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FOREWORD

This series of books on Radiotracers in Biology and Medicine is on the one hand an unbelievably expansive enterprise and on the other hand, a most noble one as well. Tools to probe biology have developed at an accelerating rate. Hevesy pioneered the application of radioisotopes to the study of chemical processes, and since that time, radioisotopic methodology has probably contributed as much as any other methodology to the analysis of the fine structure of biologic systems. Radioisotopic methodologies represent powerful tools for the determination of virtually any process of biologic interest. It should not be surprising, therefore, that any effort to encompass all aspects of radiotracer methodology is both desirable in the extreme and doomed to at least some degree of inherent failure. The current series is assuredly a success relative to the breadth of topics which range from in depth treatise of fundamental science or abstract concepts to detailed and specific applications, such as those in medicine or even to the extreme of the methodology for sacrifice of animals as part of a radiotracer distribution study. The list of contributors is as impressive as is the task, so that one can be optimistic that the endeavor is likely to be as successful as efforts of this type can be expected to be. The prospects are further enhanced by the unbounded energy of the coordinating editor. The profligate expansion of application of radioisotopic methods relate to their inherent and exquisite sensitivity, ease of quantitation, specificity, and comparative simplicity, especially with modern instrumentation and reagents, both of which are now readily and universally available. It is now possible to make biological measurements which were otherwise difficult or impossible. These measurements allow us to begin to understand processes in depth in their unaltered state so that radioisotope methodology has proved to be a powerful probe for insight into the function and perturbations of the fine structure of biologic systems. Radioisotopic methodology has provided virtually all of the information now known about the physiology and pathophysiology of several organ systems and has been used abundantly for the development of information on every organ system and kinetic pathway in the plant and animal kingdoms. We all instinctively turn to the thyroid gland and its homeostatic interrelationships as an example, and an early one at that, of the use of radioactive tracers to elaborate normal and abnormal physiology and biochemistry, but this is but one of many suitable examples. Nor is the thyroid unique in the appreciation that a very major and important residua of diagnostic and therapeutic methods of clinical importance result from an even larger number of procedures used earlier for investigative purposes and, in some instances, procedures used earlier for investigative purposes and, in some instances, advocated for clinical use. The very ease and power of radioisotopic methodology tempts one to use these techniques without sufficient knowledge, preparation or care and with the potential for resulting disastrous misinformation. There are notable research and clinical illustrations of this problem, which serve to emphasize the importance of texts such as these to which one can turn for guidance in the proper use of these powerful methods. Radioisotopic methodology has already demonstrated its potential for opening new vistas in science and medicine. This series of texts, extensive though they be, yet must be incomplete in some respects. Multiple authorship always entails the danger of nonuniformity of quality, but the quality of authorship herein assembled makes this likely to be minimal. In any event, this series undoubtedly will serve an important role in the continued application of radioisotopic methodology to the exciting and unending, yet answerable, questions in science and medicine!

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Dr. Colombetti graduated from the Litoral University in his native Argentina with a Doctor in Sciences degree (summa cum laude), and obtained two fellowships for postgraduate studies from the Georgetown University in Washington, D.C., and from the M.I.T. in Cambridge, Mass. He has published more than 150 scientific papers and is the author of several book chapters. He has presented over 300 lectures both at meetings held in the U.S. and abroad. He organized the First International Symposium on Radiopharmacology, held in Innsbruck, Austria, in May 1978. He also organized the Second International Symposium on Radiopharmacology which took place in Chicago in September, 1981, with the active participation of more than 500 scientists, representing over 30 countries. He is a founding member of the International Association of Radiopharmacology, a nonprofit organization, which congregates scientists from many disciplines interested in the biological applications of radiotracers. He was its first President (1979/1981).

Dr. Colombetti is a member of various scientific societies, including the Society of Nuclear Medicine (U.S.) and the Gesellschaft für Nuclearmedizin (Europe), and is an honorary member of the Mexican Society of Nuclear Medicine. He is also a member of the Society of Experimental Medicine and Biology, the Coblenz Society, and the Sigma Xi. He is a member of the editorial boards of the journals Nuklearmedizin and Research in Clinic and Laboratory.
PREFACE

In many ways radiation biology cannot be considered a study unto itself. Exposure to ionizing radiations in particular, produces no unique effects. Rather, its action is to increase the frequency of occurrence of a wide variety of phenomena that naturally occur in living populations. Consequently, radiation biology is simply the study of natural phenomena—heightened in incidence by irradiation. It is an immense, diffuse discipline, far too large to be placed between two covers.

This book, then, which calls itself, Radiation Biology, is much less than that. For example, not all radiations are considered, only ionizing radiations. Also, most, though not all, the essays restrict their remarks to mammalian cells, tissues and organs, leaving out nearly all the animal kingdom and, practically speaking, all the plants.

Even so, the title, Radiation Biology, may not be so wide of the mark, for the effects of ionizing radiations (at least) are considered on many of the fundamental life processes; cell replication, transmission of genetic material, mutation, reproduction and development as well as on functions depending on intercellular relationships, tissue and organ functions, and immune response.

The book was not planned as a primer, but for advanced biology students. It includes an essay on physics basic to understanding interactions of ionizing radiations and living matter, but little basic biology.

No effort was made to achieve uniformity of style or form of exposition among the various essays. Each contributor is an expert in his or her discipline, and it was felt best to permit each to tell his or her story in the way that best suited them. The assumption was that their theme development and language is the result of many hours of intense thought and research and would be hard to improve upon — and — in any case, variety among essays can only be refreshing to the reader.

The editor considered it his function to cull out inevitable repetition that occurs when a number of authors separately consider related topics, to correct occasional lapses in English and the even more occasional error of fact that he was capable of noticing. There is, nevertheless, some repetition and overlap, but this is deliberate. Repition, per se, is not necessarily bad and where it served as reinforcement or a convenience to the reader, it remained. Doubtless, there also remain lapses in English and errors in fact. This proves only the fallibility of even the most careful scrutiny and effort of both author and editor.

The book may be used as a text and read from cover to cover. However, the intention was that each essay would stand alone as well. To an extent all lean on the physics chapter and, of course, the reading of the essays in sequence enhances understandings of each of them.

The book has several unusual features. The long essay by Wolsky is an attempt to explain effects of irradiation on developmental processes rather than, as in the usual case, on development alone. Grdina’s essay describes an exciting new technique and its power to extract information. There is a section about at least one application of radiation biology—that to various branches of medicine. This is included so that students can read and appreciate how facts learned in the laboratory can be put to work and how much remains to be learned to be pressed into the service of humankind.

There are gaps. An essay on sensitizers and protectors, normal tissue models and regeneration and repopulation are desirable. However, none could be obtained without waiting so long that material in hand would become seriously outdated. Even with these gaps, this is a strong book, one that makes an important contribution to the teaching and reference literature.

Lelio G. Colombetti
Donald J. Pizzarello
THE EDITOR

Donald J. Pizzarello is Professor of Radiology at New York University Medical Center in New York City. He is the author of numerous research reports and co-author of three books, Basic Radiation Biology, which is going into its third edition, Medical Radiation Biology, going into its second edition and Concepts in Cancer Care, which appeared in mid-1980.

