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HEAVY-ION DOSIMETRY

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INTRODUCTION

A comprehensive and accurate definition of the physical characteristics of a radiation field is a necessary, but not sufficient, condition for understanding (and predicting) the probability of observing a biological effect. Part of the difficulty of doing this stems from the fact that very often the biological final state accessible to observation is the end result of a long sequence of events following the irradiation, when most of the information has been distributed among many degrees of freedom. Demography is not a very good starting point for the study of photosynthesis, yet that is, in essence, what we are often forced to do.

In some cases, the observed effect only depends on average properties of the radiation field, e.g., the absorbed dose. Thus, for example, we are able to predict that 50 percent of the human population exposed to approximately 500 rads of low LET radiation will die. However, even here there are effects that cannot be attributed to dose, and nobody could say for sure what the LD50 of neon ions for humans might be. It is one of our objectives to ensure that experimental data on this topic never come into existence.

Even within its limitations, the concept of absorbed dose represents significant progress, especially if one takes into account an understanding of the actual averaging procedures used in arriving at it, to which Harald Rossi and his colleagues have contributed so much. The measurement of absorbed dose alone is also sufficiently demanding that an entire subfield has sprung

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up around it--the science and art of radiation dosimetry. However, none of us who have an interest in this field are content with simply measuring one quantity when we know, as stated above, that a deeper understanding is required.

Accordingly, this lecture will deal with some of the more important physical characteristics of relativistic heavy ions and their measurement, with beam delivery and beam monitoring, and with conventional radiation dosimetry as used in the operation of the BEVALAC biomedical facility for high energy heavy ions (Lyman and Howard, 1977; BEVALAC, 1977). Even so, we shall not be able to discuss many fundamental aspects of the interaction of relativistic heavy ions with matter, including important atomic physics and radiation chemical considerations, beyond the reminder that such additional understanding is required before an adequate perspective of the problem can be attained.

Heavy ion beams were first accelerated to relativistic energies in the Princeton Particle Accelerator in 1971, following suggestions made by Cornelius Tobias thirty year earlier (Vosburgh, 1973). At present, the only operating facility is the Berkeley BEVALAC, a schematic diagram of which is shown in Fig. 1. The SuperHILAC is a heavy ion linear accelerator, which is operated in a time-shared mode as the injector of the Bevatron, a weak-focusing synchrotron. The BEVALAC has accelerated beams with masses up to iron. Beams are first accelerated to 8.5 MeV/nucleon in the SuperHILAC, then bent into an 800-ft transfer line, where they are transported into the Bevatron for acceleration up to energies of 2 GeV/nucleon. The beams used for biomedical research are carbon, neon, and argon, with energies determined by their desired range in tissue (400 to 500 MeV/nucleon). Dose rates for 20-cm diameter field sizes are typically between 100 and 300 rad/min, but focused beams can be obtained with dose rates of the order of 5000 rad/min. The beam is pulsed, with a frequency dependent on the maximum field strength required for each beam energy, typically at a rate of 15 pulses per minute. The beam has a microscopic time structure (that can be smoothed out upon extraction) of typically 40-70 nsec "buckets" every 400-700 nsec.

The BEVALAC Biomedical Facility is an area specially designated for tumor, tissue, cellular, molecular, neurodevelopmental and space radiobiology, radiography, and radiological physics. The Biomedical Facility has its own control room, three irradiation caves, and two preparation rooms. Figure 2 is a floor plan of the facility, showing two of the irradiation areas. The third irradiation area, known as the "minibeam" cave (because it is intended for use with narrowly focused beams), is on top of the shielding where the beam is

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Fig. 1. Schematic diagram of the BEVALAC high-energy heavy-ion facility.
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Fig. 2. Floor plan of the BEVALAC Biomedical Facility. Reprinted, by permission, from BEVALAC, 1977.

incident at an angle of 30° from below. Cave I is intended for therapy and diagnosis, and has a patient positioner and related equipment (Alonso et al., 1979a). Cave II is intended for physical, chemical, and biological research. The minibeam is intended for neurophysiological studies with radiation, and consists of an electrostatically shielded room.

SOME CHARACTERISTICS OF HEAVY ION BEAMS

Physical characteristics of high energy heavy ions that are of interest in their application to biomedical research are summarized in Table 1 (Tobias, 1973). In practice, these properties are influenced by the following factors:

1. The mean free path for nuclear interactions of heavy ions with energies of therapeutic interest is comparable to their range, as shown in Fig. 3. The calculated curves are based on geometrical cross sections and range-energy tables. For the energies of interest here, it may be seen that approximately two-thirds of the incident primary beam will interact with nuclei in the absorbing material to produce secondary fragments. An experimental Bragg peak, illustrating the geometric dose distribution, is shown in Fig. 4, including calculated contributions due to secondary particles (J. Lyman, private communication).

