Nuclear Medicine Pioneer, Hal O. Anger, 1920–2005

Hal O. Anger, the inventor of the first successful radioisotope camera and numerous other innovations that moved nuclear medicine from a laboratory application to a routine and essential part of clinical practice, died on October 31 at his home in Berkeley, CA. He was 85 years old. In 1998, Newsline writer Eleanore Tapscott talked with Anger and with many of those who were influenced by his innovations. The resulting article is reprinted here in its entirety from the March, 1998, issue of The Journal of Nuclear Medicine's *Newsline section as a tribute to one of the disciplines most creative and far-thinking founders.*

With his invention of the first clinically successful radioisotope camera (the scintillation, or Anger gamma, camera) more than 40 years ago, Hal O. Anger, BS, DSc, created the foundation for the sophisticated imaging systems available today. A quiet, modest and unassuming gentleman, Anger firmly resists labels that would depict him as a scientific or nuclear medicine icon. Instead, he views his work and accomplishments as an outgrowth of his desire to create products that would help people. It is apparent, however, that Anger was quite influential in changing nuclear medicine from a static imaging technique to one that highlights its tomographic and functional capabilities.

Anger was born in Denver in 1920. He had an avid, lifetime interest in science. While in high school, he often listened to a University of California–sponsored program, "The University Explorer," that discussed, among other things, Ernest Lawrence's cyclotron and the radioactive isotopes that it could produce. After graduation from high school, he began his undergraduate training at Laguna Beach Junior College in California before transferring to the University of California Berkeley (UCB), where he received a bachelor of science degree in 1943. As an undergraduate, a course of great interest to him was one simply titled "Research," taught by Professor Jean V. Lebacqz. "The course was so interesting to me," Anger recalls, "because it gave me an opportunity to build things."

Toward the end of his college career, he invented a radar pulse, which he later learned had been invented independently by the British, that was used by the Allies in World War II. After graduation from UCB in 1943, he continued working on radar research in the Radio Research Laboratory at Harvard University until the end of the war.

Still interested in the emerging field of radioisotope research, Anger applied for employment at UCB's Lawrence

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A Personal Note

I went to the Donner Laboratory in July 1962 to see if I could do research. Dr. John Lawrence, the director of the laboratory, hired me because he needed a radiologist to align the proton beam from the Berkeley cyclotron to treat the pituitary of patients with endocrine-responsive cancer, acromegaly, and diabetic retinopathy. I had just finished my radiology residency and was not sure whether I was going to be a diagnostic radiologist or a radiation oncologist. At the time, I had virtually no interest in nuclear medicine. I dutifully listened when Lawrence told me he had an engineer who had developed an interesting nuclear medicine imaging device and who really needed to collaborate with a physician. I said I would certainly like to find out about it, and he introduced me to Hal O. Anger. Hal gave me a few reprints about his camera, which he had recently finished. From that moment, I was intrigued and would go on to work with Hal at Donner for two years and as long-distance colleagues for many more. Luck and curiosity on my part started my relationship with Hal. But his personality had as much to do with it as anything. Although many individuals have noted that he was quiet and unassuming. I worked in Hal's lab, and he was the boss—although he was never bossy. When we disagreed, common sense and science were always used to resolve differences. I was attracted to nuclear medicine not only by Hal's camera, which took better pictures than I was used to seeing, but by Hal's personality, which made it very easy to work with him. For more than 40 years, Hal was a good friend. We are very fortunate to have had him in our field.

Alexander Gottschalk, MD
Professor of Radiology
Michigan State University Medical Center

Hal Anger created the foundation for sophisticated imaging systems in use today.

Photo courtesy of William H. Blahd, MD

Hal Anger and Benedict Cassen at the International Conference on Peaceful Uses of Atomic Energy in Geneva, Switzerland, in 1955.

Radiation Laboratory [Donner] in 1946, where he remained until his retirement in 1982. Anger soon began assistingDrs. John Lawrence and Cornelius Tobias on their project, the use of the 184-inch cyclotron beam as a radiation-delivering method to treat human disease. As that project did not require all of his time, he began his work on gamma-ray imaging in 1951.

Early Advances in Nuclear Medicine

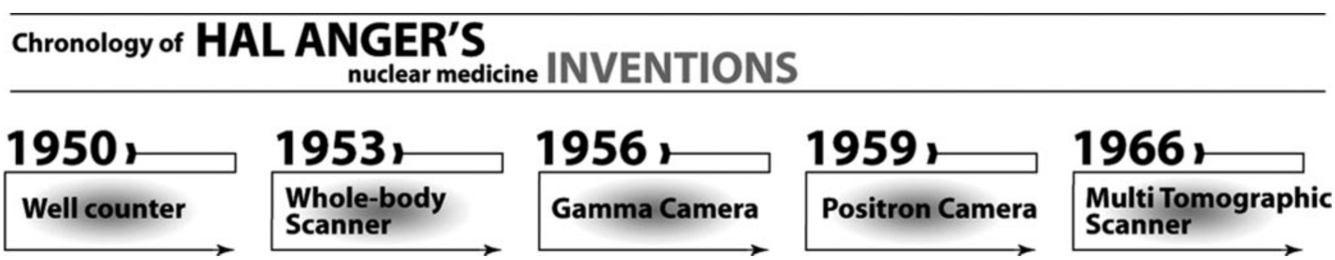
Anger's employment at Lawrence Radiation Laboratory seems fortuitous in view of the many advances in nuclear medicine being made at the laboratory: from Lawrence's cyclotron to Glenn Seaborg's and Jack Livingood's creation of ^{131}I to the discovery of ^{99m}Tc by Segré, Seaborg, and Perrier.