He is much in demand as a lecturer, having served as Visiting Professor in medical centers in nearly all parts of North America, most frequently discussing presumed hazards of exposure to low doses of ionizing radiations. In addition to these professional audiences, Dr. Pizzarello frequently addresses lay groups concerned, generally, about current and future exposure of human beings to artificial sources of ionizing radiations.

Aside from the foregoing, Dr. Pizzarello regards himself as an ordinary fellow who loves his family; music; literature; good food, drink and conversation; despises all physical exercise (except swimming, which he thinks of as a form of lying down) and excessively hot weather.
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Section I
Basic Radiation Biology
# Chapter 1

## BASIC PHYSICS

Robert J. Barish

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I. INTRODUCTION

A. Matter and Energy

Our concepts of energy and matter have undergone a considerable evolution in this century. The theory of quantum chromodynamics predicts the existence of hundreds of subatomic particles, many of which have already been observed in high energy physics experiments. To understand the physics of radiobiology, however, we can be content with one of the earlier atomic models where there are only three fundamental particles. In this model, electrons swing in orbits around a nucleus which is composed of protons and neutrons.

B. Atomic Structure

Each atom consists of a nucleus containing protons and neutrons, and orbital electrons which surround it. The electrons exist in orbits with discrete energy levels whose values are quantized; i.e., they can take only these energy values and not any in-between. This concept was first proposed, and its consequences worked out, by Bohr in 1913. He assumed that electrons could make a transition from one energy level to another and that the transition would correspond to the absorption or emission of radiation whose quantum energy would be equal to the difference in energy of the two levels.

The electrons can be thought of as occupying “shells” which are identified by the letters K, L, M, ..., successively as one gets farther from the nucleus. The electrons in the inner shells are more tightly bound to the atom than those in the outer shells. This model accounts for the observation of such phenomena as the line spectra emitted when a material is excited in an electric spark. The wavelength of the emitted light corresponds to the energy difference between the electron shells. Some electrons are raised to higher orbits and the observed spectrum is created as they jump back to their normal orbits. By supplying enough energy, an electron can be liberated completely from the atom thus creating a positively charged atom or molecule and a free electron, each of which may interact with its surroundings. In most cases, the free electron will soon attach itself to a neutral molecule to form a negative ion so that the net result is an “ion pair”. The capture of another electron by the positively charged atom or molecule will often lead to the release of energy in the form of a single “bundle” — a photon. Alternatively it may lead to the breakup of the molecule; i.e., to chemical change.

C. Mass Energy Equivalence

The mass of an atom is less than the combined masses of the component parts — neutrons, protons, and electrons — which make it up. The difference is accounted for by the binding energy holding the parts together, quantified by Einstein’s famous relationship of equivalence between mass and energy, \( E = mc^2 \). If \( \delta m \) is the decrease in
mass when a number of neutrons, protons and electrons combine to form an atom, \( E = \Delta m c^2 \) is released in the process. This same amount of energy would be required to break the atom into its constituents. Mass and energy are not measured in the same units but a direct conversion is possible using the Einstein formula. For example, if an electron could be completely converted into energy, the energy would be:

\[
E = (9.11 \times 10^{-31} \text{kg})(3 \times 10^8 \text{ m sec}^{-1})^2 = 8.2 \times 10^{14} \text{J} \quad (1)
\]

A special energy unit, the electron volt (eV), has long been used in radiological physics although it is not part of the S.I. system* (1 eV = 1.6 \times 10^{-19} \text{ J}). \( E \) in Equation 1 is therefore 5.1 \times 10^5 \text{ eV} or 510 keV. Thus 510 keV of energy could conceivably be converted into the mass of one electron, a phenomenon that happens in certain interactions of radiation with matter.

Radiation may broadly be divided into two types — particulate in which the individual energy carriers have mass and may be electrically charged, and electromagnetic where the energy carriers are photons which have no charge and have zero mass.

D. Electromagnetic Radiation

Many familiar physical manifestations such as light, radio waves, and radar are examples of electromagnetic radiation. X-rays and gamma rays are also in this category. Their names are associated with their means of production. X-rays arise from electron transitions in the inner shells of atoms or from the deceleration of charged particles in matter. Gamma rays are associated with the release of energy from the atomic nucleus. The physical properties of electromagnetic radiation can be fully explained only if these radiations are considered to have a dual nature and to behave sometimes as waves and sometimes as particles. Using light as an example, the wave nature is demonstrated by the fact that this radiation undergoes interference, diffraction, refraction, reflection, and polarization. The waves are characterized by their velocity of propagation \( c = 3 \times 10^8 \text{ m sec}^{-1} \) in a vacuum, and by their wavelength \( \lambda \) and frequency \( \nu \). These are related by the formula \( c = \lambda \nu \). The particulate nature of light is based on the fact that energy carried by the radiation is always absorbed in the form of discrete "bundles" or "quanta". These individual bundles are called photons. Each photon has no mass but travels with the velocity, \( c \), given above. The minimum amount of a particular electromagnetic radiation is one single photon of the appropriate energy. Thus, in the examples given earlier in this chapter, an electron transition in an atom can lead to the production of a photon whose energy is characteristic of a particular electron energy level difference in that material. This photon is properly called a characteristic X-ray. Similarly, a photon whose energy exceeds 1020 keV can be converted into two electrons (one negative, one positive) in the interaction mentioned earlier.

E. Particulate Radiation

Particulate radiation may be of many types. The nuclear particles, neutrons or protons, may be liberated from the nucleus and emitted as particulate radiation following the interaction of high energy radiation with matter or as a result of nuclear fission. Alpha particles which consist of two protons plus two neutrons may be emitted from the nucleus in radioactive decay. Electrons also may be liberated from the atom. If they are produced as a consequence of radioactive decay they are called beta particles. They may also be knocked out of their orbits as a result of the interaction of radiation with matter. Physics research has led to the production of many other particles which

* Systeme Internationale, an international system of units and definitions.
are not easily found in nature. Some of these, like pi mesons, may in the future have some application in radiation biology.

II. PHOTON INTERACTIONS WITH MATTER

A. Photoelectric Effect

In the 1890s, it was observed that light falling on a metal surface could cause a loss of charge from the metal. There was a minimum optical frequency at which this would occur. Light of lower frequency (longer wavelength) would not eject the electrons which, as we now know, caused the charge loss, regardless of the intensity or the length of application of the light. These observations could not be explained by the existing theories. In 1905, Albert Einstein put forward a simple hypothesis to explain this process called the photoelectric effect. He proposed that energy of light was carried by individual quanta, called photons, each with energy \( E = h\nu \), where \( h \) is Planck's constant and \( \nu \) is the frequency. If the energy of the photon is great enough, \( \nu \) is high enough, an orbital electron can be ejected from an atom of material it strikes. In the photoelectric interaction, the photon gives up all of its energy and disappears. This absorption of the photon leads to the release of an electron whose kinetic energy is equal to the difference between the photon energy and the energy holding the electron to the atom. The likelihood of the photoelectric interaction per electron varies with \( E^2 \) and \( Z^3 \) where \( E \) is the photon energy and \( Z \) is the atomic number of the material. Thus the process dominates at low energies for a given material. In biological materials, the photoelectric effect is most important for photon energies up to around 50 keV.

