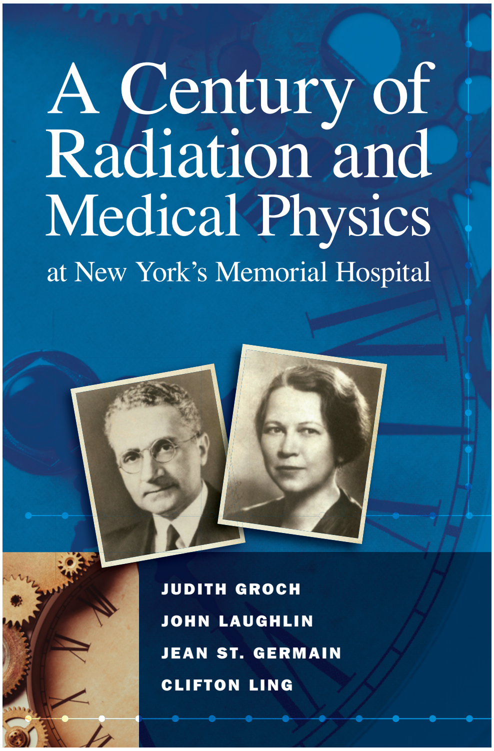

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John S. Laughlin:
A Founder of Medical Physics


John S. Laughlin

John Seth Laughlin (1918–2004) was born in Canton, Missouri. He received his B.A. from Willamette University in 1940, an M.S. from Haverford College in 1942, and his Ph.D. in nuclear physics from the University of Illinois in 1947. At the start of his career at the University of Illinois, Laughlin conducted research on particle accelerators, particularly on the early cyclotrons with P. Gerald Kruger and Donald Kerst.

In 1940, Kerst developed the betatron, a high-energy device used to accelerate beta particles (electrons) in a circular orbit. In addition to providing an increasing magnetic flux to induce electrons to accelerate and acquire energy, Kerst shaped the pole faces to establish a stable equilibrium orbit, with the electrons injected tangentially near this orbit. The accelerated electrons had a relatively monoenergetic spectrum, and their energy was easy to control. Kerst's first betatron operated at 2.3 MeV, the second at 20 MeV, and the next at 300 MeV.

During this period at the University of Illinois, Laughlin helped with the installation of the betatron and was involved in the first therapeutic applications of high-energy x-rays using a 20 MeV betatron, originally devoted to physics. In 1948, a graduate student at the University of Illinois developed a glioblastoma, and it was decided to use localized irradiation following surgery. Radiologist Henry Quastler and physicist Donald Kerst carried out a treatment with high-energy x-rays using 20 to 30 fields all angled and coming in from different directions, perhaps a precursor of conformal radiation therapy developed almost half a century later.

Although the dose was tumoricidal out to the margins of the lesion, the patient eventually died. A postmortem revealed no viable neoplastic cells in the irradiated region. This first use of high-energy photons pioneered the medical use of the betatron.

The Allis-Chalmers Manufacturing Company developed a commercial version of the betatron for reliable medical use. In 1948, one of these devices, a 24 MeV betatron, was installed at the Saskatoon cancer clinic in Canada under the direction of Dr. Harold E. Johns. Another device was installed at the University of Illinois, and nine months later in March 1949. In 1950, Dr. R. S. Harvey, chairman of radiology at Illinois, John Laughlin, and Lewis Haas, another graduate student, also at Illinois, started treating a relatively small number of patients using the betatron's high-energy electron beam.

Dr. James J. Nickson became chairman of Radiation Therapy at Memorial in 1950 and recruited John Laughlin to Memorial in 1951. There, he oversaw the installation of a 24-MeV betatron, donated by the Kress Foundation, and devoted to medical use. Its installation, completed in 1953, was the first high-energy electron-beam machine to be installed in a U.S. cancer center. A variety of high-energy accelerators were used almost exclusively for nuclear physics research; the betatron turned out to have practical applications in medical therapy and diagnosis. The absorption of electrons was shown to be quite different from the absorption of x-rays. As a consequence, the energy dissipated by the electrons was fairly uniform along the beam and terminated at a finite range. In a 1953 article published in *Electronics,* Laughlin wrote that low-energy x-ray beams produce their maximum dose on the skin, do not penetrate to great depths in tissue, are not well defined because of scatter, and are particularly destructive to bone. By contrast, he explained, the high-energy x-ray beam of the betatron is effective in irradiating deep-seated tumors with minimum damage to surrounding tissue. The maximum radiation dose is produced 3 cm to 5 cm below the patient's skin, and its side scatter is negligible. At these energies the beam is well-defined, permitting effective localization of the dose.

