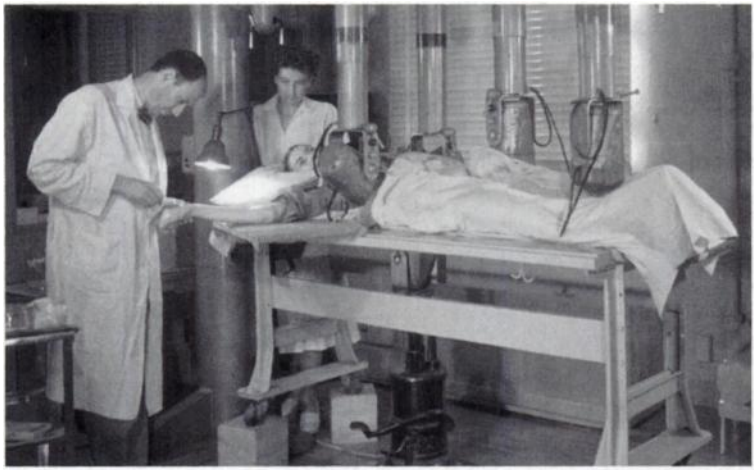
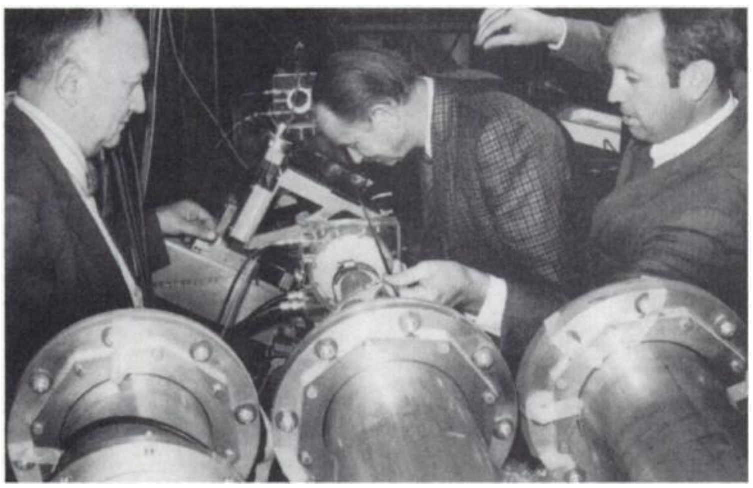
NEWSLINE

Donner Laboratory: The Birthplace of Nuclear Medicine





Top photo: The movement of radioactive tracers through the body was an early application of the Multiprobe Detector "Monster" for in vivo kinetic analysis.

Bottom photo: The first known human experiment which demonstrated the mechanism for light flashes, which were observed by astronauts on the Apollo missions to the Moon. (From left) Drs. Cornelius Tobias, Thomas Budinger, and Edward McMillan make the first observations of accelerated nitrogen ions.

Many nuclear medicine historians claim that the genesis of nuclear medicine in the United States took place more than 60 years ago when John Lawrence took a leave of absence from his faculty position at Yale Medical School to visit his brother Ernest Orlando Lawrence at his new radiation laboratory (now known as the Ernest Orlando Lawrence Berkeley National Laboratory) in Berkeley, CA. Ernest Lawrence, who invented the cyclotron in 1929 (for which he won the 1939 Nobel Prize in Physics), established the laboratory in 1931 and had already committed much of the fledgling lab's research program to the discovery and production of artificial isotopes. Excited by the possibilities for using these isotopes in medicine, John Lawrence left Yale in 1936 to join his brother, founding a program which later evolved into the Donner Laboratory and sparking the birth of a new field of medicine and research. Because of his lifelong contributions and pioneering work, John Lawrence became known as the "father of nuclear medicine."

"John Lawrence saw the opportunities for diagnostic and therapeutic uses of the radiation beams and isotopes being produced through the then-new cyclotron," said Thomas F. Budinger, Head of the Center for Functional Imaging (CFI) at Berkeley. One of the opportunities Lawrence saw was the use of radioactive iron for the study of hematology, which was a field of expertise for Lawrence, who was a hematologist and endocrinologist by training and author of one of the first definitive clinical texts on polycythemia vera. Having worked at Harvard as an endocrinologist under Harvey Cushing, MD, it wasn't surprising that Lawrence became interested in treating "Cushing's" disease with radioactive beams.