In addition to the primary ionization that is a result of the photoelectric ejection of an electron, two other subsidiary processes may occur. The first is a filling of the vacancy created in the electron shell from which the photoelectron came. The jump of an outer electron to the inner vacancy is accompanied by the emission of characteristic X-radiation which may then produce its own ionization elsewhere. Sometimes the characteristic X-ray's energy is absorbed in the outer shells of the same atom, releasing electrons from these higher orbits. These are called Auger electrons, and contribute to the general distribution of secondary effects.

B. Compton Scattering

It is also possible for a photon to collide directly with any of the atomic electrons. If the binding energy of the struck electron is small compared with the photon energy, it may be considered “free” and in the collision, the photon transfers enough energy to knock the electron out of the atom. The photon is left with lower energy and is deflected away to interact again elsewhere. Thus the outcome of this event is a recoil electron and a scattered photon which share the initial photon energy (minus the electron binding energy). The physical principles of this interaction were discovered by A. H. Compton in 1923. He combined elements of Einstein’s quantum theory of light and some parts of the special theory of relativity to predict the relationships of energy transfer and angle of deflection in this interaction. The Compton process is the dominant interaction in biological materials over the wide energy range of 50 keV to 20 MeV. Since the process involves relatively “free” electrons, it is independent of the atomic number of the absorber and all materials absorb about the same amount of radiation per electron by this process. There is a practically linear decrease in the likelihood of Compton scattering over its broad energy range.

C. Pair Production

Pair production provides a practical demonstration of the conversion of energy into
matter. When a high energy photon passes sufficiently close to the nucleus of an atom it can interact with the Coulomb field and wink out of existence to be replaced by two electrons, one negatively and one positively charged. For this to happen, the photon must have sufficient energy at least to equal the rest mass energy equivalence of the two particles. As we calculated earlier, this value is 1.02 MeV. If the photon has higher energy than this threshold value, the rest is shared as kinetic energy between the electron and positron (positively charged electron). After creation of the electron-positron pair, the two particles lose energy by excitation and ionization of the surrounding material. Ultimately the positron slows down enough to recombine with a free electron. The two electron masses are annihilated, creating two photons each with an energy of 510 keV. These two photons travel off in opposite directions (to conserve momentum) and are available to produce further ionizations. The likelihood of pair production per electron is linearly proportional to Z and rises approximately linearly with E from the threshold value of 1.02 MeV. In biological materials this process becomes important at energies above 20 to 30 MeV.

D. Photodisintegration

High energy photons can interact with the atomic nucleus causing expulsion of a nuclear particle or particles. The release of any of the nuclear particles is possible including individual neutrons, protons, or alpha particles as well as various combinations. In order for these particles to be expelled, the photon energy must be greater than the binding energy of the last nucleon. For most light elements this is on the order of 10 to 15 MeV. For heavy elements it is about 7 MeV. The probability of this interaction in any given nucleus forms a peak around a certain "resonance" energy. Photodisintegration is responsible for the neutron contamination associated with linear accelerators producing high energy photon beams. Additionally, the atoms which have been disrupted are unstable and undergo radioactive decay with the emission of other particles or gamma photons.

E. Effective Atomic Number

Although biological materials contain many types of atoms, it is possible to think of an "effective atomic number" (Z_{eff}) for them as if they were elemental. This value can then characterize their absorption behavior as the photon energy is changed. Commonly applied values for Z_{eff} are 13 for bone, 7.4 for muscle, and 6 for fat. Thus, at a given photon energy, the amount of energy being absorbed or scattered in neighboring materials may be very different depending on their Z dependence at that energy.

This phenomenon is exploited in diagnostic radiology where the photon energies used lie in the range where the photoelectric effect dominates. The dependence of the interaction on Z^3 of the absorbers means, for example, that bone will be much more likely than soft tissue to absorb a photon. Thus the "shadows" cast by the two materials will vary considerably in intensity. This variation will provide good contrast in the resulting radiograph.

F. Quantitative Photon Interaction

We have described briefly how the occurrence of particular photon interactions is a function of both photon energy and the atomic number of the absorber. If a beam of photons is incident on an absorber, and a detector is placed on the exit side, the number detected will be less than the number incident because of losses due to absorption and scattering. The overall loss is called the "attenuation" of the beam. The probability per unit path length that a photon will be absorbed or scattered is a summation of the probabilities of each possible interaction. This probability is usually called \( \mu \) or \( \mu(E,Z) \) since it is a function of energy and atomic number. In experiments with monoenergetic
narrow beams of photons it is found that the number of photons which is transmitted through an absorber is dependent upon the thickness of the absorber and the number of incident photons. If \( N(x) \) is the number of noninteracted photons which have penetrated a distance \( x \) into the absorber, we can write an expression for the decrease in beam intensity as \( -dN(x) = \mu N(x) dx \) where \( \mu \) serves as the constant of proportionality. This expression can be rearranged to be \( \frac{-dN(x)}{N(x)} = \mu \) \( dx \). The term on the left is the fraction of photons which have penetrated a distance \( x \) into the absorber and which subsequently interact in the distance \( dx \). The equation can be integrated to give \( N = N_0 e^{-\mu x} \) where \( N_0 \) is the number of incident photons and \( e \) is the base of the natural
FIGURE 3. Absorption curve for a beam of X-radiation showing the change in energy with increasing depth. This change is reflected in the increased thickness of the second HVT compared with the first.

logarithms. The quantity $\mu$ is called the linear attenuation coefficient. The units of $\mu$ are length$^{-1}$, e.g., if $x$ is in cm, $\mu$ must be cm$^{-1}$. The equation $N = N_0 e^{-\mu x}$ produces a linear plot on semilog paper (Figure 1). The linear attenuation coefficient can be plotted as a function of photon energy. Such a plot for water in Figure 2 shows a characteristic shape. The curve really is a composite of the individual attenuation coefficients of the three main interaction processes — photoelectric absorption, Compton scattering, and pair production. It thus falls steeply in the region where the photoelectric effect dominates, falls linearly in the Compton region, and rises past the pair production threshold.

The photon beam from an X-ray generator is not homogeneous. The distribution of photon energies depends on the operating voltage, the electrical waveform, and the inherent and added filtration. As lower energy photons are more readily attenuated, there is greater loss of photons from the beam in the top layers of the absorber than in subsequent layers. Thus, the plot of attenuation vs. absorber thickness deviates from linearity by becoming progressively less steep until a point is reached where there is relatively little energy difference between the remaining photons and the curve then becomes practically straight (Figure 3). To simplify comparisons between photon beams the concept of half-value thickness (HVT) was introduced. The HVT is the thickness of absorber required to reduce the number of incident photons to one half of the original value. For monoenergetic beams where the relationship $N = N_0 e^{-\mu x}$ applies, the equation becomes $\frac{1}{2}N_0 = N_0 e^{-\mu(HVT)}$. This expression reduces to $0.693 = \mu(HVT)$. Thus, provided either the linear attenuation coefficient or half-value thickness is known, the other can be calculated.