When the betatron's high-energy electrons are used, bone does not absorb any more dose per unit mass than soft tissue, circumventing a serious limitation in lower-voltage x-ray therapy. The maximum depth of penetration is proportional to the incident energy, while the decrease near the end of the penetration is fairly steep. Thus, the healthy tissue at greater depth is not exposed. Furthermore, Laughlin wrote, the betatron's electron beam could be used to treat lesions near the surface with finite maximum depth of penetration proportional to the incident energy.

The original betatron installed at Memorial was donated to the Smithsonian Institution in 1977.

In 1952, Laughlin was appointed chairman of the newly reconstituted Department of Medical Physics at the Memorial Hospital for Cancer and Allied Diseases and Chief of Biophysics at the Sloan-Kettering Institute. With the arrival of John Laughlin at Memorial, many gifted men and women were attracted to the growing staff. Medical physics experienced a period of growth and expansion with a brilliant flowering in an alliance between radiation physics and radiation therapy. Over approximately three decades, Laughlin's pioneering and legendary research eventually included every aspect of medical physics: advancing the quality of medical imaging and diagnostic radiology, improving the accuracy of radiation dosimetry and radiation safety, optimizing the delivery of radiation treatment, and studying the biological effects of radiation.

Laughlin made significant contributions to x-ray dosimetry and nuclear medicine. A few examples include an early interest in bone marrow dosimetry, the construction of a dual-headed gamma camera, the introduction of computer analysis in imaging applications, the potential for total-body scanning, the installation of a cyclotron for the production of short-lived radionuclides, and the placement of the first PET camera at the hospital.

A strong advocate of teaching, Laughlin and his colleagues taught hundreds of residents, graduate students, and radiological physicists. Many of the leaders in the current field of medical physics throughout the country received training in the "Memorial Program" created in this period.

In the mid-1950s, Rosalyn Yalow, a nuclear physicist and a close friend of Laughlin, and Solomon Berson had developed a radioimmunoassay procedure for insulin, based on the principle of competitive binding by antibodies of natural and labeled hormones. The method became the basis for numerous assays in diagnostic and physiological research, and for this work Yalow received the Nobel Prize for Medicine in 1977.

A Cyclotron at the Sloan Kettering Institute

Although cyclotron-produced radionuclides were used for biomedical research almost from the time that Ernest Lawrence dedicated his 60-inch unit as a medical cyclotron, such use was uncommon. Then in 1965, cyclotrons were installed at the Washington University School of Medicine by Michel TerPogossian and also at Massachusetts General Hospital by Gordon Brownell, who used cyclotron-produced positron emitters for metabolic studies.

In 1967, Laughlin installed a cyclotron at Memorial Sloan-Kettering Cancer Center in the new Kettering laboratory building, which had opened in 1964. A prototype machine designed and built by the Cyclotron Corporation could accelerate helium-3 ions as well as protons, deuterons, and helium-4 ions. The short-lived positron emitters were eventually widely used in PET scanning. This cyclotron was removed in 1995 and a new cyclotron was installed in the Citigroup Biomedical Imaging Center (CBIC), a consortium collaboration between MSKCC and the Weill School of Medicine of Cornell University.

Radiation Oncology: Coming of Age

In building Memorial's fledgling radiation therapy department, the recruitment of Laughlin for the physics department and the fostering of brachytherapy (by Dr. Ulrich Henschke and subsequently by Dr. Basil Hilaris) were significant development led by Dr. James Nickson. With great foresight, Dr. Florence Chu wrote, Dr. J. Nickson also established a Radiobiology Laboratory and expanded the department by increasing the staff and its meager equipment to include a 2-MeV x-ray machine and a 24-MeV betatron.