Anger began his work on imaging studies in 1951, but the rectilinear scanner, invented by Benedict Cassen in 1950, was the device that first introduced imaging to nuclear medicine. The scanner obtains data by detecting and analyzing the intensity of the emitted radiation at a predefined location by moving laterally across the object being imaged, building the image line by line.

By 1952, Anger had completed the first prototype for the gamma camera, a pinhole camera that used a thallium-activated sodium iodide crystal as the detector and a photographic plate. The drawback to this model was its low sensitivity; lengthy exposure times (an hour or longer) were required. However, its significant advantage over the rectilinear scanner was that the gamma camera could capture an entire organ at once.

Anger continued to work to refine the camera further, and in late 1956, a few months after the cyclotron project was stopped for 2 years, he developed the design now seen in current camera systems. In this version of the camera, which consists of a 4-inch scintillator and 7 photomultiplier tubes (PMTs), the sodium iodide crystal is coupled to a close-packed array of PMTs. Scintillation light (hence the name scintillation camera) from an absorbed gamma is spread over several tubes, and centroiding logic ("Anger" logic) calculates the position of each photon event within the crystal. "Anger's use of PMTs to determine exactly where the flash of light occurs so that an image could be made was a revolutionary idea," said H. William Strauss, MD, SNM president and chief of nuclear medicine at Stanford University, Stanford, CA. An image of tracer distribution in the body could be made quickly, facilitating the use of dynamic function studies, added Strauss. "What Anger did was brilliant and is so hard to improve on," said Stanley J. Goldsmith, MD, New York Hospital–Cornell Medical Center, New York. Nuclear medicine now had an imaging device that could image the heart, brain, liver, kidneys, and bone with higher resolution than the rectilinear scanner. Only in the past few years has anyone designed a gamma camera that differs significantly from Anger's original design.

Anger summarized his findings in an article titled "Scintillation Camera," which was published in *Review of Scien-*



tific Instruments in 1958. In June of that year, he conducted a demonstration of the camera at the SNM Annual Meeting. Said William J. MacIntyre, PhD, Cleveland Clinic Foundation, OH, who attended the meeting, "It was a remarkable demonstration. The members were very impressed with Anger's invention." Clinicians had been following Anger's research over the years and found it progressive, said MacIntyre. Four years later, Anger completed development of the first 11-inch camera. During this time, Anger was also at work on the first positron camera.

In the summer of 1962, Alexander Gottschalk, MD, came to the Lawrence Berkeley Laboratory (LBL) to work with Anger to investigate the clinical uses of the camera. In the 2 short years that Gottschalk was at LBL, Anger recalls, he began to use ^{68}Ga-EDTA with the positron version of the camera to localize brain tumors. More notably, however, Gottschalk was the first to use ^{99m}Tc-pertechnetate with the gamma camera, amply demonstrating in static brain images and dynamic blood flow studies in the heart and other organs the speed with which images could be obtained by using ^{99m}Tc.

Early Marketing of the Camera

Despite early clinical interest, it took several years before the Anger camera was routinely used. Manufacturers, on the other hand, questioned the product's viability and its ultimate value to nuclear medicine. However, John Kurantz, the founder of Nuclear–Chicago Corp., was unwavering in his support of the camera and was instrumental in its initial mass production. This camera, which used an 8-inch scintillator and 19 small PMTs, was the only such camera made by Nuclear–Chicago Corp. The first commercial Anger camera was delivered in 1962 to Ohio State University Hospital for use by William Myers, PhD, in his studies on small animals. That camera now belongs to the Smithsonian Institution.

One factor that affected widespread use of the camera was the natural human response to change. "People were comfortable using the rectilinear scanner," explained MacIntyre. That scanner could accurately depict static studies and successfully did the job. Even as late as 1973, 15 years after the gamma camera's development, a proficiency testing program conducted by the Council of American Pathologists revealed that more than half of the respondents were using the scanner despite the availability of the gamma camera. Today, however, gamma cameras are standard features in most hospitals, and rectilinear scanners are not to be found.

Anger's invention certainly helped jump-start the imaging instrumentation industry. For many years the only gamma camera manufacturers were Nuclear–Chicago Corp., Ohio Nuclear Corp., and Picker Corp. In time, other manufacturers, both domestic and foreign, developed and released their own cameras, all based on Anger's original design.