For the heterogeneous beams produced by X-ray generators, the half-value thickness in conjunction with the peak operating voltage provides a reasonable means of comparison of the penetrating abilities of two beams. But two beams with identical HVTs generated with the same operating voltage may still not be identical. Their attenuation curves might coincidentally cross at the HVT (Figure 4). A second quantity, the homogeneity coefficient, uses the second HVTs (that thickness in which the beam intensity is reduced from $\frac{1}{2}$ to $\frac{1}{4}$ its original value) in a comparison. The homogeneity coefficient is defined as $(\text{first HVT})/(\text{second HVT})$. For a homogeneous beam the value is unity. Coincidence of both HVTs and a match of homogeneity coefficients at least insures a reasonable match in beam characteristics. Unfortunately, much of the radio-
radiation biology contains references to experimental beams in which only the peak operating voltage and added filtration of a generator is presented. This makes it difficult to infer accurate dosimetric information about the experiment.

III. CHARGED PARTICLE INTERACTIONS

When charged particles travel into matter, their paths are marked by excited and ionized atoms. The Coulomb field of the moving charged particle interacts with that of the electrons in the material and the collisions result in a transfer of the particles' energy into the absorber. They also interact with the Coulomb field of the nucleus and by so doing produce secondary X-ray emissions. Ultimately, the particles reach the end of their range of travel by giving up their kinetic energy in these interactions and then stop and are incorporated into the structure of the material.

A. Electron Interactions

The interaction of electrons with matter is characterized by energy loss through both collisional and radiative mechanisms. The equality of mass between the incoming electron and the bound electron it interacts with, prevents it from following a straight path. Instead, the electron interacts in a series of collisions that may deflect it widely from its original direction and motion.

Along its path of interaction, the electron leaves a trail of ionized and excited atoms. If one of the orbital electrons of the material is given sufficient kinetic energy in a collision it will be ejected and carry on to produce a series of secondary interactions of its own. In addition, Coulomb interactions with the nuclei of the absorber lead to the production of X-rays. The deceleration of the electron in the nuclear interaction has as a consequence the emission of X-ray energy which is called "bremsstrahlung" from the German meaning "braking radiation". Of course, the removal of orbital electrons from the absorber by collision leads to the production of characteristic X-rays when the electrons readjust their positions. So two types of radiative interactions occur in the absorber. An X-ray machine uses a target material which is struck by electrons and is chosen to optimize the amount and type of these radiative interactions.

B. Heavy Charged Particles: Alphas, Protons, Other Heavy Ions

The heavy charged particles have masses which are thousands of times greater than the mass of an electron. Thus, there is an enormous difference in the velocity of these
particles compared with the velocities of electrons having the same energy. A proton and an electron with the same velocity ionize and excite the molecules along their track in about the same proportion, but the energy of this proton would be more than 1000 times greater. A proton having the same energy as an electron would be traveling with a much lower velocity and would therefore ionize a greater number of molecules along every part of its path to create a denser track. A doubly charged particle, such as an alpha particle, makes a pattern of ionization that is four times as dense as that of a singly charged particle of the same velocity.

The track of a heavy charged particle is characterized by two important features. The first is its linearity which holds until the very end of the track when a small amount of deviation called "straggling" occurs. The second is an increase in the number of ions formed per millimeter near the end of the track. When a heavy particle first enters a material it produces ions at nearly a constant rate. As the particle slows down, the ionization per mm increases until it reaches a maximum a few mm from the end of its range. It then falls off rapidly to zero as the particle stops. This effect is illustrated in Figure 5 where the ionization is plotted against distance in the absorber. The maximum value occurs at what is called the "Bragg peak".

C. Neutron Interactions

Neutrons are uncharged particles which are almost equal in mass to protons and about 1800 times as heavy as electrons. They interact by direct collision with the nuclei of the target material and can undergo either a scattering or an absorption in the reaction.

With the relatively light nuclei of biological materials, the main interaction is elastic scattering. In this process part of the energy of the incoming neutron is transferred into kinetic energy of the struck nucleus. The fractional energy loss is greatest when the nucleus has a mass comparable to that of the neutron and decreases continuously as the nuclear mass increases. Thus for water, which has an abundance of hydrogen, each scattering leads to the transfer of a considerable fraction of the neutron energy into kinetic energy of the single proton which is the hydrogen nucleus. This proton is projected as a fast secondary particle into the surrounding material where it ionizes many more molecules. Hence a single primary collision of the neutron leads to a majority of the resulting ions being formed along the paths of the secondary particles which, in the case of water or other hydrogenous material, are protons.

Once the neutrons have transferred their kinetic energy and have been slowed down, they can interact with the absorber nuclei in several other processes. One such process is radiative capture. Here the neutron coalesces with the struck nucleus forming a new atom. The compound nucleus that results may be radioactive so that a whole spectrum of decay radiations may be initiated. The neutron absorption may lead to a breakup of the atom with the release of fragments including neutrons, protons, or larger groups.
Table 1

<table>
<thead>
<tr>
<th>Radiation type</th>
<th>L_{n,T} keV/\mu m</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{60}$Co</td>
<td>0.239</td>
</tr>
<tr>
<td>22 MV X-ray</td>
<td>0.19</td>
</tr>
<tr>
<td>2 MeV electron</td>
<td>0.20</td>
</tr>
<tr>
<td>200 kVp X-ray</td>
<td>1.7</td>
</tr>
<tr>
<td>$^3$H betas</td>
<td>4.7</td>
</tr>
<tr>
<td>50 kV X-ray</td>
<td>6.3</td>
</tr>
<tr>
<td>5 MeV proton</td>
<td>10.0</td>
</tr>
<tr>
<td>Thermal neutrons</td>
<td>20.0</td>
</tr>
<tr>
<td>5.3 MeV alpha</td>
<td>43.0</td>
</tr>
</tbody>
</table>


of nucleons carrying either single or multiple charge. These particles will contribute to dense local ionization near the site of the initial neutron absorption.

D. LET

The loss of energy by an interacting particle can be described by a quantity called linear energy transfer (LET). LET is defined\(^1\) as the quotient of dE by dl where dl is the average distance traversed by a particle and dE is the average energy loss in dl due to collisions with energy transfers less than some specified value $\Delta$. Thus $L_a = (dE/dl)_\Delta$.

LET usually has dimensions of keV $\mu$m$^{-1}$. ICRU 16 tabulates specific LET data\(^2\) and Table 1 presents some values of LET to help put their magnitude in perspective. Notice that for an individual particle, the LET has a constantly changing value as the particle slows down.