Table 1. Some Important Characteristics of High Energy Heavy Ion Beams

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1.	Stable particles, i.e., intensity, energy, and beam purity are controlled by accelerator.
2.	Well-defined range in matter, dependent only on initial energy, i.e., minimal straggling.
3.	Reduced multiple scattering which allows the design of sharply defined beams.
4.	Well-defined geometrical pattern of energy loss in matter. For monoenergetic beam, leads to increasing dose as a function of depth, up to a peak region located at a depth dependent on the initial energy, with a sharp fall-off at the distal end of the beam.
5.	High LET, leading to reduced oxygen enhancement ratio and higher biological effectiveness.
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Fig. 3. Mean free path for nuclear interactions of heavy ion

with energies of therapeutic interest compared to their range. Reprinted, by permission, from Schimmerling et al., 1973.

2. Multiple scattering, mainly due to many independent small-angle deflections by Coulomb scattering with the nuclei in the medium, results in beam broadening. This can be used to advantage in the beam flattening schemes discussed below, but constrains the design of collimators and air paths in the beam. Secondary fragments, in addition, will contribute a penumbra due to the combination of their own multiple scattering distribution with the angular distribution resulting from nuclear interactions.

3. The beams produced at accelerators are not mono-energetic. When the beam range is controlled by a variable absorber, the initial energy spread is broadened by straggling. The fact that slower particles lose energy at a higher rate results in a slightly asymmetric energy distribution, especially near the Bragg peak, and a broadening of the peak that depends on the amount of absorber interposed.

4. The finite thickness of ionization chambers commonly used to measure Bragg curves results in a measured peak width determined by the average ionization in the chamber.

Fig. 4. Bragg curve for an unmodified argon beam. Reprinted, by permission, from Lyman and Howard, 1977a.

5. The relative biological effectiveness (RBE) is related to the LET_{∞} as shown in Fig. 5, showing a compilation of results obtained for cells (E. Blakely, private communication). However, many sources of variability still exist, and LET by itself is insufficient to predict biological effects completely.

The inadequacy of LET_{∞} as a predictor of biological effect may be seen more clearly in Fig. 6, showing the inactivation cross sections for human kidney cells irradiated with carbon, neon, and argon beams (Blakely et al., 1979). According to model predictions, the curves should be a function of Z^4/β^4 , where Z is the charge of the ion and β its velocity (in units of the speeds of light, c). In the case of hypoxic cells, the data are, rather, a function of $Z^4/\beta^{4.6}$, indicating a velocity dependence of biological effects not described by LET_{∞} alone. Blakely et al. conclude that the description of the biological effects of heavy ions requires at least three variables, e.g., fluence, velocity, and charge.

Fig. 5. Relative biological effectiveness as a function of LET for a variety of mammalian cells. Courtesy of E. A. Blakely.

The radiation dosimetry of heavy ions thus deals with the situation depicted schematically in Fig. 7 (with apologies to R. Magritte): the beam is delivered to a target site, and must be adequately characterized and monitored in order to provide a well-defined physical input for biomedical evaluation. The primary beam, shown coming from the left, interacts with the components of the beam line used to measure it, and becomes modified by them. The beam and its reaction products then interact with the target and its supporting structures, both directly and indirectly via subsequent scattering.

The incoming beam properties are: the atomic mass, A , and the charge, Z , of its constituents, the fluence, $\phi_0(x,y)$ in the plane perpendicular to the beam, the velocity, β (or energy per nucleon, ϵ), the velocity spread, $\Delta\beta/\beta$ (or energy spread, $\Delta\epsilon/\epsilon$; sometimes a more useful quantity is the momentum spread, $\Delta p/p$), the spatial location of the beam, and the angle the beam makes with the propagation axis, z ($x' = dx/dz$, $y' = dy/dz$).

The material in the beam will consist of beam transport elements (magnets), vacuum windows and air gaps, beam delivery

Fig. 6. Inactivation cross sections for human kidney cells irradiated with carbon, neon, or argon beams. Reprinted, by permission, from Blakely et al., 1979.

devices (collimators, beam flatteners, ridge filters, variable thickness absorbers), and beam monitoring and measurement devices (ionization chambers, wire chambers, scintillation counters). These materials are characterized, in turn, by their density, ρ , their total cross section for nuclear interaction, σ_T (or attenuation length $\lambda = 1/n\sigma_T$, where n is the number of nuclei/cm³), various differential cross sections describing the angular and energy distributions of nuclear interaction secondaries, denoted by $d^2\sigma/d\Omega dE$, their radiation length L_{rad} (a thickness of material relating to multiple scattering), the average ionization potential, I_{ave} , that enters into the stopping power, and their own atomic mass, A_T , and number, Z_T .

