ELEMENTS
OF RADIOBIOLOGY

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By

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PREFACE

For a number of years, the author has given a course in radiobiology to second year students in radiologic technology, as well as an occasional lecture to radiology residents. More recently, radiobiology has become a mandatory subject in the curriculum of approved radiologic technology schools.

In this book, the author has expanded and thoroughly updated his lecture notes so as to conform to the required curriculum. Since the book is directed both to technology students and beginning radiology residents, emphasis has been placed on the essentials of radiobiology.

After a brief historical introduction, basic physics and cellular biology pertinent to radiobiology are treated separately, followed by chapters on their interplay: modes of action of x and gamma rays, response of cells and tissues, cellular radiosensitivity, and factors affecting cell response to ionizing radiation.

Because of the growing interest in radiation hazards, fully one-third of the book deals with this important subject. Thus, it includes chapters on whole body effects, hazards to embryo and fetus, late effects on body tissues, genetic effects, and population exposure (health physics).

Radiobiology has become such an integral part of irradiation therapy that an introduction to radiation oncology and an overview of available radiation modalities have been included. Finally, there is a brief discussion of radiotherapy: equipment, goals, planning, and terminology.

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Joseph Selman, M.D.
Tyler, Texas

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Chapter I

INTRODUCTION

Three remarkable events, in rapid succession, ushered in the era of radiology. In 1895 Wilhelm Conrad Roentgen discovered x rays through their ability to excite fluorescence in a barium platinocyanide screen. The following year Henri Becquerel first observed the radiations emitted by a uranium-containing mineral, a phenomenon later called *radioactivity* by Marie Curie. Then, in 1898, Marie and Pierre Curie announced their discovery of radium. In each instance the important product was *ionizing radiation.*

The biologic effects of such radiation soon became apparent when Becquerel noticed a skin reaction—reddening and irritation—accidentally induced by radium he had been carrying in a tube in his vest pocket. Later, Pierre Curie deliberately exposed a small area of his own skin to radium and closely observed the consequent radiation effects.

History of Radiobiology

We may define radiobiology as the branch of science that deals with the modes of action and the effects of ionizing radiation on living matter. This important discipline has contributed in no small measure to our understanding of the factors involved in population exposure to radiation, as well as tumor response to irradiation, although radiotherapy still remains largely empirical (i.e., based on practical experience).

We can date the beginning of experimental radiobiology to Bergonié and Tribondeau who, in 1904, exposed rabbits' testes to x rays. Their observations of radiation effects on testicular reproductive cells are embodied in the law that bears their names. This law simply relates radiation sensitivity or responsiveness of a tissue, to the fraction of cells that are actually dividing (i.e., in mitosis) or have the potential to divide in the future. While this law holds generally and has been verified in a great many different types of tissue, it is subject to certain exceptions that will be brought out later.

In the 1920s it was already widely accepted that the *biologic effects* of radiation result from the ionization it produces in tissues. It soon became apparent that two different processes are involved: (1) direct effects by ionization along charged particle tracks and (2) indirect effects by free radicals and other entities that diffuse (spread) away from the ionization tracks. This second process, *activation of water*, received a great deal of attention in the 1930s by H. Fricke (1936), and later by D. E. Lea (1947) and L. H. Gray (1953).

Another important step in the advance of radiobiology was the discovery by Thoday and Read (1947) that oxygen increases the frequency of chromosome breaks over and above that predicted from the indirect ionizing effect of radiation such as x and gamma rays. It turns out that oxygen enhances the indirect effect exerted by free radicals. This, the *oxygen effect*, was also studied by Gray, an outstanding pioneer radiobiologist.

In 1956 Puck and associates reported the first successful culture of mammalian cells in artificial media, much like bacteria, thereby opening the door to large scale investigation of cellular response to radiation under controlled laboratory conditions. They used cells derived from a carcinoma of the uterine cervix in a patient named Helen Lane; these cells are called HeLa cells. Puck and associates exposed such cells to various doses of radiation and plotted cell survival curves. Based on curves of this kind, Elkind in the 1950s was able to show that cells can recover from sublethal (less than fatal) doses of radiation.