E. Production of X-Rays

As described in the section on electron interactions, two types of X-radiation are produced when electrons bombard the target of an X-ray tube. The first type, characteristic radiation, is related to the electron transitions in the target material. The second type, bremsstrahlung, is produced in a continuous spectrum of energies up to the energy of the interacting electron. For a monoenergetic electron beam striking a thin target, a plot of the theoretical spectral distribution of X-ray photons is shown in Figure 6. Most of the curve is due to bremsstrahlung. Superimposed on the continuous spectrum are peaks caused by the characteristic X-rays emitted as the result of principal electron transitions in the target. As the figure illustrates, most of the radiation is of low energy with a continual decrease in the number of photons emitted per energy interval until the maximum energy value is reached. The maximum photon energy is determined by the peak operating voltage on the X-ray tube.

Once the X-rays are produced, they interact with many absorbers on their way to the object being irradiated. They interact with the target itself, the glass walls of the X-ray tube, the oil insulation surrounding the tube, and with the tube housing window. The $\varepsilon$ materials provide an "inherent filtration" which removes photons from the beam. Since the low energy photons are more readily absorbed, the low energy end of the spectrum is reduced to a greater degree than the high energy end. Usually, addi-
FiguRE 6. Theoretical "unfiltered" X-ray spectrum that would result from the bombardment of an X-ray target by electrons.

FiguRE 7. Actual spectral distribution of X-rays from a generator showing K characteristic radiation on the filtered bremsstrahlung curve.

tional material in the form of thin aluminum and/or copper sheets is also placed in the beam before it emerges from the collimator of the X-ray machine. This "added filtration" insures that the resulting X-ray beam will have a predominance of high energy photons, and hence most of the radiation energy will be sufficiently high so as to traverse more than just the surface of the irradiated object. The nature and amount of added filtration together with the operating voltage that is accelerating the electrons to the target determine the penetration and energy characteristics of the final beam. These characteristics are usually referred to as "beam quality". The filtered spectrum of an X-ray beam is illustrated in Figure 7. The lowest energy photons have been removed by filtration and the resulting spectrum demonstrates the characteristic radiations of the target as well as the high energy bremsstrahlung which remains after filtration.

IV. RADIATION QUANTITIES AND UNITS

The units of radiation dosimetry have been changed to conform with the broad-based S.I. system. Since much of the radiobiological literature contains references to
earlier dosimetric quantities, it is best to examine these concepts with some historical perspective.

A. Exposure and Dose

In the early part of this century, no common system of radiation dosimetry was in practice for either of the two sources of ionizing radiation then known — X-rays or radiation from the decay of radioactive materials. The search for a physical standard was consolidated with the formation of the International Commission on Radiological Units and Measurements (ICRU) in 1925. The approach adopted as standard at that time relied on measurements of the ionization of air produced by the radiation. The practicality, simplicity, and reproducibility of air ionization dosimetry kept it in favor until the development of high energy radiation equipment and the introduction of charged particle beams prompted a change to a different approach.

The unit of quantitative ionometry adopted in 1928 and kept, with some changes in definition, for over 50 years was the roentgen (R). This unit had at different times been referred to as a unit of “quantity” (1928), of “dose” (1937), of “exposure dose” (1956), and finally of “exposure” (1962). At all times its basis in quantifying the ionization of air had been unchanged. The roentgen was defined as $2.58 \times 10^{-4}$ C kg$^{-1}$. This represented the ratio of the charge of the ions liberated by the radiation to the mass of air in the irradiated volume. For reasons given below, the roentgen has not survived as a unit, although ionization in C kg$^{-1}$ may still be cited in quantitative dosimetry.

The roentgen had limited usefulness as a quantity for evaluating the local chemical and biological effects which occurred in materials exposed to radiation. The interaction processes of radiation with matter are dependent on the atomic number and electron density of the irradiated material as well as the energy of the radiation. The same “exposure” to two different materials might lead to a considerably different energy absorption in each case with different physical consequences as a result. In addition, experimental difficulties make it impossible to carry out exposure measurements for high-energy photons (>3 MeV). Other difficulties arose when energetic charged particle sources became available. Their energy deposition was also quite different from those of the earlier X-ray and gamma ray sources. By 1953, the ICRU had recognized the difficulties inherent in using exposure as the primary quantity in radiation dosimetry. Instead the quantity “absorbed dose” was defined as the amount of energy imparted to a unit mass of the irradiated material. The unit of absorbed dose was the rad, with a magnitude of 100 erg gm$^{-1}$. The corresponding S.I. unit of absorbed dose is the gray (Gy), which has a magnitude of 1 J kg$^{-1}$. Thus, 1 Gy = 100 rad or 1 rad = 1 centigray.

The relationship between exposure and absorbed dose is complex as it is a function of the mass energy absorption coefficients of the irradiated material. These coefficients are strongly dependent on the energy of the radiation and of course depend on the structure of the material. In the case of the usual broad spectral distribution of photon energies from X-ray generators, it may be difficult or impossible to relate some of the older literature reports of “exposure” or “exposure dose” to actual absorbed dose.

B. RBE

Radiobiological experiments have shown that both the type and the spectral distribution of radiation influences the biological effects observed. There is strong correlation between the LET and these effects. As might be expected, high LET radiations produce a greater effect by virtue of their more concentrated release of energy. The consequences of these differences are embodied in the concept of relative biological effectiveness (RBE). RBE is defined as: “a ratio of the absorbed dose of a reference radiation to the absorbed dose of a test radiation to produce the same level of biolog-
ical effect, other conditions being equal. When two radiations produce an effect that is not of the same extent and/or nature, an RBE cannot be specified. Since RBE is a ratio of two doses, it is dimensionless.

C. Dose Equivalent

In the field of radiation protection, an attempt is made to provide a dosimetric quantity which is related to the presumed radiation risk. This quantity, called dose equivalent (H), has the same dimensions (J kg\(^{-1}\)) as absorbed dose and is obtained by multiplying the actual absorbed dose by two modifying factors. The first factor, Q, provides an influence related to radiation quality and is directly related to LET. It is thus similar to RBE. The second factor, N, represents other modifications and is presently assigned a value of 1 for external sources. The International Council on Radiation Protection (ICRP) has recommended other values of N for sources deposited in bone. Thus dose equivalent \(H = \text{dose} \times Q \times N\) J kg\(^{-1}\). The special unit of dose equivalent is the sievert (Sv) which has a magnitude of 1 J kg\(^{-1}\). Formerly, the unit of dose equivalent was the rem, with a magnitude of 100 erg gm\(^{-1}\). Thus 1 Sv = 100 rem or 1 rem = 1 centisievert.

It must be emphasized that the concept of dose equivalent is only defined in the field of radiation protection. It is not proper to use RBE in radiobiology work in the same manner in which Q is used in the field of radiation protection.

V. RADIOACTIVE DECAY

The nuclear particles in any atom are in constant motion with energy being continually transferred between them. In a stable nucleus, no particle ever acquires enough energy to break away from the strong nuclear attractive forces. In a radioactive nucleus, it is possible for a particle to gain enough energy to escape. Exactly when this will occur is a matter of pure chance for a single nucleus. If there are many nuclei, a certain percentage will disintegrate over a given period of time. The light atoms, with relatively small numbers of nuclear particles are stable. Most of the heavier elements have radioactive species. Radioactive elements achieve stability by undergoing one or more of the following processes: alpha decay, beta minus decay, beta plus decay, electron capture, internal conversion, isomeric transition, and fission.