Quantities that relate to the interaction of the beam with the material in the beam line are the range, R , which can be scaled to a good approximation as $(AZ^2)R_p$ (R_p = range of a

Fig. 7. Schematic of heavy-ion irradiation arrangement showing the beam and material properties relevant for radiation dosimetry. The integral signs are only used as a mnemonic to denote the thick target attenuation and velocity degradation.

proton with the same velocity) (Schimmerling et al., 1973), and is, as noted, generally also of the order of magnitude of the attenuation length for the energies considered here, the mass stopping power (since thicknesses are more conveniently measured in g/cm^2), $(1/\rho)(dE/dx)$, which also can be scaled to a good approximation as (Z^2/B^2) with respect to the stopping power of heavy ions with different charge (the logarithmic term in the stopping power formula varies slowly), and the "dose," $D = \phi \cdot dE/dx$. The latter is an approximation to the absorbed dose, since $dE/dx \equiv LET$, and the existence of charged particle equilibrium cannot always be established.

Finally, the actual beam incident on the target may consist of varying contributions of secondaries, with atomic number Z , $Z-1$, $Z-2$, etc., (experimentally, pickup reactions leading to fragments with $Z+1$, or $4+1$, etc., are not observed, and are not favored kinematically). For each of these species, isotopes with mass A , $A-1$, $A-2$, etc., may also be assumed to exist, and the observed flux and velocity distributions will be the integrated

result of all the interactions. In practice, these contribute a small, but not negligible, amount of the actual delivered dose.

BEAM DELIVERY AND SPATIAL DISTRIBUTION

Beam energies at the BEVALAC Biomedical Facility are selected by specifying certain fixed maximum ranges adequate for research and clinical work (Lyman and Howard, 1977; Alonso et al., 1979a, 1979b). The values used most often are listed in Table 2 (BEVALAC, 1977). The restriction to a fixed set of energies is of considerable practical importance in order to obtain reproducible beam line tunes easily, limiting the number of necessary ridge filters, and allowing intercomparison of data obtained in standard beam configurations.

Table 2. Commonly Used Beams at the BEVALAC Biomedical Facility.

Ion	Nominal Energy (MeV/amu)	Rate (particle/pulse; rad/min)	Range to Bragg Peak (cm)
${}^4_2\text{He}$ (Kevatron)	225	3×10^8 to 1×10^9 p/pulse 10 to 50 rad/min	30.4
${}^{12}_5\text{C}$ (Bevatron)	400	5×10^7 to 2×10^8 p/pulse 20 to 80 rad/min	25.9
${}^{12}_6\text{C}$ (BEVALAC)	400	5×10^8 to 2×10^9 p/pulse 350 to 1500 rad/min	25.9
${}^{20}_{10}\text{Ne}$ (BEVALAC)	400	2×10^8 to 1×10^9 p/pulse 250 to 1200 rad/min	14.6
${}^{40}_{18}\text{Ar}$ (BEVALAC)	500	2×10^7 to 5×10^7 p/pulse 200 to 500 rad/min	12.3

Circulating beam in the Bevatron is extracted by means of a resonant extraction system, and provides a "spill" length of up to 1500 msec per Bevatron pulse. Shorter spill can be provided without RF structure. The beam size at the object focus F1 is about 3 cm high, and may be reduced by collimation. The energy spread of the extracted beam is approximately 0.3 percent (BEVALAC, 1977).

The residual range of the primary beam energy can be reduced, in order to accommodate the requirements of different irradiations, by inserting an absorber in the beam. A variable absorber is used to meet these varying requirements. Figure 8 shows a schematic diagram of the 15-cm diameter variable water column used at the BEVALAC Biomedical Facility. The maximum depth is 30 cm of water, variable by computer or manual control. The minimum thickness is the 0.6 cm of the lucite windows. The window is moved by a piston driven by a stepping motor, and is read out to $0.1 \text{ mm} \pm 1 \text{ digit}$.

Another possible design, used for the minibeam area (Schimmerling et al., 1977a), is shown in Fig. 9. This design is based on a double wedge, with some advantages due to its simplicity, lower cost, faster response, and easy exchange of

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Fig. 8. Diagram of variable water absorber. Reprinted, by permission, from BEVALAC, 1977.

