report 35, International Commission on Radiation Units and Measurements, Washington, D.C.

Janni, J.F. (1982). Proton range-energy tables 1 keV-10 Gev. Atomic Data and Nuclear Data Tables, 27:147-529.

Johns, H.E. and Cunningham, J.R. (1974). The Physics of Radiology, Charles C. Thomas, Springfield, IL.

Kanai, T., Kawachi, K., Kumamato, Y., Ogawa, H., Yamada, T. and Matsuzawa, H. (1980). Spot scanning system for proton radiotherapy. Med. Phys. 7:365-369.

Karlsson, B.G. (1964). Methoden zur Berechnung und Erzielung einiiger fur die Tiefentherapie mit hochenergitischen Protonen gunstiger Dosisverteilungen. Stralentherapie 124:481-492.

Kellerer, A.M. and Chmelevsky (1975). Concepts of Microdosimetry III. Mean values of the microdosimetric distributions. Rad. Envior. Biophys. 12:321-335.

Kellerer, A.M. and Rossi, H.H. (1972). The theory of dual radiation action. Curr. Top. Radiat. Res. Q. 8, 85-158.

Kellerer, A.M. and Rossi, H.H. (1978). A generalized formulation of dual radiation action. Radiat. Res. 75:471-488.

Koehler, A.M., Schneider, R.J. and Sisterson, J.M. (1975). Range modulators for protons and heavy ions. Nucl. Instrum. Meth. 131:437-440.

Koehler, A.M., Schneider, R.J. and Sisterson, J.M. (1977). Flattening of proton dose distributions for large-field radiotherapy. Med. Phys. 4:297-301.

Kristensen, M. and Sundbom, L. (1981). Sensitivity dependence of an A-150 walled ion chamber to air humidity. Phys. Med. Biol. 26:903-905.

Lam, G.K.Y. (1982). Technique of range modulation for a clinical pi-meson beam. Rev. Sci. Instrum. 53:1067-1071.

Lam, G.K.Y. and Skarsgard, L. (1983) Physical Aspects of the Pion Beam at TRIUMF. In: Pion and Heavy Ion Radiotherapy: Pre-Clinical and Clinical Studies. pp. 83-90. (L. Skarsgard, ed.), Elsevier, North Holland.

Larsson, B. (1961). Pm-therapeutic physical experiments with high energy protons. Brit. J. Radiol. 34:143-151.

Larsson, B. (1980). "Dosimetry and Radiobiology of Protons as Applied to Cancer Therapy and Neurosurgery". In: Advances in Radiation Protection and Dosimetry in Medicine (1980) pp. 367-394. (R. H. Thomas and V. Perez-Mendez, eds.) Plenum Press, New York.

Laughlin, J.S. (1974). Annual Progress Report for U.S.E.R.D.A. Contract EY-76-5-02-3522, 1974.

Laughlin, J.S. and Genna, S. (1966). "Calorimetry". In: Radiation Dosimetry, Vol. 2, 2nd ed. pp. 389-441. F. H. Attix and W. C. Roesch, eds., Academic Press, New York.

Laulainen, N. and Bichsel, H. (1972). Energy removed by delta rays from finite volumes in passage of charged particles. Nucl. Instrum. Meth. 104:531-539.

Lea, D.E. (1962). Actions of Radiations on Living Cells. 2nd ed., Cambridge University Press, London.

Lehman, C., Alonso, J., Grunder, H., Hoyer, E., Staples, J. and Voelker, F. (1979). "A Three-Dimensional Beam Scanning System for the Irradiation of Large Volumes in Particle Therapy". In: Proceedings of the First Int. Seminar on the Uses of Proton Beams in Radiation Therapy. Vol. 1, pp. 112-122. Atomistadt, Moscow.

Lyman, J.T. (1983). 'Computer Modeling of Heavy Charged Particle Beams". In: Pion and Heavy Ion Radiotherapy: Pre-Clinical and Clinical Studies. pp. 139-147 (L. Skarsgard, ed.), Elsevier, North Holland.

Lyman, J.T. (1984). "Heavy Charged-Particle Beam Dosimetry". In: Advances in Dosimetry for Fast Neutrons and Heavy Charged Particles for Therapy Applications. pp. 267-280 IAEA, Vienna.

Lyman, J.T. and Howard, J. (1977). "Biomedical Research Facilities and Dosimetry". In: Biological and Medical Research with Heavy Ions at the Bevalac, 1974-1977, Lawrence Berkeley Laboratory Report, LBL-5610 (April 1977) pp 26-35.

Lyman, J.T., Fabrikant, J.I. and Frankel, K.A. (1985). Charged-particle stereotactic radiosurgery. Nuc. Instrum. and Meth. in Phys. Res. B10/11:1107-1110.

McDonald, J.C. and Goodman, L.J. (1982). Measurements of the thermal defect for A-150 plastic. Phys. Med. Biol. 27:227-233.