A. Nomenclature

Atoms are characterized by two quantities: their atomic number and their mass number. Atomic number, Z, refers to the number of protons in the nucleus. This is also the number of electrons in a neutral atom since charge is balanced. The atomic number of an element determines its chemical and physical characteristics and is therefore unique to each element.

Mass number, A, refers to the total number of particles in the nucleus of the atom. The number of neutrons in the nucleus is, of course, A - Z. The usual method of denoting an atomic species, called a nuclide, is to use the form \(^{\text{Z}}\text{M}\) where M is the chemical symbol for the particular element. A nuclide that undergoes radioactive decay is called a radionuclide.

It is possible to have atoms of the same element which vary in the number of neutrons in their nuclei. Such species are all "isotopes" of the particular element. Thus deuterium, \(^{\text{2}}\text{H}\), tritium, \(^{\text{3}}\text{H}\), and ordinary hydrogen, \(^{\text{1}}\text{H}\) are all isotopes of hydrogen. Tritium is also a radionuclide since it undergoes radioactive decay. Like hydrogen, a number of elements have more than one stable isotope in addition to the radioactive forms.
B. Alpha Decay

Alpha disintegration occurs mainly in heavy nuclei. In this decay a helium nucleus, two protons and two neutrons, is ejected. The decay can be represented by the equation \[ _2^4\text{He} \rightarrow _0^2\text{He} + _2^4\text{He} (\pm \gamma) \].

Sometimes the nucleus is left in an excited state following alpha decay. It can achieve stability by the emission of a gamma ray photon. At other times, even for the same radionuclide species the alpha decay can proceed directly to the “ground state” of nuclear energy so that no gamma rays are released. This explains the ( + \gamma) in the decay equation above. The decay scheme for radium is presented in Figure 8. Radium can decay via either of the two paths illustrated. In 98.8% of the decays, a 4.79 MeV alpha particle is emitted and radium’s daughter, radon, is created in the ground state. In 1.2% of the decays, the disintegration leads to an excited state of radon which releases its energy in the form of the 0.18 MeV photon.

C. Beta Decay

Beta particles are simply electrons or positrons designated \( \beta^- \) or \( \beta^+ \). Since the nucleus contains no electrons, their origin is in the conversion of neutrons into protons and vice versa.

\( \beta^- \) decay occurs in neutron rich nuclei, \( \beta^+ \) decay in proton rich nuclei. The reactions are: \( _n\beta^- \rightarrow _p \beta^- + \nu \) and \( _p \beta^+ \rightarrow _n \beta^+ + \bar{\nu} \) where \( \nu \) is a neutrino and \( \bar{\nu} \) an antineutrino. These are neutral particles that are extremely light compared with electrons and interact very little with matter. A typical reaction for \( \beta^- \) decay is \( _2^4\text{He} \rightarrow _2^4\text{He} + _0^2\text{He} + \beta^- + \nu \). For \( \beta^+ \) decay it is \( _2^4\text{He} \rightarrow _2^4\text{He} + \beta^+ + \bar{\nu} \). The gamma rays are released if the nucleus is left in an excited state following the decay.

Whereas in alpha decay the particles are emitted with the discrete energies noted in the decay scheme, in beta decay the situation is different since the \( \beta \) particle shares the available energy with the neutrino. This means that there is a continuous spectrum of beta energies from a single beta emitter. The neutrino energy ranges from zero, where the beta receives all the energy, to the opposite case where the neutrino receives it all leaving the beta with no kinetic energy. The decay scheme for \( ^{32}\text{P} \) is shown in Figure 9. A plot of the spectrum of beta energy in this decay is shown in Figure 10. Notice that \( E_{\text{max}} = 1.7 \text{ MeV} \) but the average value of beta energy is only around 0.7 MeV.

The decay scheme for \( ^{60}\text{Co} \) is shown in Figure 11. The nickel is created in an excited state and achieves stability by the emission of two gamma rays in cascade.

D. Electron Capture

Alpha and beta decay are processes in which active nuclei eject particles and in so doing achieve energy stability. Some radionuclides of the proton-rich type decay in an
alternative path to $\beta^+$ emission. Instead of the proton changing into a neutron by losing a $\beta^+$, it does so by capturing an electron from a nearby orbit, usually the K shell. The reaction is: $\uparrow p + \downarrow e \rightarrow \downarrow n + \nu + (\gamma)$. Thus the atom's own orbital electron is used to convert the proton to a neutron. The resulting vacancy in the electron shell will cause the emission of characteristic radiation and/or Auger electrons. Atoms which are proton rich usually decay by both electron capture and beta plus ($\beta^+$) decay in different proportions. This is illustrated in Figure 12 which is the decay scheme for $^{22}\text{Na}$.

E. Internal Conversion

As we have described, a gamma ray may be emitted following alpha or beta decay if the daughter nucleus has been created in an excited state. In some disintegrations this excess energy may be lost in a process called internal conversion. Here, the energy of the excited nucleus is given to an electron in the K shell of the atom. The electron is ejected, leaving a vacancy in the shell. Of course, characteristic X-rays and Auger electrons may then also be released.
F. Isometric Transitions

If radioactive decay results in the creation of a nucleus in an excited state, gamma rays can be emitted. Usually this emission follows very quickly. There are, however, atoms where the time interval between the decay and the emission of the gamma ray can be minutes or even years. These delayed releases are called isomeric transitions. Atoms whose nuclei are in this excited state are called isomers of their unexcited sister atoms. An isomeric state is usually denoted by the letter m attached to the mass number of the nuclide, e.g., $^{99m}$Tc or $^{113m}$In.

G. Fission

In the process of fission, the nucleus of a heavy atom (high Z) splits. Two atoms with intermediate values of Z are created and about 200 MeV of energy is released in the form of neutrons and gamma rays. The neutrons which are released have the potential to induce other surrounding nuclei to fission which may lead to a “chain reaction”. The nuclides which are created from fission are generally radioactive and undergo radioactive decay through a series of elements until reaching a stable form.

H. Artificial Radionuclides

In addition to the naturally occurring radionuclides, it is possible to induce radioactivity by bombarding stable atoms with particles or photons of sufficient energy. The use of cyclotrons and nuclear reactors to create these artificial species is of great importance in radiobiology and nuclear medicine. For example, $^{99m}$Tc is a radionuclide that is widely used in nuclear medicine because of its favorable energy and half life. It is obtained by the neutron irradiation of molybdenum in the reaction:

$$^{98}_{42}\text{Mo} + ^{1}_{0}\text{n} \rightarrow ^{99}_{42}\text{Mo} + ^{\gamma}_{-}\text{n} \quad 66 \text{ hr} \rightarrow ^{99m}_{43}\text{Tc} + ^{\beta^-}_{-}\text{c} \quad 6 \text{ hr} \rightarrow ^{99}_{43}\text{Tc} + ^{\gamma}_{-}\text{n}$$

I. Quantitative Radioactive Decay

In 1902 Rutherford and Soddy observed the activity of a sample of radioactive material. They found that the number of atoms which decayed in a short time, dt, was directly proportional both to the number of atoms present and to the length of the time interval.