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Fig. 9. A double-wedge variable absorber. Reprinted, by permission, from Schimmerling et al., 1977a.

absorber material. Its disadvantages are the limited dynamic range, due to the minimum thickness required in the thinner wedge, and the maximum practical dimensions of the larger wedge. A double wedge is, of course, necessary in order to present a constant thickness surface to the finite beam spot. It is possible, and often necessary, to obtain a dose distribution in the target volume (e.g., a tumor region) that differs from that shown in Fig. 4. Such a distribution may be synthesized by shifting the range of the particles in a time short compared with that of the irradiation. The desired dose distribution in the target volume will then be the time-averaged superposition of Bragg curves of the type shown in Fig. 4.

There are several means of accomplishing this goal. For example, Tobias (private communication) has suggested the use of a wedge, performing a programmed motion under computer control, to obtain the desired dose distribution curve, since the faster response of this type of variable absorber is required for implementing the concept. At the present time, prescribed dose distributions are achieved with the use of spiral ridge filters, a photograph of which is shown in Fig. 10. These consist of a brass plate with a precisely machined spiral groove. The exact shape and depth of the groove determine the form of the spread Bragg curve.

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Fig. 10. A spiral ridge filter. Reprinted by permission, from BEVALAC, 1977.

Examples of such spread Bragg curves are shown in Fig. 11 for carbon, neon, and argon beams with "short" ($\sim 15 \text{ g/cm}^2$) and "long" ($\sim 25 \text{ g/cm}^2$) ranges, and for "narrow" (4 g/cm^2) and "broad" (10 g/cm^2) spreads. The shape of these curves is not flat (isodose), but falls off at the distal end to compensate for the greater RBE, and to yield a constant biological effect (isoeffect criterion). It should be noted that RBE is a function of the biological end point, and therefore the ridge filter will not result in isoeffect curves for different end points (i.e., cell-survival level). As may be evident from Fig. 6, this is true a fortiori for aerated and hypoxic cells—an isoeffect curve for one will not in general be an isoeffect curve for the other.

The spiral ridge has a "dead spot" at the center, where the groove cut ends. For radiobiology experiments, which in general do not require very large beam spots, this problem is circumvented by positioning the filter off-axis from the beam. This is not possible for the large beam spots used in therapy, and the dead region is blocked out by the second scatterer of the beam flattening system described below.

In addition to obtaining a prescribed dose distribution in depth, it is also necessary to define the lateral distribution of the beam. In practice, the simplest way of accomplishing this is by generating a uniform transverse distribution and shaping it to the final contours with collimators. The lateral spreading of the beam into a uniform field is done with the scattering-foil occluding ring system developed at Harvard (Koehler et al., 1977), and at the Berkeley 184-inch Synchrocyclotron (Crowe, 1975). A lead foil, typically 0.6-cm thick, located 10 m upstream of the target volume, scatters the beam into a symmetric Gaussian distribution. A second scatterer, consisting of the ridge filter, an additional 4-mm brass plate, a central brass cylinder, and a concentric brass ring, is positioned approximately 4 m downstream of the first scatterer. The central brass cylinder and the concentric ring block out the central region and an eccentric portion of the Gaussian distribution. The brass plate on the filter acts as a diffuser, filling in the blocked-out regions, so that, after traversing the path to the target, the beam profile is completely flat with an intensity variation of no more than 2 percent over the entire 20-cm diameter field. Approximately 40 percent of the original beam intensity lies within this field, thus providing better beam utilization than would be possible by blowing up the beam size and selecting a uniform central region with collimators. A photograph of the assembled ridge filter with occluding rings is shown in Fig. 12.

Operation of this system requires great alignment accuracy, and several alternatives are under study and development. One

Fig. 11. Bragg curves spread with a ridge filter for different incident beam energies and filter range. Reprinted, by permission, from, Lyman and Howard, 1977a.

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Fig. 12. A spiral ridge filter covered with an occluding ring. Reprinted, by permission, from Lyman and Howard, 1977a.

such an alternative is the use of a beam "wobbler," shown schematically in Fig. 13 (Alonso, private communication). The device consists of a rotating dipole field, provided by a stationary sextupole magnet, which sweeps the beam in a circular pattern to fill in a ring-shaped region, and is turned off to fill in the central region. Further development will ultimately lead to a full three-dimensional, computer-controlled scanning system, receiving its input from treatment-planning and CT

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Fig. 13. Beam delivery wobbler system. Courtesy of J. Alonso.

scanning computers. A prototype scanning magnet and power supply have already been constructed. A schematic diagram of the concept is shown in Fig. 14.

Verification of the beam flatness can be accomplished approximately with the concentric-ring ionization chambers described below. For greater accuracy, exposed photographic emulsions and densitometry scans had to be used until recently. This involved six to eight exposures covering a dose range of 1:100, so that a dose vs. film density calibration was obtained simultaneously.