McDonald, J.C., Laughlin, J.S. and Freeman, R.E. (1976). Portable tissue equivalent calorimeter. Med. Phys. 3:80-85.

McDonald, J.C., Ma, I-C., Liang, J., Eenmaa, J., Awschalom, M., Smathers, J.B., Graves, R., August, L.S. and Shapiro, P. (1981a). Calorimetric and ionimetric dosimetry intercomparisons. I. U.S. neutron radiotherapy centers. Med. Phys. 8:39-43.

McDonald, J.C., Ma, I-C., Mijnheer, B.J. and Zoetelief, H. (1981b) Calorimetric and ionimetric dosimetry intercomparisons. II $d + T$ neutron source at the Antoni Van Leeuwenhoek Hospital. Med. Phys. 8:44-48.

McDonald, J.C. and Domen, S.R. (1986). A-150 plastic radiometric calorimeter for charged particle and other radiations. (submitted to Nucl. Instr. Meth. in Phys. Res.-A)

Mijnheer, B.J., van Wijk, PC., Williams, J.R. and Bell K. (1983). The influence of air humidity on gamma-ray calibrations and neutron absorbed-dose meausrement with different types of A-150 plastic tissue-equivalent ionization chambers. Phys. Med. Biol. 28:277-284.

Müller, J. W. (1979). Some second thoughts on error statements. Nucl. Instr. Meth. 163:241-251.

Mustafa, A.A.H. and Jackson, D.F. (1981). Small-angle multiple scattering and spatial resolution in charged particle tomography. Phys. Med. Biol. 26:461-472.

NAS, (1964). “Studies in penetration of charged particles in matter”. Nat. Acad. Sci. Nat. Res. Council Publ. 1133.

Nuton, D.H., Harris, S.J. and Doust, C.E. (1981). The energy dependence of $\overline{W}$ in argon/methane gas for 300 keV to 1.8 MeV protons. Phys. Med. Biol. 26:245-251.

Paciotti, M., Bradbury, J., Inoue, H., Rivera, O. and Sandford, S. (1981). Beam characteristics in the LAMPF biomedical channel. IEEE Trans. Nucl. Sci. NS-28:3150-3152.

Painter, L.R., Arakawa, E.T., Williams, M.W. and Ashley, J.C. (1980). Optical properties of polyethylene: Measurements and applications. Radiat. Res. 83:1-18.

Paretzke, H.G. (1980). "Advances in Energy Deposition". In: Advances in Radiation Protection and Dosimetry in Medicine, Vol. 2, pp. 51-73, R.H. Thomas and V. Perez-Mendez, eds. Plenum Press, New York.

PART II (1977). Particles and Radiation Therapy (1977). Second International Conference Int. J. Radiat. Oncol. Biol. Phys. vol 3 (complete).

PART III (1982). Int. J. Radiat. Oncol. Biol. Phys., vol 8 (complete).

Powers, W.E., Kinzie, J.J., Demidecki, A.J., Bradfield, J.S. and Feldman, A. (1973). New system of field shaping for external-beam radiation therapy. Radiology 108:407-411.

Raju, M.R. (1980). Heavy Particle Radiotherapy. Academic Press, New York.

Raju, M.R., Amols, H.I., Dicello, J.F., Howard, J., Lyman, J.T., Koehler, A.M., Graves, R. and Smathers, J.B. (1978). A heavy particle comparative study. Part I: Depth-dose distributions. Brit. J. Radiol. 51:699-703.

Richman, C. (1981). The physics of cancer therapy with negative pions. Med. Phys. 8:273-291.

Richman, C., Aceto H., Jr., Raju, M.R. and Schwartz, B. (1966). The radiotherapeutic possibilities of negative pions. Am. J. Roentgenol. 96:777.

Rossi, H.H. (1971). Measurement of Radiation Quality, Nuclear News, pp. 53-56 (November, 1971).

Rossi, H.H. and Failla, G. (1956). Tissue-equivalent ionization chambers. Nucleonics 14:32-37.

Rossi, H.H. and Rosensweig, W. (1955). Measurement of neutron dose as a function of linear energy transfer. Radiat. Res. 2:417-425.

Rubach, A. (1976). Neutron Dosimetry with Spherical IC. Diss. U. Wash. (June 1976).

Rubach, A. and Bichsel, H. (1982a). Neutron dosimetry with spherical ionization chambers I. Theory of the dose conversion factors r and W_n. Phys. Med. Biol. 27:893-904.

Rubach, A. and Bichsel, H. (1982b). Neutron dosimetry with spherical ionization chambers III. Calculated results of tissue-equivalent chambers. Phys. Med. Biol. 27:1231-1243.

Rubach, A. and Bichsel, H. (1982c). Neutron dosimetry with spherical ionization chambers IV. Neutron sensitivities for C/CO_2 and tissue-equivalent chambers. Phys. Med. Biol. 27:1455-1463.