Other Innovations

"As important as the gamma camera is to nuclear medicine," says Thomas F. Budinger, MD, PhD, LBL, Berkeley, CA, "Hal is responsible for another device critical to nuclear medicine, the well counter. It is the most widely used of nuclear medicine instruments, as it is found in every laboratory that deals with isotopes. It is the standard for the safe use of isotopes."

Developed in 1950, the well counter is a device that measures small amounts of radioactive substances. "The well counter was an extremely clever idea," says Dennis D. Patton, MD, professor of radiology and optical sciences, University Medical Center, Tucson, AZ, "because the previous method (a plain, flat sodium iodide scintillation detector) was inefficient. Anger thought to drill a hole through the crystal so that the sample could be placed inside it to get 98% efficiency." What is particularly significant, notes Budinger, is that, despite modern additions of digitized signal and robotic devices to facilitate sampling, modern well counters still use Anger's basic design.

And the list of Anger's prolific developments continues. Whole-body scanning, in which the scanner uses an array of 10 scintillation detectors to scan the whole body, was introduced in 1953. Anger cites as pioneering Myron Pollycove, MD's research using the first whole-body scanner and ^{50}Fe to study iron kinetics and hemoglobin synthesis in humans.

In 1959, Anger developed the first positron camera and the principle of coincidence detection. Donald van Dyke, MD, a research physiologist, did pioneering work using the positron camera by demonstrating that blood flow and marrow distribution in various disease states could be imaged using ^{32}Fe and ^{18}F made by LBL chemist Yukio Yano in the Berkeley cyclotron, said Anger. According to Pollycove, now a Visiting Medical Fellow with the Nuclear Regulatory Commission, Anger's development of the positron camera helped facilitate the study of blood disorders with ^{52}Fe. "With the positron camera and ^{52}Fe," said Pollycove, "you could get better distribution and visualization of the iron kinetics." Additionally, use of the positron camera made it possible to use oral or intravenous administration of ^{52}Fe, said Pollycove.

In 1966, Anger developed the first multiplane tomographic scanner, a camera that images multiple planes in the body simultaneously. Nuclear–Chicago Corp. manufactured the camera, which in time was superseded by SPECT instrumentation.

Professional Commendations

The holder of 15 U.S. patents as well as the author of numerous journal articles and book chapters, Anger is the recipient of many major awards and honors, including the John Scott Award in 1964 for the development of the positron camera; Guggenheim Fellowship, 1966; Gesellschaft fur Medizin Award, 1971; honorary doctorate in science, Ohio State University, 1972; Nuclear Medicine Pioneer Citation, SNM, 1974; Modern Medicine Award for

Distinguished Achievement, 1975; SNM First Western Regional award for distinguished contributions to nuclear medicine, 1976; Centennial Year Medal, Institute for Electrical and Electronics Engineers (IEEE), 1984; Societé Française de Biophysique Medal, 1988; Georg de Hevesy Memorial Medal, Vienna, 1991; and Honorary Member and Fellow, American College of Nuclear Physicians, 1992.

In 1994, the Education and Research Foundation for the Society of Nuclear Medicine paid tribute to Anger by awarding him the first Cassen Prize, a $25,000 award to a scientist whose work has made a major advance in nuclear medicine science. According to Patton, who served as president of the seven-member Cassen Prize Committee when Anger was nominated, the selection of Anger was unanimous, and there was no discussion of other nominees.

Current Activities

Since his retirement in 1982, Anger has maintained professional memberships in both SNM and IEEE. Anger keeps abreast of instrumentation developments by reading the literature and attending occasional meetings and conferences. The last instrumentation that Anger finds most intriguing is ADAC's Meuhllener dual PET scanner and Digirad's solid-state gamma camera, a notable advancement, given that the camera is about the size of a laptop computer because solid-state detectors are used instead of the crystals and PMTs used in larger traditional gamma cameras. It is interesting to note that despite the fact that solid-state gamma-ray detector research has been ongoing for many years, the solid-state gamma camera, which was approved by the Food and Drug Administration in May 1997, could make new inroads for nuclear medicine imaging in much the same way the Anger gamma camera did.

"It has been very satisfying to see the development of PET and SPECT and the advances in image resolution and clarify," Anger observed. "I had an extraordinary opportunity at Donner to follow through on my ideas and make the [devices] work." To say that Anger's innovations were the catalyst for the emergence of nuclear medicine may be an understatement, but the development of the first clinically successful radioisotope camera had far-reaching implications for nuclear medicine. "Improvements in the Anger camera, including SPECT and the deployment of different designs for positron imaging, can be seen as an offshoot of Hal's original work," said Budinger. Perhaps Anger's contributions to the field are best summarized by Strauss: "It's hard to say where nuclear medicine would be without Anger's contributions."

Eleanore Tapscott
SNM, 1998