This procedure is time-consuming and cumbersome, and has led to the development of a multiwire, multiplane proportional chamber for reconstruction of beam profiles. The instrument, called MEDUSA (Alonso et al., 1979b), integrates the charge collected from a single beam pulse on capacitors connected to each of the 64 signal wires in each of the 16 planes. The planes are rotated at equal intervals around 180° , perpendicular to the beam. The integrated charge profile from each plane constitutes a projection of the beam intensity (but not of dose!). The beam profile is reconstructed from the 16 different projections, using algorithms developed for CT scanning. Ultimately, reconstruction is expected to take 2 seconds, sufficient to

Fig. 14. Schematic depiction of a three-dimensional scanning method. Reprinted, by permission, from Lawrence Berkeley Laboratory Report LBL-7230.

enable interactive beam tuning. Accuracy of the device is expected to be better than 0.5 percent intensity resolution. A photograph of the assembled chamber is shown in Fig. 15, and a reconstructed beam profile is shown in Fig. 16. The beam profile was obtained with a copper bar and lead brick placed in front of the chamber. The sharpness of the edges is a good indication of the spatial resolution of the instrument (10 percent to 90 percent in 3 pixels) and its ability to reconstruct asymmetric patterns.

DOSIMETRY

It must be emphasized that dosimetry serves both a predictive and an archival function. It is as important to know the physical characteristics of beams that will be delivered as it is important to know the characteristics of beams that have been delivered. Most of the methods described in this section are

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Fig. 15. MEDUSA chamber. Reprinted, by permission, from Alonso et al., 1977b.

used for beam verification. Instruments used for routine operation at the BEVALAC presently measure dose intensity distributions. Microdosimetric measurements have been made, and are described in other lectures of this course. Other studies of beam quality will be discussed below.

The most useful monitor for the heavy ion beams is a parallel plate ionization chamber. The basic ionization chamber used in biomedical dosimetry at the BEVALAC (1977) consists of three foils mounted on insulating frames in a gas-tight aluminum

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Fig. 16. Reconstruction of a radiation field obstructed by a rectangular metallic absorber after smoothing the raw data. Reprinted, by permission, from Alonso et al., 1977b.

housing, as shown in Fig. 17. The three foils are a quadrant foil, a high voltage foil, and a concentric, ringed foil. The foils are constructed of thin plastic membranes and gold plated on both sides in the appropriate pattern. The charge collected by the various electrodes is integrated and measured by linear, seven-decade voltage-to-frequency converters.

The signals from diametrically opposed quadrants in the quadrant foil can be added and modulated with a sine-wave generator. When the resultant signals are applied to the x- and y-sweeps of an oscilloscope, the resultant Lissajous pattern is a circle or ellipse with semi-axes or radius proportional to the beam intensity, centered on a location that can be referred to the beam position. In this way, a continuous indication of relative intensity and position is obtained.

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Fig. 17. Ionization chamber foils. Reprinted, by permission, from BEVALAC, 1977.

The ringed foil allows monitoring of the dose as a function of radial distance from the beam axis (Lyman et al., 1975) as well as a measurement of total dose (when the beam spot is smaller than the active area of the chamber). A photograph of the disassembled chamber is shown in Fig. 18.

Figure 19 shows a scale drawing of the ionization chamber used in Princeton (Schimmerling et al., 1976). This chamber is similar in geometry, and does not feature multiple electrodes. Emphasis in this design was placed on eliminating the use of adhesives that could contaminate the filling gas with organic vapors. Also noteworthy in this design are the provisions for vacuum baking for initial cleanup, and the pierced foils at each end of the chamber, used for damping microphonic noise, to which this type of instrument is extremely susceptible.

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Fig. 18. Disassembled components of the ionization chamber used in the LBL Biomedical facility (drawn schematically in Fig. 17. Reprinted, by permission, from BEVALAC, 1977.

The Berkeley chamber is flushed with dry nitrogen gas, while the Princeton chamber used argon. The choice of filling gas is determined by the desire to have a well-defined material as well as by the advisability of using the chambers in the electron collection mode. The latter, especially, is important in order to deal with the high ionization of heavy ions, and to collect the produced charges in a time which is short relative to recombination lifetimes. Nitrogen and argon have low electron

Fig. 19. Scale drawing of the ionization chamber used at Princeton. Reprinted, by permission, from Schimmerling et al., 1976.

affinities, and are useful for this reason. When ionization chambers, such as the one shown in Fig. 19, are used in pulse mode, it is further important to minimize electron collection times to ensure proper linearity (collection of all the produced charge) and maximize counting rates. In that case, propane and methane give the highest electron mobilities and are the filling gas of choice. Tissue-equivalent gases that have the same electron density as muscle tissue are also used in order to avoid errors introduced by the calculation of absorbed dose in tissue from the measured ionization.

