Radiation Therapy

by R. Stewart Harrison

R. Stewart Harrison, MD, radiologist and director of radiation safety for the California Institute of Technology.

During the depressed thirties there were at least three questions that confronted radiologists seeking to control or cure cancer below the surface of the skin:

(1) At that time the unit of ionizing radiation was based on the amount of ionization produced in air. Would one unit produce the same effect in tissue at all photon energies?

(2) Would the amount of ionization produced in a cubic centimeter of tissue n centimeters from the surface always bear a constant relation to the amount produced in the first cubic centimeter, regardless of photon energy? And, if there was a difference, would it be therapeutically useful?

(3) It was already known that some cancers were on the average somewhat more sensitive to ionizing radiation than surrounding or intermingled normal cells. Could this relative sensitivity be enhanced by increasing the energy of the photons?

These questions were answered within the decade by cooperative research undertaken at Caltech and elsewhere.

In 1928 C. C. Lauritsen built the world's largest x-ray tube—750,000 volts—for physics experimentation. In 1933 Albert Soiland, a prominent Los Angeles radiologist, documented the beginning of the medical use of radiation produced by this tube in an article published in *Radiology*, February 1933:

"During the summer of 1930 the writer was invited by Dr. R. A. Millikan and Dr. C. C. Lauritsen of the California Institute of Technology to inspect the high voltage x-ray tube installation at the Institute. Dr. Lauritsen, who had been experimenting with the 1,000,000-volt transformer set at the Institute, had succeeded in building a large x-ray tube of glass through which 5 milliamperes of current operated successfully at 750,000 volts. This equipment, which

A relatively short and unfamiliar chapter in the history of Kellogg Laboratory written by a member of the Caltech research team in radiology in the thirties who subsequently became director of the radiology department of the Huntington Memorial Hospital in Pasadena.

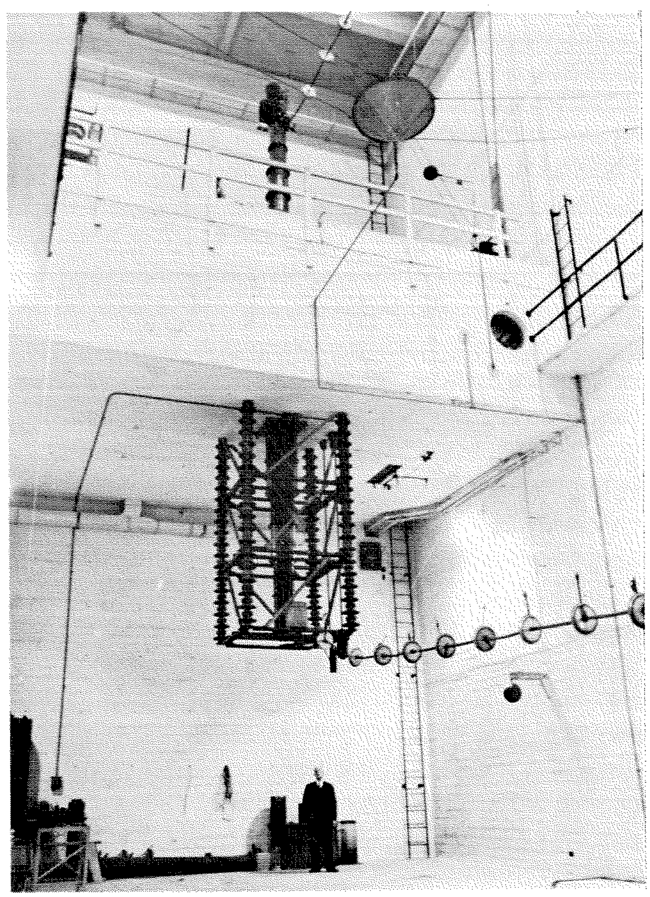
was designed for physical research purposes only, had been in successful operation for many months. It occurred to Dr. Lauritsen that the radiation produced by this tube might have some biologic effect which could be utilized in the treatment of disease. Because the writer was much impressed by Dr. Lauritsen's achievement, he suggested, after consultations with Dr. Millikan and Dr. Lauritsen, that he be permitted to put the tube to clinical tests. . . .

"Dr. Lauritsen has more recently constructed a tube with a capacity of 1,000,000 volts potential, and further research work is going on in the new Kellogg Laboratory. This department is under the immediate charge of Dr. Seeley G. Mudd, who has become greatly interested in the work and devotes his time and energy to the furtherance of the clinical experimentation. Dr. Mudd is assisted by Dr. Clyde K. Emery and by my clinical associates, Dr. William E. Costolow and Dr. Orville N. Meland as collaborators."