Nickson's most difficult task was to try to achieve total independence for the Radiation Therapy department from the "cancer specialist" surgeons. Following Memorial's long-standing tradition, the surgeons (and internists) refused to surrender their radiotherapy privileges, even though the techniques had developed at a pace far beyond their grasp. Weary of the endless battle, Nickson resigned in 1965 and moved to the University of Chicago. His associate, Dr. Marvin Glicksman, also left for the pion project at the Los Alamos Laboratory. Dr. Ralph Phillips, who had previously taken leave for illness, returned eventually to become the Chairman of Radiation Therapy. Phillips served until his retirement in 1968 when Dr. Giulio D'Angio of Philadelphia was recruited to be department chairman.

D'Angio strengthened the training programs and created new treatment and research programs for pediatric and other cancers, and he studied the radiosensitizing effects of hyperthermia. D'Angio also established a total skin electron bean therapy (TSEB) protocol, using linear accelerator electrons to treat skin lesions, and put Dr. Lourdes Nisce in charge of the program. This treatment protocol required major support from Medical Physics, including the construction of whole-body chambers to monitor the doses, the tailoring of blocks to lower the dose to the lung, and precise dose calibration at different treatment distances. Like his predecessors, however, D'Angio struggled with the surgical orientation of Memorial's clinical programs. He resigned in 1976, returning to pediatric oncology practice in Philadelphia.

Dr. Florence Chu served as Chairman of the Department of Radiation Therapy, later renamed the Department of Radiation Oncology, from 1977–1984. Born in Shanghai, China, in 1918, Florence Chu came to Memorial in 1949 as a special fellow in radiation therapy and entered the Department of Radiation Therapy under Dr. Phillips. After 1984, Chu remained in the department for two more years.

Chu worked to upgrade the five treatment units and to replace these units one by one. With the strong support of the physics team led by Laughlin, there were further developments in brachytherapy and, in addition, a sea change in the treatment policy for early-stage breast cancer. Memorial was known for advocating radical and supraradical mastectomies, but with mounting clinical data, the surgeons reluctantly accepted the newer treatment of breast-conserving surgery (lumpectomies) followed by focal radiotherapy.

In 1984, Dr. Zvi Fuks, previously chairman of Radiation and Clinical Oncology at the Hebrew University–Hadassah Medical School in Israel, became chairman of the Radiation Oncology department. As a further indication of the change in emphasis, Dr. Samuel Hellman, previously at the Joint Center for Radiation Therapy of Harvard Medical School, was named Physician-in-Chief of Memorial Hospital, the first non-surgeon to hold this position.

In the late 1950s and early 1960s, brachytherapy techniques still used radium needles and radon seeds. Given the growing concern about the harmful effects associated with the use of radium, the use of brachytherapy faced mounting problems from physicians, nurses, and patients, as well as from state, city, and hospital radiation safety regulations. Many hospitals, including Memorial, found it increasingly difficult to recruit and retain personnel willing to care for patients using high-energy radioactive materials.

If someone wanted training in modern brachytherapy, according to Dr. Basil Hilaris, author of a detailed book on the history of brachytherapy, the only place available in the late 1950s and early 1960s was Memorial Hospital. There, Dr. Ulrich Henschke and his group, including Dr. Hilaris, were developing innovative techniques based on afterloading and using iridium as a substitute for radium.

Henschke had arrived at Memorial Hospital in 1955, after working on afterloading at Ohio State with Dr. W. Myers, on small ^{60}Co and ^{198}Au radioactive sources. There he made practical the principle of afterloading radioactive sources for intracavitary or interstitial applicators.

Henschke remained at Memorial until 1967, at which point he left for Howard University where in 1970 he was appointed professor of radiotherapy. Upon Henschke's departure, Hilaris took over the clinical leadership in brachytherapy. In 1979, he was named chief of Memorial's newly formed Brachytherapy Service in the Department of Radiation Oncology, a position he held until 1988. Some two-thirds of all brachytherapy techniques used in the United States originated at Memorial, where over the years, the growth of the technology surrounding afterloading and the use of radium-substitute materials was a highly successful collaboration. Writing in 1989, Laughlin noted that in the 1960s these major innovations were important for using brachytherapy sources and in reducing radiation exposure for the staff.