Suppose there are N(t) atoms present. The mathematical expression for the decay is \(dN(t) = -\lambda N(t) dt\) where \(\lambda\) is the constant of proportionality. In physical terms, \(\lambda\) represents the probability per unit time that an atom will decay. This equation can be rearranged in the form \([dN(t)/dt] = -\lambda N(t)\). Notice that the left hand side of the equation now is the activity, the time rate of change in the number of radioactive atoms. Thus, the activity, \(A\), is \(\lambda N\) where the negative sign is dropped because we need only the absolute value of the rate of radioactive decay. The solution of this equation is similar to the solution of the equation for the absorption of photons in matter as
they both have the same mathematical form. Using similar calculations, the solution 
\[ N = N_0 e^{-\lambda t} \]
is obtained. Here \( N_0 \) is the number of atoms initially present and \( N \) is the 
number remaining at time \( t \). The quantity \( \lambda \) is called the decay constant and is the 
probability of decay per unit time. Because \( t \) has units of time, \( \lambda \) must have units of 
reciprocal time, e.g., if \( t \) is in seconds, \( \lambda \) must be seconds\(^{-1} \). Since \( A = \lambda N \) and \( A_0 = \lambda N_0 \) we can substitute for \( N \) and \( N_0 \) and obtain 
\[ A = A_0 e^{-\lambda t} \]
which is the equation that Rutherford presented in 1902.

Activity, as the number of disintegrations per unit time, is an important concept for 
which a special unit has been created. This unit is the becqueral (Bq) which is defined 
as 1 disintegration per second (1 sec\(^{-1} \)). Before the advent of S.I. units, the standard 
unit of activity was the curie (Ci). This unit was based originally on the activity of one 
gram of radium and equal to \( 3.7 \times 10^{10} \) sec\(^{-1} \). Thus 1 Bq = \( 2.7 \times 10^{-11} \) Ci.

J. Half Life

The half life, \( T_{\frac{1}{2}} \), is the time at which \( N(t) \) the number of radioactive atoms remain-
ing at time \( t \) becomes equal to \( N_0/2 \). That is, when half of the radioactive atoms have 
decayed. Substituting these values in the decay equation gives an expression that is 
similar in mathematical form to the equation for half-value thickness derived earlier. 
The solution is \( T_{\frac{1}{2}} = 0.693 \lambda^{-1} \) which enables calculation of either the decay constant 
or the half life when one of the two is known.

VI. RADIATION MEASUREMENTS

A. Radiation Dosimetry

The most widely applied form of radiation dose measurement relies on the ionization 
of a mass of air contained in a device called an ionization chamber. The chamber 
encompasses two electrodes which are held at a high potential difference. As radiation 
passes through the air in the chamber, some of the molecules are ionized and the ions 
so produced are collected on the electrodes of opposite sign. The electrodes may be 
connected to a current measuring system for a dynamic readout of the ionization rate, 
or there may be a charge collection system which can read out the total collected 
charge. The ratio of the collected ionic charge of one sign to the mass of air in the 
chamber is the radiation exposure in Coulombs per kilogram (C kg\(^{-1} \)) or roentgens 
(R).

Once an exposure measurement is obtained, it is possible to derive the absorbed 
dose. Dividing the collected charge in coulombs by the charge of an individual ion, 
\( 1.6 \times 10^{-19} \) C, yields the number of ion pairs created in the mass of air. Multiplying 
the result by \( (\bar{W}/e) \), the amount of energy needed to produce an ion pair in air \( (5.4 \times 10^{-18} \) J), yields dose in J kg\(^{-1} \) or gray. To relate this calculation of absorbed dose in 
air to the dose that would be absorbed by some other medium, it is necessary to correct 
for differences in energy absorption of the two different materials. This is accomplished 
by multiplying the dose in air by the ratio of the mass energy absorption coefficients. These coefficients are similar to the linear attenuation coefficients, \( \mu \), defined 
earlier. They are a measure of the energy absorption in the material whereas \( \mu \) is a 
measure of both absorption and scattering processes.

An accurate measurement of radiation exposure relies on the collection of all of the 
ions produced by both the primary radiation and the secondary particles which it liber-
ates. This poses a problem for high energy radiation where the ranges of these parti-
cles are long. For this and other reasons it is not practical to measure exposure for 
photon energies greater than about 3 MeV. A solution of this difficulty is to measure 
dose directly using cavity ionization techniques based on the Bragg-Gray principle.\(^{11} \)

These measurements are accomplished by putting a small air-filled ionization cham-
ber in a block of the medium under consideration. Usually in radiobiological or medical dosimetry that medium is water, so a water tank or block of water-equivalent plastic is used. The energy given to the air in the chamber is obtained by multiplying $(\overline{W}/e)$, the energy needed to produce a single ion pair by the total number of ion pairs created. This value is multiplied by a quantity $S_{mg}$ which is the ratio of the difference in energy absorption in air and in the medium. $S_{mg}$ is called the mass stopping power ratio. Thus if $J_g$ is the ionization in the chamber in ion pairs per kg, the absorbed dose is $J_g(\overline{W}/e)S_{mg}$. This is the Bragg-Gray formula.

### B. Ionization Methods

In proper radiation dosimetry, the ionization chamber is operated with sufficient voltage between the collecting plates to insure that all of the ions which are produced by the radiation are collected. If not, recombination can occur between positive and negative charges as they pass near one another on their way toward opposite electrodes. Figure 13 is a plot of the ionization current vs. the collection voltage showing the plateau region (A) where essentially all of the ions are being collected and increasing the voltage does not yield any more.

If the voltage is increased further, the ions begin to be increasingly accelerated under the influence of the electric field and eventually they have sufficient kinetic energy to cause secondary ionizations in the air in the chamber. In region B of the figure this effect is seen as a proportional increase in ionization current with increasing collection voltage. Thus the detection system becomes more sensitive to low levels of radiation by virtue of a higher current output for a given amount of ionization. In this situation the radiation detector produces a current pulse which is proportional to the energy deposited by the detected particle and as such is useful in many measurement situations where sensitivity and energy discrimination is required.

If the voltage in the chamber is increased further, the Geiger region is encountered (region C of the curve). Here the output of the measuring device is independent of the size of the event which triggers it. Since the initial ionization causes a charge "avalanche" of secondary ionizations, each event saturates the system for a brief time. In this circumstance a heavily ionizing alpha particle or a lightly ionizing beta particle passing through the chamber produce pulses of the same size. The actual size of the pulse depends on the applied voltage. In the Geiger region, amplifications of up to $10^6$
can be obtained. Thus a detector system operating in this region can detect individual particle interactions which would be unmeasurable in an ionization chamber. These detectors are usually designed to count the interactions which occur in the tube and as such usually display their output in "counts per second" or similar units. They can however be calibrated to indicate exposure or dose rate if certain conditions of geometry and energy limits are met.

Geiger counters may take different forms depending on their applications. The detector walls are designed to be as transparent as possible to the radiations of interest.