Rubach, A., Bichsel, H. and Ito, A. (1983). Neutron dosimetry with spherical ionization chambers V. Experimental measurements and comparison with calculations of the cavity size dependence of the specific ionization. Phys. Med. Biol. 28:913-924.

Salzmann, M. (1979). Measurements at the πE3 single beam correlated to dosimetry and therapeutic planning for the pion applicator. Rad. Environm. Biophys. 16:219-223.

Schimmerling, W. (1980). "Heavy-Ion Dosimetry". In: Advances in Radiation Protection and Dosimetry in Medicine, Vol. 2, pp. 479-516, R.H. Thomas and V. Perez-Mendez, eds. Plenum Press, New York.

Schimmerling, W., Vosburgh, K.G., Todd, P.W. and Appleby, A. (1976). Apparatus and dosimetry for high-energy heavy-ion-beam irradiations. Radiat. Res. 65:389-413.

Schimmerling, W., Subramanian, T.S., McDonald, W.J., Kaplan, S.N., Sadoff, A. and Gabor, G. (1983). "Physical Characterization of Energetic Heavy-ion Beams". In: Biology and Medicine Division Annual Report 1981-1982, pp 41-43. Lawrence Berkeley Laboratory Report, LBL-14986 (April 1983).

Schneider, R., Schmidt, R.A. and Koehler, A.M. (1974). Physical preparations of cancer therapy at the Harvard Cyclotron. Bull. Amer. Phys. Soc. 19:31 (abstract).

Seiler, P.G., Dietlicher, R., Wemmers, G., Salzmann, M. and Moline, A. (1982). Two-dimensional measurement of pion-induced beta activity in extended foils. Phys. Med. Biol. 27:709-714.

Shonka, F.R., Rose, J.E. and Failla, G. (1958). "Conducting plastic equivalent to tissue, air and polystyrene". In: Proceedings of the Second International Conference on Peaceful Uses of Atomic Energy, Vol. 21, pp. 160-166, United Nations, New York and Geneva.

Shortt K. (1979). Absolute Dosimetry of Negative Pions. Thesis, University of British Columbia (Nov. 1979).

Shukovsky, L.J. and Fletcher, G.H. (1973). Time-dose and tumor volume relationships in the irradiation of squamous cell carcinoma of the tonsillar fossa. Radiology 107:621-626.

Smathers, J.B., Otte, V.A., Smith, A.R., Almond, P.R., Attix, F.H., Spokas, J.J., Quam, W.M. and Goodman, L.J. (1977). Composition of A-150 tissue-equivalent plastic. Med. Phys. 4:74-77.

Thomas, R.H. and V. Perez-Mendez, eds (1980). Advances in Radiation Protection and Dosimetry in Medicine. Plenum Press, New York, 1980.

Thomas, R.H., Lyman, J.T. and Decastro, T.M. (1980). A measurement of the average energy required to create an ion pair in nitrogen by high-energy ions. Radiat. Res. 82:1-12.

Tobias, C.A., Anger, H.O. and Lawrence, J.H. (1952). Radiological use of high energy deuterons and alpha particles. Am. J. Roentgenol. 67:1-27.

Tochilin, E., Goldstein, N. and Lyman, J.T. (1968). The quality and LET dependence of three thermoluminescent dosimeters and their potential use as secondary standards. In: Proceedings of Second International Conference on Luminescence Dosimetry, USAEC and ORNL Conf. 680920 (U.S. Atomic Energy Commission, Washington, D.C.).

Verhey, L.J., Koehler, A.M., McDonald, J.C., Goitein, M., Ma, I-C., Schneider, R.J. and Wagner, M. (1979). The determination of absorbed dose in a proton beam for purposes of charged particle radiation therapy. Radiat. Res. 79:34-54.

von Essen, C.F., Blattmann, H. Crawford, J.F., Fessenden, P., Pedroni, E., Perret, C., Salzmann, M., Shortt, K. and Walden, E. (1982). The Piotron: Initial performance, preparation and experience with pion therapy. Int. J. Rad. Oncol. Biol. Phys. 8:1499-1509.

Williams, J.R. (1980). Problems in neutron dosimetry associated with the incorrect composition of tissue-equivalent gas. Phys. Med. Biol. 25:501-508.

Wilson, R.R. (1964). Radiological use of fast protons. Radiology 47:487-491.

Zaider, M. and Dicello, J.F. (1978). RBEOER: A FORTRAN Program for the Computation of RBEs, and OERs, Survival Ratios, and the Effects of Fractionation Using the Theory of Dual Radiation Action, Los Alamos National Laboratory report LA-7196-MS.

Zirkle, R.E. (1940). Killing of bacteria, mould spores and yeast by α-rays. J. Cell. Comp. Physiol. 16:221.