

HISTORY CORNER

Hal Anger: Nuclear Medicine's Quiet Genius

Hal Anger is one of those individuals who have made truly revolutionary contributions to nuclear medicine. As we continue to celebrate the SNM's half-century anniversary, it seems an appropriate time to remind our colleagues of Anger's work. Millions of patients all over the world have benefited from diagnosis and treatment that depended on the use of the Anger camera and the innovations made possible by its development. Yet many of our younger colleagues are unfamiliar with the story of its genesis and the ingenuity and dedication that Anger brought to this and other innovations in our field.

Anger was born on May 24, 1920, in Denver, CO. His father was a first-generation German-American and his mother was British-American. When he was 5 years old, his family moved to Long Beach, CA, where he entered the Long Beach public schools. Showing an early interest in electronics, he built a television set from scratch while at Long Beach Junior College in the late 1930s—an impressive feat at a time when the technology was new. From Long Beach, he entered the engineering school of the University of California at Berkeley, where he was inspired by J.V. Lebacqz, who was at work on a seminal text on pulse generators. Anger received his bachelor's degree in electrical engineering in 1943. During World War II, Anger was among those who worked to develop radar at Harvard's Radio Research Laboratory.

Anger went to work in 1948 at the Donner Laboratory, part of the larger Berkeley Laboratory that had been founded by the Nobel laureate Ernest O. Lawrence in 1931. John H. Lawrence, Ernest's brother, was head of the Donner Laboratory, and, like his staff members, was dedicated to finding new ways to apply radioisotopes in medical diagnosis and treatment. Anger's immediate boss was Cornelius (Toby) Tobias, one of the many Hungarian refugees who came to the United States in the pre-war years and who contributed so much to the development of the radiation sciences. Tobias was a founding member of the Donner Laboratory and pioneered the study of the biologic effects of cosmic rays. At the lab, he worked with Luis Alvarez and Emilio Segré, who would also become Nobel laureates. Tobias's career at the lab spanned more than

The monthly excerpts from past years of SNM annual Highlights Lectures do not appear in Newsline this month so that this well-deserved tribute could be published. The Highlights feature will resume next month with excerpts from 1986.



Hal Anger in 1965 with the whole-body scintillation scanner at the Donner Laboratory. The small holes in the foreground are part of the collimator. From the collection of Henry N. Wagner, Jr., MD.



Anger is known internationally for his achievements in imaging technology. This photo was taken at the Deutschen Gesellschaft für Nuklearmedizin in 1966. From the collection of William G. Myers, MD.

40 years, and among his many accomplishments were the use of ^{11}C in studies of oxygen deprivation in pilots and the use of xenon gas as an anesthetic. Tobias is best known for his work in radiation therapy, using the fifth in a series of cyclotrons engineered by Ernest Lawrence. It was to this 184-inch cyclotron that Anger was assigned as an engineer.

Among the first projects Tobias assigned to his new employee was modification of the 184-inch cyclotron so that it could be used for irradiation of pituitary tumors with high-energy deuterons. The cyclotron had been converted during World War II to a large-scale spectrograph (or "calutron") for the production of ^{235}U for the first atomic bomb. After a mass spectrograph was built in Oak Ridge (TN) to produce

large amounts of fissionable uranium and plutonium isotopes, the Berkeley cyclotron was reconfigured for biologic and medical purposes. In addition to engineering this modification, Anger also worked briefly with Alvarez on the development of contrast agents for cholecystography.

The first of Anger's major contributions to biochemistry and nuclear medicine was the invention of a workable well counter in 1950. The device used anthracene crystals arranged around a well-like compartment to assay radioactivity in liquids placed in small glass vials (*Rev Sci Instrum.* 1951;22:912-914). Well counters soon became the most widely used instruments in radiation chemistry.

The January 1951 issue of the journal *Nucleonics* carried news of the invention of the rectilinear scanner by Benedict Cassen, chief of medical physics at the University of California at Los Angeles. Anger recognized that the mechanical movement of the crystal radiation detector back and forth over the patient's body was a serious limitation. Only photons directly under the moving scanner could be detected at any given time; the rest of the emissions were "wasted." Anger set out to develop a device that could simultaneously record emissions from large areas at the same time.

The first gamma camera report by Anger was published in 1952 on the use of a pinhole camera for in vivo studies of a tumor using ^{131}I (*Nature.* 1952;170:200-201). Gamma photons from ^{131}I in a patient with metastatic cancer near the skin were used to produce images on a large piece of photographic paper with a pinhole collimator in front of a thallium-activated sodium iodide crystal that was 5/6-inch thick. The apparatus was developed further, as reported in 1954 (Berkeley, CA: University of California Radiation Laboratory, Publication 2524, 1954).

The first Anger scintillation camera was described in 1957 in an article entitled "A new instrument for mapping gamma-ray emitters" (Berkeley, CA: University of California Radiation Laboratory, Publication 3653, 1957). This camera used a sodium iodide crystal 4 inches in diameter, optically coupled with 7 photomultiplier tubes. Although Anger had previously had little contact with Ernest O. Lawrence, Tobias brought the laboratory director to see the new invention. Lawrence immediately noted that it would be to Anger's advantage if the lab could get the invention released from the Atomic Energy Commission (AEC), so that the inventor could seek patent rights. With help from Tobias and John Lawrence, the AEC released the rights to Anger, who, in 1958 obtained U.S. patent #3011057 on the scintillation camera that would be known by his name. The instrument was exhibited at the 1958 SNM annual meeting and later that year at the meeting of the American Medical Association. Despite early problems with the small detector size and relatively poor detection efficiency (at first only patients who had received therapeutic doses of ^{131}I could be imaged), the invention was well received and went on to meet with great commercial success.