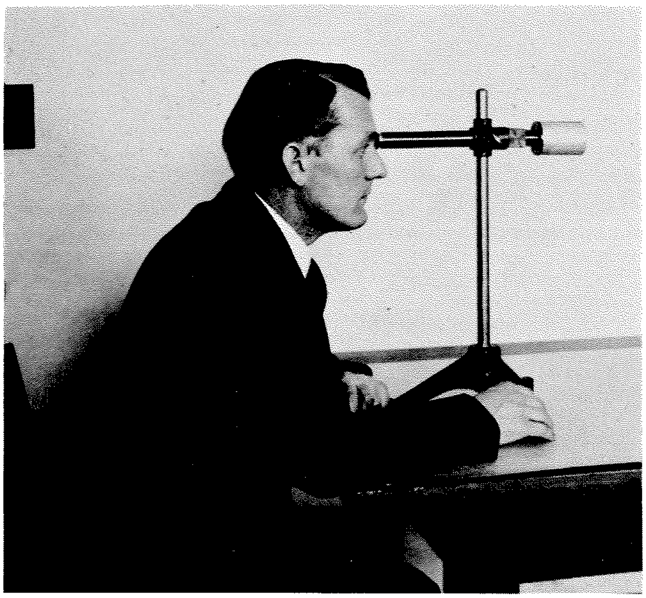
After the early 1930's Lauritsen was devoting his energy to physics, but admitted a primary duty, usually fulfilled during the night hours, of having the x-ray tube ready for an 8 a.m. starting time.

Seeley Mudd directed the clinical applications of the beam. Among those who participated in the work were Drs. Clyde Emery, George Sharp, Leo Levi, Melville Jacobs, Stewart Harrison, Henri Coutard, Mildred Wehrly (later to become an MD and radiation therapist at Orange County Hospital); and Virginia Johnson (later Kotkin). Among the graduate students who were engaged in the operation of the tube were Wilson Brubaker, H. Richard Crane, William A. Fowler, Thomas Lauritsen, and Louis Ridenour, Jr.

In his spare time, Lauritsen attacked the dose problem. The roentgen, which was proposed as a unit in 1926, measured the intensity of a beam of x-rays in air by counting the ion pairs produced. Its definition was ambiguous and the measurement doubtful or impossible at high energy. In September 1933 he wrote in the *American Journal of Roentgenology and Radiation Therapy*:



The upper and lower ends of the 30-foot x-ray tube—designed and built by C. C. Lauritsen and his associates in 1928—protrude from the concrete target enclosure in which patients were given radiation therapy at Kellogg.



C. C. Lauritsen takes readings of radiation intensity using an early model of the quartz fiber electroscope which he developed for measuring x-rays.

". . . This is satisfactory in practice as long as the problems dealt with are similar in nature and the quality of radiation is the same, but we have no right to expect that a given number of roentgens will produce the same effect regardless of the quality of the radiation. As a matter of fact, we can expect this to be so only in very special cases. It is much more reasonable to assume that equal effects are produced when equal quantities of energy are absorbed in a given volume."

"Obviously," he reported later in 1935, "any effect, whether physical or biological, is produced by that part of the energy which is truly absorbed in the volume under consideration. The energy which goes on through and the energy which is removed from the beam by scattering can have no effect within the volume. . . ."

The debate about dosage was vigorous, both here and in Europe. Professor Holfelder, a senior professor of radiology in Germany, claimed that "an increase in tube voltage above 200,000-volt peak is an illogical error that is accompanied by a completely unnecessary expenditure of money and results in a step backwards from what we already know." (I have tried to recapture in translation the professor's innate modesty.) Under Lauritsen's guidance, I showed that the more significant *depth* dose steadily increased with higher photon energy—a fact later confirmed experimentally. Such a phenomenon was of great interest to radiation therapists, who were concerned with possible damage to superficial tissues when treating deeper ones.

From 1930 to 1939 Mudd and his colleagues treated 746 patients with inoperable malignant lesions at the Kellogg Laboratory.

"It is obvious," they reported in 1938, "that it is too early to draw final conclusions regarding supervoltage irradiation. Fortunately, therapy of this type is being carried on in a number of laboratories in this country and abroad. It is to be hoped that cooperation between these clinics will result in a better understanding of the proper use of this agent."

In a final article that appeared in 1940, Mudd does not go beyond this, and it becomes apparent that the work of those days produced a clearer understanding of the problem, some improvement in the distribution of energy absorption when deep seated cancer is treated, but no evidence of a change in relative sensitivity; in short, "no breakthrough."

Early in 1939 the clinical studies were discontinued; all concerned were caught up in the steadily worsening world situation. After the war, by about 1950, cobalt 60 with a nearly monochromatic 1.3 MeV radiation was becoming available in sufficient quantity for clinical use in radiation therapy. With increasing energy of the primary photon (or particle) the absorption at deeper levels relative to the skin improved significantly. At these energies the roentgen fell into disuse and Lauritsen's workaday unnamed unit—100 ergs absorbed in 1 cubic centimeter of tissue—got its own name, the "rad," and, in 1956, became the official unit.

Cobalt 60 with its present known advantages of improved percentage depth dose, skin-sparing resulting from build up, decreased relative bone absorption, preferentially forward scatter—all predictable and predicted from the work in the thirties—is now used in the treatment of the vast majority of patients with deep cancer. (The machinery is also reliable and, for the energy and intensity available, not expensive.)

There is still no clear-cut evidence for a change in the relative sensitivity of normal cells and cancer cells, but a report from Louis Rosen at Los Alamos in December 1968 concludes *inter alia* that high energy negative pions, with high linear energy transfer on absorption, damage anoxic cells more readily than low L.E.T. radiation for the same damage to normal tissue. This will be a most interesting development if confirmed.