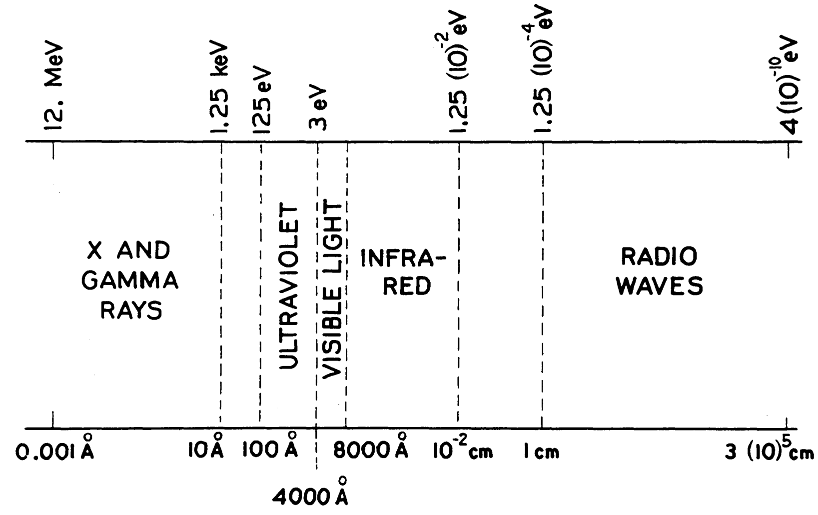
It should be noted that a definite interrelation exists among the three disciplines of radiation physics, biology, and radiobiology. *Radiation physics* deals with the spread of energy through space and its absorption in matter. *Biology* comprises all the available knowledge about living organisms. As noted at the outset, *radiobiology* includes the interaction of ionizing radiation with living systems. Later we shall describe the salient features of experimental radiobiology and show how they relate to radiotherapy.

Chapter II

PHYSICAL PROPERTIES OF X- AND GAMMA-RAY BEAMS

Nature of Photon Radiation

Photon beams, whether x rays or gamma rays, consist of electromagnetic radiation characterized by high frequency and short wavelength. They belong to the general electromagnetic spectrum (i.e., range of frequencies) as illustrated in Figure 2.01.



$$1\ \text{Å} = \frac{1}{100{,}000{,}000}\ \text{cm} = 10^{-8}\ \text{cm} = 10^{-10}\ \text{M}$$

Figure 2.01. Electromagnetic spectrum. Useful range of wavelengths and energies is as follows:

Diagnostic x rays	0.1 to 1 Å (124 to 12.4 kV)
Cobalt 60 gamma rays	0.01 Å (1.25 MeV)
Linac; betatron	0.0005 to 0.002 Å (25 MV to 6 MV)

X rays arise in association with the following processes:

1. Change in velocity (i.e., speed or direction) of high-speed electrons.
2. Transition of electrons between atomic shells, from higher to lower energy levels.
3. Rapid oscillation (vibration) of electrons.

Gamma rays—physically identical to x rays—originate in the nuclei of certain radionuclides during radioactive transformation (decay).

All electromagnetic radiation consists of simultaneous electric and magnetic waves that proceed through space in step with each other as shown in Figure 2.02. Ordinarily, only one of these waves is used by way of illustration, as in Figure 2.03.

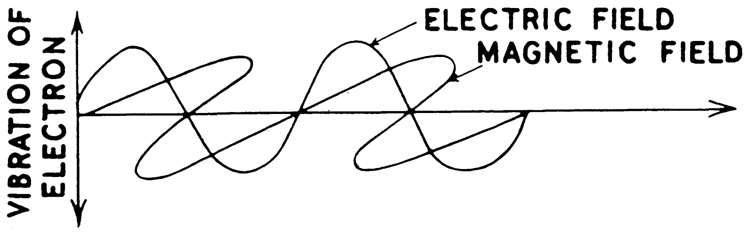


Figure 2.02. Electromagnetic wave form. The electrical and magnetic components of an electromagnetic wave oscillate (vibrate) in mutually perpendicular planes.

Electromagnetic waves have the properties of *frequency*, symbolized by the Greek letter ν (*nu*) and *wavelength*, symbolized by the Greek letter λ (lambda). Frequency designates the number of vibra-

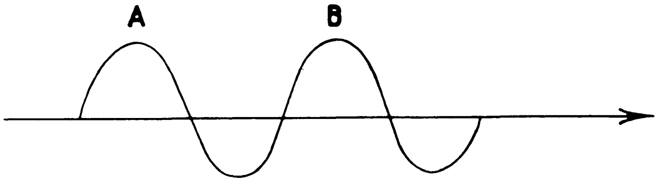


Figure 2.03. Ordinary representation of an electromagnetic wave, comprising only one component. The distance between two successive peaks, such as A and B, is the wavelength. The part of the wave between two corresponding points such as A and B is one cycle, and the number of cycles per second is the frequency.

tions or cycles per second for a particular electromagnetic wave, measured in hertz (1Hz = 1 cycle/sec). The distance between two successive crests in the wave such as *AB* in Figure 2.03 is the wavelength.