The Era of Cobalt

Beginning in 1951 in the United States, reactor-produced cobalt-60 (^{60}Co) was advocated for several years for both externally and internally administered radiation treatment. The first commercial ^{60}Co teletherapy machines ("tele" from the Greek means *at a long distance*) became available in the 1960s. Harold Johns and his associates described the installation of such a machine in Canada, and the design was adapted for commercial purposes by Atomic Energy of Canada, Ltd.

Because ^{60}Co had the major advantage of not requiring associated power supplies, complicated acceleration apparatus, and had an energy just high enough to provide some skin sparing. Although linear accelerators eventually became the primary method for radiation treatment, cobalt units had a major advantage in that they could be installed almost anywhere.

The production of ^{60}Co permitted very high activities, leading to higher dose rates than the 250 kVp x-ray units. In addition, the availability of ^{60}Co spelled the end of radium teletherapy, along with the need to dispose of the seminal element and dismantle its housing.

The cobalt source was contained in a sealed capsule placed in a treatment head containing depleted uranium shielding and with trimmers to refine the treatment field. The source head was mounted on a gantry capable of rotating a full 360 degrees with the patient under treatment at the center of the rotation.

Because ^{60}Co decays with a half-life of 5.25 years, the sources had to be replaced periodically to maintain the desired treatment dose rate, typically from 100 to 150 rad/min. The source drawer moved from the treatment position to a shielded position by means of a hydraulic system. Since the source could never be turned "off," there would be some measurable radiation levels, so-called "leakage" radiation, at all times. The higher photon energies also meant that a more heavily shielded room was required than that needed for the 250 kVp x-ray units. Moreover, the entire facility required more space.

1967: New Department—the Firestone Center

A new Radiation Therapy department was planned in the 1960s where newer machines would be installed adjacent to the existing betatron. Planning and construction took place from 1965 to 1967, at which point the new department opened as the Russell Firestone Radiation Therapy Center. The complement of machines included the existing betatron, three ^{60}Co units, and one of the first commercially available linear accelerators, a Clinac 6 manufactured by Varian Associates, Inc. The department also used the 250 kVp machines for specific treatments until their removal after the construction of a new outpatient building in 1972.

In 1968, the James Ewing Hospital, built in 1947 by New York City for indigent patients and staffed by Memorial Hospital physicians, was merged with Memorial Hospital and renamed the Ewing Pavilion. The renovated division functioned initially as a hospital and was subsequently renovated in 1982 as the Schwartz Laboratory building, housing clinical and research laboratories and clinical offices.

The Arrival of Linear Accelerators

Before and during World War II, in England and the United States, oscillator tubes capable of relatively high power output at microwave frequencies were developed for the military and applied to radar. After the war, groups at Stanford University and in England led the development of linear accelerators designed for medical use.

In the decade following World War II, with the development of particle accelerators—especially the betatron and the linear accelerator—a new era arrived with the potential for optimal radiation treatment with high-energy x-rays and electrons. According to Laughlin, by 1982, in the United States alone, hospitals were using approximately 700 linear accelerators and 35 betatrons for cancer therapy.

The first medical linear accelerator was installed at the Hammersmith Hospital in England in 1953. In 1956 in the United States, Henry Kaplan used a Varian 6 MV linear accelerator to treat patients at Stanford University School of Medicine. Varian then manufactured a commercial 6 MV linac with a 360-degree rotation that was installed at UCLA in 1962. At Memorial, the first linear accelerator was installed in 1966 during the renovation of the department described above.