When Alexander Gottschalk was sent by Paul Harper at the University of Chicago to the Donner Laboratory to work

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The Importance of $^{99\text{m}}\text{Tc}$ and the Early Success of the Anger Camera

The limited number of photons from radionuclides such as ^{131}I did not produce very impressive images with the original Anger camera. Fortunately, in 1960, Stang and Richards advertised on the cover of the bulletin of the Brookhaven National Laboratory the availability of $^{99\text{m}}\text{Tc}$, obtainable from a ^{99}Mo generator. Paul Harper at the University of Chicago recognized that $^{99\text{m}}\text{Tc}$ had physical characteristics that were ideal for nuclear imaging: (a) It was metastable, decaying to ^{99}Tc without emitting radioactive particles, which meant that it could be administered safely in large doses, an extremely important advantage for the scintillation camera; (b) Its 160-keV photon emission was suitable for the human body; and (c) It was readily available by elution from the ^{99}Mo generator.

At the Oak Ridge Laboratory, officials of 3 major radiopharmaceutical companies stated at a scientific meeting in 1960 that "hospitals will never undertake the chemical elution of a generator in preparing doses for administration to patients." Fortunately, this viewpoint was not shared by other scientists, and $^{99\text{m}}\text{Tc}$ was on its way to becoming a workhorse of nuclear imaging.

Another key person in the development of the Anger scintillation camera was the late William G. Myers of Ohio State University, one of my predecessors as historian of the SNM. As a graduate student at Ohio State, Myers's doctoral thesis was on the potential role of the cyclotron in biomedicine as the source of positron-emitting radiotracers. Myers had participated in the atomic bomb testing at Bikini before becoming an internist and nuclear physician. He traveled every summer to the Donner Laboratory to direct a course in the use of radioactive tracers in biomedicine. He recognized immediately the importance of the invention of the scintillation camera and became its strongest proponent. He persuaded Charles Doan, head of the Department of Internal Medicine at Ohio State, to place an order for the first commercial version of the scintillation camera. This was to be built under the leadership of John Kuranz, president of Nuclear Chicago, a new business. Kuranz's employee, Edward Reible, was assigned to work with Anger to build the camera. After substantial delays, the camera went into production and became one of the first wide commercial successes of nuclear medicine practice.

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with the new Anger camera in July 1962, he immediately recognized the importance of Anger's work. In 1963, the 2 researchers described the localization of brain tumors with the "positron scintillation camera" (*J Nucl Med.* 1963;4:326–330). This represented the first clinical use of the positron scintillation camera and was an extension of the camera with an instrument that Anger had described in 1958 (*Rev Sci Inst.* 1958;29:2733). Gottschalk arranged for Anger to move the new device to the Alta Bates Hospital in Berkeley, where patients with brain tumors could be imaged.

The radionuclide used by Anger and Gottschalk was the positron-emitting ^{68}Ga , with a half-life of 68 minutes. This nuclide was obtained by elution from a germanium–gallium generator system. The chemist at Donner, Yukio Yano, carried out the preparation of the ^{68}Ga tracer. The new camera had an 11.5-inch diameter sodium iodide crystal, which made it possible to examine the entire brain. Anger and Gottschalk studied 25 patients and compared the results with those from the ^{203}Hg -neohydrin rectilinear scanner images.

At the annual meeting of the SNM in Berkeley in 1964, Anger and Gottschalk presented a talk on the diagnostic applications of the scintillation camera, using ^{203}Hg -neohydrin and ^{131}I -hippuran. Anger also collaborated with another Donner physician, Donald Van Dyke, in applying positron-emitting ^{52}Fe to the use of the camera in imaging the distribution of iron in the bone marrow of patients with hematologic disorders and Paget's disease. The results of this work were also presented at the 1964 SNM annual meeting. By 1965, Anger

and Gottschalk had modified the camera with focused collimation rectilinear scanning to provide the first instrument capable of producing multiple images focused at different depths from a single scan of a patient.

In recognition of his work, Anger received a Guggenheim fellowship in 1965 to extend his research efforts. After a long and fruitful tenure at the Berkeley laboratory, Anger retired in 1982. He published more than 90 journal articles, 22 book chapters, and held 14 U.S. patents during his career. His accomplishments have been recognized with numerous awards and honors, including the 1991 von Hevesy Prize from the Georg von Hevesy Foundation, based in Zurich, Switzerland. In 1994, he was the first person to receive the SNM Education and Research Foundation's Cassen Prize for distinguished achievement in nuclear medicine. He continues to live in California, where he pursues a lifelong interest in photography.

Anger's contributions to nuclear medicine—and the effects these had on the subsequent technical direction of the field—cannot be summarized in the limited space available here. Many innovations still under development depend heavily on insights and innovations that Anger brought to the field more than 50 years ago. It is clear that the nature of 21st-century nuclear medicine has been profoundly affected by this unassuming, original, and inventive individual.

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