The measured charge, or ionization, in the chamber can be related to the energy loss in the chamber and, hence, to the absorbed dose, if the average energy required to produce one ion pair, W , is known. This quantity is not easily calculated in an accurate form (Myers, 1968), and has become the object of revived theoretical and experimental interest (Dennis, 1972; ICRU, 1979) in the light of its importance for charged particle dosimetry.

The experimental determination of W requires an independent measurement of beam intensity in order to determine the average ionization per incident beam particle. W in argon was determined (Schimmerling et al., 1976) for nitrogen ions of 520 MeV/u by using carbon activation detectors to monitor the beam passing through the ionization chamber, based on the measured $^{12}\text{C}(^{14}\text{N}, x)^{11}\text{C}$ cross section (Skoski et al., 1973). The value of W obtained, 26.2 ± 1.8 eV/i.p., was in good agreement with the value of 26.3 ± 0.1 for alpha particles in argon (Myers, 1968). Stephens et al. (1976) have used thermoluminescent dosimeters to measure the fluence of 250 MeV/A carbon ions, and obtained a value of 36.6 ± 0.7 eV/i.p. for W in the nitrogen gas used at the BEVALAC. Subsequent measurements report values of 35.3 ± 1.5 eV/i.p. for neon at 375 MeV/A and 34.6 ± 1.4 eV/i.p. for 429 MeV/A argon ions in nitrogen (Thomas et al., 1978). The difference between these values is not statistically significant, and the authors of this work conclude that the average value of $W = 35.2 \pm 0.9$ eV/i.p. in nitrogen may be taken as the best value presently available, independently of particle charge or velocity. This is to be compared with the value of $W = 34.9$ eV/i.p. used for routine BEVALAC operations (1977).

All these measurements rely upon a two-step procedure to establish the absolute beam fluence. In a first step, the method is calibrated at low intensities, where the signal-to-noise ratio in ionization chambers operated in the current mode is too small for reliable comparison. In this mode scintillation counters (Schimmerling et al., 1976) or nuclear emulsions (Skoski et al., 1973; Stephens et al., 1976), can be used for absolute counting. The second step, at intensities within the operational range of the ionization chamber, compares the secondary standard (activation foils, thermoluminescent dosimeters, etc) with the ionization current. Figure 20 shows the typical efficiency of thermoluminescent detectors relative to ^{60}Co gamma rays and comparison with some theoretical models (Patrick et al., 1976).

It is possible to circumvent this two-step procedure by using the ionization chamber in a pulse mode (Epstein et al., 1971) and counting beam particles directly. This is done in the fragment dose experiments described below. Preliminary measurements (Schimmerling et al., unpublished results) show agreement between the value obtained for 525 MeV/A argon ions in propane and the value calculated using Bragg's rule, $W = 29.6$ eV/i.p. Similarly, measurements by Goodman and Colvett (1977) have shown that the value of W for argon ions in air and TE gas is not significantly different from that obtained with a ^{137}Cs source. It seems safe to conclude that, except perhaps for a narrow region beyond the Bragg peak where the velocity of the heavy ions becomes comparable with that of orbital electrons, W values of heavy

Fig. 20. Efficiency of thermoluminescent detectors relative to ^{60}Co . Reprinted, by permission, from Lawrence Berkeley Laboratory Report LBL 6710.

ions differ by less than 5 percent from those of lighter charged particles.

The accuracy of absolute dosimetry is dependent upon W , a knowledge of the stopping power, the dimensions of the ionization chamber, and the method of charge collection. The accuracy of W measurements is, as we have seen, not much better than 5 percent. Stopping power cannot be calculated to an accuracy better than a few percent at the present time, and experimental measurements are also not more accurate, for the energies and ions considered here. Improvements in these accuracies would require quite sophisticated and fastidious experiments. Thus, the accuracy of absolute physical dose determinations cannot be assumed to be better than 5 to 10 percent.

Fortunately, evaluations of the merits of radiation therapy rely on relative observations and reproducibility of dose measurements can be attained at the few percent level or better, as evidenced by preliminary results of recent intercomparisons. These comparisons utilized 1 cm^3 tissue-equivalent ionization chambers to eliminate sensitivity to field shapes, and referred the measurements to ^{60}Co doses. This work is being performed

under the auspices of the Charged Particle Dosimetry Group (CPPDG) of the American Association of Physicists in Medicine.

Figure 21 shows the complete panoply of instrumentation used for routine high-energy heavy ion dosimetry at the BEVALAC, mounted on a standard alignment bench. The beam is incident from the left, and the instruments in the beam path, from left to right, are: collimator, upstream ionization chamber (for intensity normalization), scintillators, collimator, spiral ridge filter, variable water absorber, aperture holder, downstream ionization chamber, remote control sample translator, EG and G TE ionization chamber, alignment pointer, cross hairs and x-ray tube.