C. Scintillation Methods

A scintillation detector exploits the fact that certain crystals luminesce when exposed to radiation. The crystal is excited by the absorption of radiation and deexcites to achieve energy stability by emitting light photons. These are detected by a photomultiplier tube which is a device that converts light to electrical pulses. One of the important properties of a scintillation detector is its ability to measure the energy of the incident radiation. The amount of charge which appears at the output of the photomultiplier tube is proportional to the energy of the incident radiation. By using suitable electronics, it is possible to separate and group the signals produced by particles of different energy and to discriminate against those that are unwanted. Thus a threshold energy can be selected to eliminate background radiation. Similarly, the energy spectrum of the radiation beam can be determined by plotting the number of particles in each particular energy range.

D. Thermoluminescence Dosimetry (TLD)

Scintillation detection exploits the fact that certain crystals emit light when exposed to radiation. Thermoluminescence dosimetry utilizes the delayed emission of such light. In some materials, the action of radiation excites electrons into higher energy levels in the crystal, where they become trapped. They can be made to release from these traps by heating the crystal and in so doing, light is released with an intensity proportional to the radiation dose. A photomultiplier tube detects the light and drives the electronics of a counting system. TLD material can be used in quantitative radiation dosimetry if it is properly calibrated by exposing some of the dosimeters to known doses of radiation in the range of interest. Thermoluminescent material is available in several physical forms. Lithium fluoride and calcium fluoride are commonly used. The material may be in the form of powder, disks, or rods depending on the application. TLD can measure dose over a wide range of values — from a few nanogray to a decagray. TLD rods or chips are small in size and lend themselves well to such measurements as the output of gamma irradiators used for animals or cell cultures. TLD is also used for personnel monitoring as an alternative to the common "film badge" where its wide range of useful dose measurement is exploited.

E. Photographic Film

Dosimetric information can be obtained by measuring the blackening of photographic film exposed to radiation. Optical density is a quantitative measure of film blackening. It is defined as log(I/I₀) where I₀ and I, respectively, represent incident and transmitted light over a given area of film. Optical density can be measured simply with a film densitometer.

The response of a particular film to radiation is usually expressed in the form of a graph of optical density vs. log exposure. This curve is characteristic of the film and radiation used, and is also dependent on film processing (developing and fixing).

The film’s characteristic curve frequently has a linear portion (Figure 14). In this region there is a simple linear relationship between density and exposure which enables
dosimetry based on an interpolation between points set from calibration standards. A major limitation in using film for dosimetry arises for radiation below 200 keV, an energy range that includes scatter from higher energy sources. As Figure 15 shows, there is a marked peak in film response around 40 keV which corresponds to the K shell binding energy in silver. Thus it is difficult to do precise dosimetry using film for radiation below 200 keV in energy. Film if properly calibrated can be used to measure dose in the range 0.001 to 1.5 gray.

F. Chemical Systems

The energy deposited in an irradiation can produce chemical changes in special solutions which may be used to measure dose. In the Fricke dosimeter, radiation oxidizes an aqueous solution of ferrous sulfate to ferric sulfate. Absorption spectrometry is used to measure the magnitude of the amount of ferric ion which is produced.
In practice, a solution of Fe₂SO₄ in sulfuric acid is prepared. Following irradiation of samples of the solution, the optical density of both the irradiated samples and unirradiated controls are measured in a spectrophotometer. The change in density is related to the number of ferric ions which have been formed. The value “ferrous sulfate yield,” which is the number of ions formed by a standard amount of radiation, is used to calculate the absorbed dose. The ferrous sulfate dosimeter is useful for measurements of high dose in the range 10 to 500 gray.

G. In-Vivo Dosimetry

When irradiating biological materials in an experimental or clinical situation it is necessary to calculate accurately the dose which they will receive. This dose to the organism is evaluated by constructing a relationship to the dose at a standard reference point where a calibration of the output of the radiation producing equipment has been made. In this regard, the concept of depth dose is frequently employed. Percentage depth dose is defined as the ratio \( \frac{D_d}{D_{d\text{max}}} \times 100 \) where \( D_d \) is the dose at depth \( d \) in the material and \( D_{d\text{max}} \) is the maximum dose along the central axis of the beam of radiation. The location of \( d_{\text{max}} \) is the surface of the irradiated object for low energy radiation becoming deeper in the object for high energies as the ranges of liberated secondary electrons become longer. In experimental or clinical irradiation, the object being irradiated is positioned at a standard distance from the source. This insures that the dose at \( d_{\text{max}} \) can be easily calculated. The dose at any other depth is then determined by multiplying by the percentage depth dose. Similarly, if a specific dose is to be administered to, say, the midline of the organism, dividing by the percentage depth dose will give the dose at \( d_{\text{max}} \). This dose to a standard location is easily translated into an operating time for the radiation machine. Figure 16 illustrates the depth dose characteristics for several beam types.

Percentage depth dose is a comparison between the doses at the two points, A and B, in Figure 17. For photon irradiation the ratio of dose to those two points is influenced by two mechanisms of loss in the beam. The first, inverse square attenuation, would create a difference in dose reaching the two points even if there were no absorp-
FIGURE 17. Schematic diagram illustrating the two points which are compared in defining percentage depth dose.

FIGURE 18. Isodose curve for 60Co. In this conventional curve, normalization is made to the dose at $d_{max}$.

ing material between them. The radiation dose rate from a small source, such as an X-ray focal spot or small isotope source, falls off with the square of the distance from the source. The second factor influencing the difference in dose at the two points is absorption by the medium between them. Usually this absorption is exponential in the form $B e^{-\mu}$ where the term $B$ accounts for scattered radiation and modifies the usual "narrow beam" term. Of course, both $B$ and $\mu$ are dependent on the energy of the incident beam.

Tables of percentage depth dose are available for most beam qualities used in fundamental radiobiology. Others can be compiled by experimental measurement.

H. Isodose Charts
In addition to the dose received along the central axis of a beam, it is often desirable
to know the radiation dose at other points. To aid in this undertaking, isodose charts are created. Using a homogeneous phantom, usually a water tank, the radiation dose is measured at a large number of positions throughout the volume. The results are normalized to the dose measured at $d_{max}$ on the central axis of the beam. When all like values are connected graphically, the result is an isodose curve (Figure 18). This figure is a typical isodose curve through the central axis of a $^{60}$Co beam. The values which can be read along the axis will match those found in a table of percentage depth doses since both are normalized to 100% at $d_{max}$ on the axis.

Isodose curves provide a visual indication of the variation in dose when a single beam of radiation interacts with an absorbing medium. When calibrating the output of the radiation producing equipment used in a research or clinical situation, the reference point chosen for the output calibration is usually the position of $d_{max}$ for the individual radiation unit. Thus the dose delivered at any other point in the medium can be determined by using isodose curves and tables.

Isodose curves may also be used to evaluate the radiation dose distributions which are obtained from the use of multiple beams. They may be added together when overlaid on a crosssectional contour of the irradiated object. By renormalizing the summed values, it is possible to create a composite isodose distribution for even elaborate arrangements of multiple fields. This is frequently done in radiation therapy treatment planning.

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