The frequency and wavelength of any given electromagnetic wave have a reciprocal relationship. Since the frequency determines the number of waves per second passing a given point in space, the speed of the wave equals the frequency times the wavelength, symbolized as follows:

$$c = \nu\lambda \qquad (1)$$

where c, the speed of light, is a universal constant in air or in a vacuum. From equation (1) you can see that since c is constant for all electromagnetic radiation, *an increase in* ν *must be accompanied by a corresponding fractional decrease in* λ. For example, if ν is doubled, λ is halved; if ν is tripled, λ is reduced to $\frac{1}{3}$, since their product must always equal c, which represents 3×10^8 meters per sec in air or vacuum.

Owing to the extremely short wavelength of x and gamma rays, much smaller units of measurement are more convenient than those in everyday use. These include the angstrom (Å) having a value of 10^{-10} meters (m) or 1/10,000,000,000 m, and the micron or micrometer having a value of 10^{-6} m or 1/1,000,000 m.

Curiously enough, x and gamma rays exist not only as electromagnetic waves but also as extremely minute (tiny) bits of energy called *quanta* (plural of *quantum*) or *photons*. The energy of E of such a quantum is defined by:

$$E = h\nu \qquad (2)$$

where h is Planck's constant (6.625×10^{-27} erg-sec) and ν is the frequency of the electromagnetic wave associated with the quantum. Thus, the *energy of a quantum or photon is directly proportional to its frequency*. We shall find that the interactions of x and gamma rays with matter can be explained only with reference to the quantum aspect of radiation. These *simultaneous wave and quantum properties* express the *dual nature* of electromagnetic radiation.

On the basis of this concept, known as the *quantum theory*, an x- or gamma-ray beam consists of showers of photons or quanta (bits of energy) that carry no charge. Furthermore, *they travel with the same, constant speed in air or vacuum regardless of their energy*. Thus, x and gamma rays (as well as light) have a dual nature, behaving as both waves and particles.

Since, from equation (2), the energy of a photon is proportional to its frequency, and from equation (1), the frequency times the wavelength is constant (speed of light *c*), highly energetic (very penetrating) photons have high frequency and short wavelength; conversely, low energy (less penetrating) photons have low frequency and long wavelength. This relationship is shown in Figure 2.04.

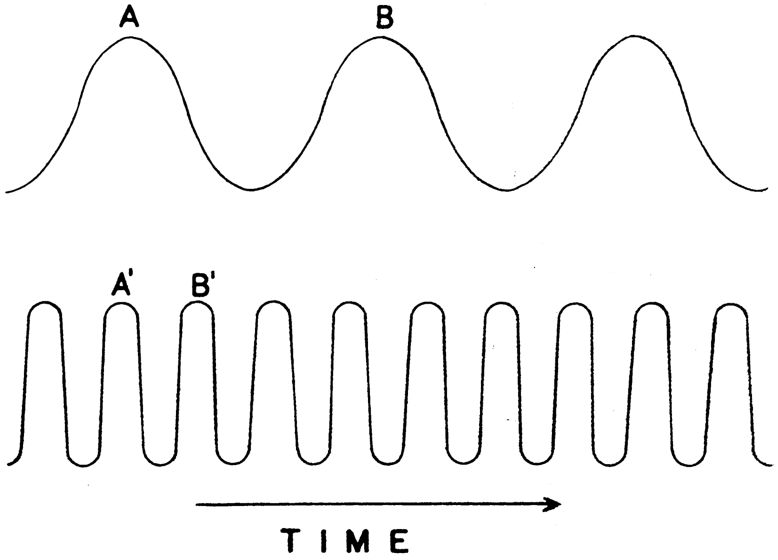


Figure 2.04. Two electromagnetic waves. The upper and lower wave trains differ in wavelength (compare AB to A′B′). The lower wave has a shorter wavelength, and therefore more peaks (or cycles) per given time interval, than does the upper wave because their velocities are identical. So the wave with the shorter wavelength has the greater frequency or number of cycles per second (Hz).

Quantity of Photon Radiation

By the term *quantity* we mean the amount based on a particular property of ionizing radiation, namely, its *ability to ionize air*. You