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Fig. 21. The instrumentation used for radiation dosimetry at the BEVALAC Biomedical Facility. Shown from left to right: brass collimator, upstream ionization chamber, collimator, spiral ridge filter, variable thickness water absorber, aperture holder, downstream ionization chamber, remote control sample translator, EG and G TE ionization chamber, alignment pointer, cross hairs and x-ray tube, and a utility fixture with a custom-poured collimator. Reprinted, by permission, from BEVALAC, 1977.

also used for alignment, and a utility fixture with a custom-poured collimator. The alignment bench for the minibeam is shown in Fig. 22, showing the double wedge, ionization chambers, and a microscope system to be used for on-line studies of cell function. The microscope is equipped with remote handling facilities, as well as a movie camera and a videotape unit for time-lapse photography. The television monitor in the figure displays a culture of neuroblastoma cells being used by T.C.H. Yang of LBL for preliminary studies.

The dose measured by the ionization chamber behind the water column is related to the absorbed dose in samples behind the ionization chamber by a displacement correction to account for the material between the sample and the chamber (measured with

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Fig. 22. Photograph of alignment bench used in BEVALAC minibeam. Shown from left to right are: upstream ionization chamber of the type shown in Fig. 19, double wedge, downstream ionization chamber, beam spot film holder, and microscope system. Reprinted, by permission from Schimmerling et al., 1977a.

the water column) and by the ratio of stopping powers in the material and the chamber gas. This procedure has been validated by Goodman and Colvett (1977) who concluded that the depth-dose distributions measured for high-energy argon ions in a water phantom and in a tissue equivalent liquid were essentially the same, after taking into account the difference in electron densities between the two liquids, at the 5 percent level. Similarly, the depth-dose distribution measured behind the water absorber was equivalent to that measured inside a water phantom. Finally, the results showed no significant difference between dosimetry in air and in tissue-equivalent gas in the cavity of a tissue-equivalent ionization chamber.

NUCLEAR INTERACTIONS AND BEAM QUALITY

As discussed in the Introduction, the mean free path of the heavy ion beams used for biomedical applications is comparable to their range. Thus, secondary and, possibly, subsequent generations of nuclear interaction products can be expected to make a significant contribution to the dose, especially in the vicinity of the Bragg peak and in the spread depth dose distribution. For the purposes of therapy planning, of course, it must be remembered that nuclear interaction products will constitute 100 percent of the exit dose. In addition, it has been shown that biological effect depends not only on the LET, but possibly on the charge and velocity in different ways. Thus, one approach to characterizing high-energy heavy-ion beams in a manner that would eliminate uncertainties about their physical characteristics from the radiobiological evaluation, is the measurement of velocity and ionization spectra for identified fragments as a function of depth.

Preliminary measurements, using only velocity spectra, showed that the present state of knowledge about fragmentation cross sections and their dependence on the incident particle energy is insufficient to permit accurate predictions (Schimmerling et al., 1977b). Estimated cross sections for fragments produced in the interaction of 251 MeV/u nitrogen ions on carbon, based on the semi-empirical model of Silberberg and Tsao (1973) and calculated as described by Schimmerling et al. (1977b), are shown in Fig. 23. These cross sections are generally in agreement with experimental data at the 20-30 percent level down to energies of 150 MeV/u. Data between 20 MeV/u and 100 to 200 MeV/u are unavailable at present. Such data are required for every element in tissue, or must be calculated by a scaling procedure. In addition, the angular distributions and energy spectra, as well

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Fig. 23. Cross sections for producing fragments from the interaction of nitrogen ions with a carbon target, as a function of velocity, estimated from the semi-empirical model of Silberberg and Tsao (1973). Reprinted, by permission from Schimmerling et al., 1977b.

as the multiplicities of light particles (neutrons, protons), must be known for an accurate calculation. Few such data are at present available.

Nuclear physics experiments provide data that are useful for biomedical purposes only after incorporation into cumbersome transport calculations of limited accuracy. Therefore, the approach of obtaining such data directly is currently being pursued at the BEVALAC. Preliminary results (Schimmerling et al., unpublished data), were obtained with the arrangement shown in Fig. 24. R is a variable thickness absorber. The detector consists of a multiwire proportional chamber to measure particle position, a channel plate time-of-flight telescope with a resolution of about 100 picoseconds (Gabor et al., 1975) (corresponding to an energy resolution of about 0.1 percent at low energies), and a pulse ionization chamber for single particle ionization measurements. S_0 , S_1 , and S_2 are scintillation detectors used to monitor the beam intensity and to impose a range requirement: a signal in all detectors except S_2 indicates that the particle stopped somewhere between S_1 and S_2 , and gives a measurement of its range. A photograph of the experimental setup is shown in Fig. 25.