Treatment Planning and Dosimetry

The advance described above was accompanied by dosimetry problems. No longer could skin reddening (erythema) be a treatment guide because the maximum deposition of energy now occurred below the surface for deep-seated lesions. With the ability to concentrate the radiation dose, it became critical to locate the target region as accurately as possible, to plan the treatment in three dimensions, and to deliver the treatment precisely. The attending dosimetry problems were far more difficult than those for orthovoltage x-rays. Thus, treatment planning became an important aspect of radiation treatment. The calculation of the energy deposited per unit mass of tissue for x-rays, electrons, and heavier particles preoccupied many radiological physicists and, according to Laughlin, the publication of studies could "undoubtedly be measured in tons."

In the mid-1950s, Laughlin and his colleagues at Memorial Sloan-Kettering developed an absorbed-dose calorimeter using a thermally isolated wafer surrounded by a homogeneous absorbing medium. Both temperatures were monitored with thermistors that were part of a bridge. The unit, fabricated of carbon and polystyrene for the dosimetry of x-ray and electron beams, was calibrated electrically by passage of a known current through the wafer.

To achieve a tumoricidal dose and yet avoid irreparable damage to irradiated healthy tissue, the radiation physician had to achieve a specified tumor dose, usually within 5% uncertainty. Failure to adequately accommodate inhomogeneities in treatment planning could substantially affect the actual tumor dose, Laughlin wrote, while an error in delivering any beam of radiation on any day of treatment could negate care in the remaining treatments. Finally, Laughlin noted, the therapy plan could require modification during treatment if check-up examinations revealed changes in the tumor's configuration or its surrounding tissue.

Brachytherapy was highly dependent on computer technology. In the late 1950s, Laughlin and his physics colleagues were instrumental in using computers to calculate the dose distributions for implanted radionuclides. An IBM 1800 computer, then considered state-of-the-art, was installed in the cellar of the Kettering Laboratory building to perform treatment planning calculations and radionuclide imaging.

K. C. Tsien, a medical physicist, had previously demonstrated the feasibility of external beam isodose computation, while other members of Laughlin's group, particularly Mary Lou Meurk and Richard Nelson, developed computational methods for interstitial and intracavitary brachytherapy. The methods for radium dosimetry relied on calculated doses to specific locations (Points A and B). The system developed by Quimby defined doses from line sources, and it was eventually replaced by the Paterson-Parker system, which allowed for volume calculations. Treatment times were specified in terms of the equivalent times previously used with radium, mg-hours radium equivalent. It was becoming increasingly evident that the dosimetry calculations were going to require more complex methods.

Automatic computation methods developed at Memorial, MD Anderson, and other institutions, provided the dose distribution throughout the volume of the implant rather than at a few points. For example, a method developed in 1976 made it possible to determine the optimum strength and location of cesium-137 sources in intracavitary applications. At 16 specific points, the clinician could determine the necessary source strength at each source position.

Simulators Arrive

Dosimetry experiments with betatrons had made it clear that since the body was not uniformly dense, corrections to the treatment plan were necessary for inhomogeneities within the treatment field. It followed that similar problems existed for other radiation modalities.

Simulators developed from modest origins, in which diagnostic x-ray tubes were mounted on improvised stands connected to, or adjacent to, a treatment couch. In one of the first attempts to measure densities in cross-sectional anatomy, Laughlin and his associates mounted a sealed source on an arm that passed transversely over the body section and detected the radiation that passed through the body.

Toshiba adapted this methodology, substituting an x-ray machine for the source, and the company installed a transverse axial tomograph in the department in the late 1960s. The results were used to modify treatment plans to account for density differences and anatomy. It soon became apparent that more accurate plans would be possible with more information.

The first commercial simulator was installed in the 1970s, using an x-ray tube as the radiation source. Simulators had the same geometry as that of the treatment machine and allowed a simulation of the patient's treatment prior to delivering the first treatment on a radiation machine. During the simulation sessions, kV x-ray images of the patient's treatment field were captured on film and reviewed by the physician. Thus, with the use of a simulator, refinements in the treatment field and patient geometry could be incorporated before the start of treatment. During patient setup for treatment, the simulation films may be compared to portal films to verify the accuracy of the radiation field to be delivered.

This concludes the first half of Chapter 4 of *A Century of Radiation and Medical Physics at New York's Memorial Hospital.*

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