Early Interests of the Donner Lab

"The development of tracers for iron and bone marrow metabolism, as well as tracers and techniques for therapy, were two early activities that he was most interested in," said Budinger. After extensive studies of the biological distribution of phosphorus-32, Lawrence used it to treat a leukemia patient, the first time that a radioactive isotope had been used in the treatment of a human disease. Lawrence went on to use phosphorus-32 to treat polycythemia vera, rationalizing that the radioactive phosphorus would inhibit the progenitors of the excessive numbers of red cells produced by this disease.

Several of the well-known radioisotopes used in nuclear medicine were discovered at the lab, including technetium-99m, carbon-14, fluorine-18, oxygen-15 and thallium-201. One of the earliest was sodium-24, which the lab created by bombarding rock salt with deuterons. Ernest Lawrence touted its properties as being nearly ideal for many medical applications, such as the treatment of cancer. Although radiosodium never lived up to those expectations, in 1937, Joseph G. Hamilton used it for human physiology studies to determine, among other things, the speed of sodium's absorption into the circulatory system when ingested.

Just as John Lawrence wanted to study bone marrow with radioactive iron, Hamilton was also interested in using radioactive iodine to study and treat the thyroid. In order to avoid medical side effects in patients, Hamilton realized that a radioisotope with a short half-life would be needed. "In the spring of 1938, he asked his colleague Dr. Glenn Seaborg, a nuclear chemist at the Lab, if he could find an isotope of iodine with a half-life of about one week," said Budinger. "Seaborg and Jack Livingood prepared a tellurium target which they bombarded with deuterons and neutrons from a 37-inch cyclotron. After a chemical separation, they found an 8-day half-life iodine-131."

Drs. Ernest and John Lawrence at the controls of the 60-inch Cyclotron completed in 1936.

The work at the new lab soon caught the attention of William H. Donner, president of the International Cancer Research Foundation (later renamed the Donner Foundation). His son's death from cancer had motivated Donner's interest in cancer research. In 1940, he visited the Lab after hearing about Lawrence's pioneering work in treating cancer with neutron beams. Impressed, Donner donated $150,000 for a building to house the new work being done in "medical physics," and construction of the new facility began the following year. A brass plaque located today at the entrance of Donner Laboratory is dedicated in memory of Joseph William Donner and reads "for the Application of Physics, Chemistry, and the Natural Sciences to Biology and Medicine."

With America's entree into World War II, Lawrence and his colleagues began adapting nuclear medicine techniques for wartime uses. The "bends" were a big problem for fighter pilots at a time when pressurized cabins didn't yet exist. "A lot of activity got pushed into researching high-altitude physiology," said Budinger. "A high-altitude chamber was built in order to understand high-altitude sickness and for the purpose of figuring out how to get pilots safely out of airplanes at high altitudes so they could survive." Donner Lab researchers used radioisotopes of inert gases to study decompression sickness, as well as other maladies. These tracer studies helped increase understanding of the circulation and diffusion of gases, and led to the development by the Lab's Cornelius Tobias of aircraft oxygen measurement equipment, which in turn led to the development of an automatic parachute opener.

Following World War II, the Donner Lab devoted some resources toward the study of radiation health effects. However, the main focus of the researchers continued to be on the physiology and biophysics of such diseases as polycythemia vera, multiple myeloma and leukemia, and the use of radioactive tracers for treatment. "This naturally led to attempts at imaging tracers," said Budinger. "There was a multiple probe device that had photo tubes with scintillators and big lead shields on gantries. It had ten arms with scintillation counters that could be positioned so that one could count over the spleen, the liver, the brain and the bone marrow. Instead of a whole body image, it did specific region images, looking at the uptake curves and creating a kinetic model from which, for example, the turnover of iron could be deduced."