Fig. 24. Schematic diagram of instrumental arrangement used for element identification of fragments emerging from a thick absorber R. S_0 , scintillator; $M(x,y)$, wire chamber; C_1 and C_2 foils of a channel plate time-of-flight spectrometer; IC , pulse ionization chamber; S_1 and S_2 , range discrimination scintillators.

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Fig. 25. Photograph of experimental arrangement shown in Fig. 24. The long pipe contains the time-of-flight spectrometer and is connected to a high-vacuum pumping system. The beam is incident from the left.

The purpose of this arrangement was to build an ionization-sensitive particle identifier with minimum mass, in order to separate the secondary particles close to the Bragg curve. The charge resolution of the ionization chamber is limited by the statistical distribution of energy losses. This "Landau tail" (Rossi, 1952) is, however, limited in a thin ionization chamber because very energetic electrons (delta rays) can only deposit a small fraction of their energy in the chamber (Epstein et al., 1971). In this sense, the ionization chamber is a "restricted energy loss detector," and its charge resolution, approximately 7 percent, is much better than would be predicted without this consideration. The counting rate of the chamber is limited by the collection time for the electrons ($\sim 3 \mu\text{sec}$). Even though this is much slower than, e.g., thin plastic scintillators, the pronounced saturation effects of these place them at a disadvantage with respect to ionization chambers in applications to

Fig. 26. Example of the saturation in scintillator output.
Reprinted, by permission, from Kidd et al., 1979.

heavy-ion dosimetry. Figure 26 shows an example of the saturation in scintillator output (Kidd et al., 1979). In experiments being set up at this time, a solid-state detector telescope (Greiner, 1972), with isotopic resolution of the order of 0.2 amu, will be used in conjunction with this apparatus.

A typical time-of-flight spectrum of 525 MeV/A argon beam, near the end of the argon range, is shown in Fig. 27. Velocity increases from right to left, with the slowest particles having the longest flight time (corresponding to the higher channels). The residual peak of argon can still be seen, as well as the substantial flux of secondary particles, mixed in the distribution to the left of argon.

Ionization pulse height spectra at a depth of 12.5 g/cm² of Lucite for an incident 525 MeV/A argon beam are shown in Fig. 28. Cuts on the data were made using the known charge resolution of the ionization chamber and the calculated velocity-ionization profile of argon in the detector. The lower left panel shows the ionization pulse height spectrum without any

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Fig. 27. Time-of-flight spectrum of 525 MeV/nucleon argon ions after traversing 12.5 g/cm² of Lucile. Time increases from left to right, and velocity correspondingly decreases from left to right.

cuts. The upper right hand panel shows the distribution of all secondary particles (corresponding to the region left of the argon peak in Fig. 27). The charge resolution is rather poor, but some structure seems evident and should be resolved in future work. Finally, the ionization spectrum for particles identified as argon is shown in the lower right hand panel of Fig. 28. The average ionization can be obtained from spectra such as this, and plotted as a function of absorber thickness to obtain the separated depth-dose curve for argon shown in Fig. 29.

Near the peak (at 14.6 g/cm²) in Fig. 29, the data are adequate to provide a crude estimate of the effect of secondaries on the dose distribution of argon. Assuming that lower-Z particles have a mean charge of $Z = 15$, and using the measured mean velocity, the estimated contribution of lower-Z secondaries to the dose is 23 percent, at an average LET_∞ of 130 keV/μm. The

Fig. 28. Ionization pulse height spectra at the exit of 12.5 g/cm^2 of Lucite for a 525 MeV/nucleon incident argon beam.

primary argon is estimated to contribute 39 percent of the dose at this point, at an LET_w of $323 \text{ keV}/\mu\text{m}$. Lighter isotopes of argon (e.g., $^{38,39}\text{Ar}$) and chlorine (e.g., ^{35}Cl) begin to stop in this region, and can be identified with the range requirement. Their contribution to the dose can be estimated as being 37%, and their average LET_w can be estimated to be approximately $490 \text{ keV}/\mu\text{m}$. The apparatus used in these experiments did not allow clear identification of the particles in the peak region itself, where they are considerably smeared in both ionization and velocity. The relative contributions of fragments can be expected to vary rapidly in this region, and it is expected that work currently in progress will yield important information about these phenomena, especially in the spread, depth-dose curve. With these data, calculation of any desired measure of beam quality, for any beam configuration, should become practical. Some of the problems that become accessible to study are discussed by Curtis (1977).

Fig. 29. Separated Bragg curve for 525 MeV/nucleon argon ions.

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