In early 1950's, Hal Anger began conducting his seminal studies on medical imaging, gradually developing the scintillation camera, also known as the Anger Camera, from which modern imaging systems such as PET and SPECT evolved. Other work at the lab included the development of the first stereotactic radiation system used to distribute a proton beam around the pituitary, the study of disorders such as Parkinson's disease and Alzheimer's disease and work in delineating the major lipoprotein components in human plasma.

Current Areas of Research

While the Donner Laboratory's focus has expanded into other areas of interest, work in nuclear medicine research is now revolves around the Center for Functional Imaging (CFI). "There are about 40 people here at the center," said Budinger. "Our main research instrumentation is a high-resolution PET with 2.6 millimeter resolution. And there's now a dedicated cyclotron which was finally commissioned last August." The new cyclotron is part of the new Biomedical Isotope Facility, led by Henry Van Brocklin, which was built to produce short-lived isotopes solely for work at the Center. An underground pneumatic tube system links the new facility to the center and can transport radioisotopes between the two buildings in eight seconds.

Current work at the Centerincludes the design and building of several new high-resolution PET cameras, including a laptop computer-sized, compact scintillation camera. The design for the new scintillation camera is being developed by CFI senior staff scientists Stephen Derenzo, PhD, Ronald H. Huseman, PhD, and William Moses, PhD, and graduate student Gregory Gruber. "We're trying to work out arrangements with some commercial people to help us build the prototype," Budinger. said "For now we're moving ahead independently with our own project. I believe we will make it work." The implications would be enormous: "This means that for less than $50,000, a nuclear physician could have a gamma camera in his or her office," said Budinger. "I think it'll be pretty convenient for patients to be evaluated post-op with an imaging device that can be maneuvered easily on something similar to the gantry of a dentist's drill system." The new compact gamma camera could possibly lead to a similar laptop-sized animal imaging system.

The major new work in instrumentation for PET at CFI is a scintillation system with a new detector design that overcomes the problem of depth of interaction. "We've been working on a silicon photo diode array which is connected to the detector system for finding the depth in the crystal at which scintillation occurs," says Budinger.

Another surprising area of interest at CFI has been in the study of nerve regeneration in patients with spinal cord injuries. "We now have the resolution on PET imaging to evaluate the usefulness of techniques used to regenerate nerve cells," said Budinger. As he sees it, the main reason medical researchers had not previously given this area of study much thought simply boils down to attitude. "When I was in the Coast Guard there was a general attitude that if something was badly damaged, like a sinking ship, then it wasn't worth trying to save it," Budinger said. "People get paralyzed by that kind of thinking."

—Jeffrey E. Williams

Directions

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both radiolabeled monoclonal antibodies and peptides holds great promise for future expansion of nuclear medicine.

These are just a few of the many areas in which JNM must act as an archive for anyone interested in nuclear medicine. The specifics of how to accomplish this are what have occupied my thoughts lately as I run. To strengthen its position as the preeminent publication in its field, the Journal will forego publishing case reports to concentrate on more substantive, multicase studies. Emphasis will once again be placed on encouraging investigators to publish their ongoing and innovative data in "Rapid Communications." These authors will be invited to subsequently elaborate on their findings in a full-length article. Also, in an effort to increase visibility for educational articles in the Journal and to provide continuing medical education (CME) credit, each special contribution will run simultaneously on the SNM's website as a CME article. In addition, when a clinical or basic science article's illustrations exceed the space limits of the Journal, some of these may appear online. These and other efforts to use the internet will be developed to expand the reach of the Journal.

As did the six distinguished editors before me, I will do everything I can to ensure that JNM offers its readers the highest quality scientific articles possible. I will work with the associate editors and the Editorial Board to see that the Journal not only reflects current advance in nuclear medicine but acts as a catalyst for those who seek answers in brand new directions. Last, but most important, the Journal belongs to the SNM; therefore, its future depends on the members at large who are its readers, its authors and its reviewers. It is their willingness to provide constructive suggestions for improvement, to understand that not all manuscripts can be published and to complete reviews in a timely fashion that has guided JNM to its great success. I look forward to being a part of that continuing journey.

—Martin P. Sandler, MD
Editor-in-Chief
The Journal of Nuclear Medicine