Nuclear Medicine Pioneer: Benedict Cassen

The Rectilinear Scanner and an Enduring Legacy of Education and Research

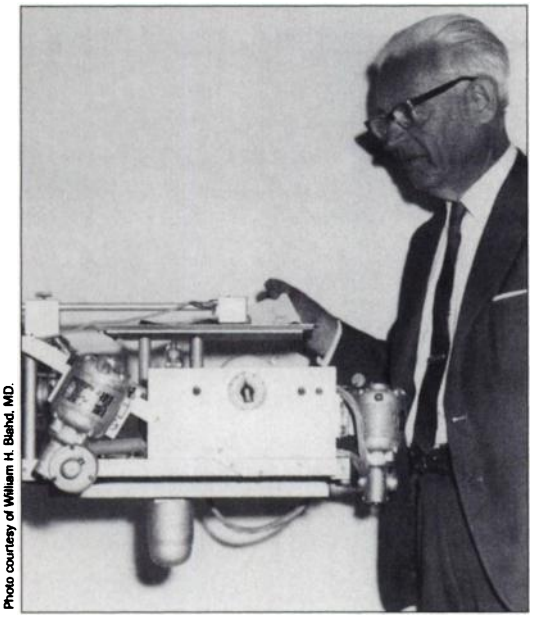

Photo courtesy of William H. Blahd, MD.

Benedict Cassen, PhD, with his rectilinear scanner (above), and Mary Wylie Cassen (below).

Lauded for his revolutionizing 1950 invention, the rectilinear scanner, which was the first instrument capable of imaging organs in the body, the late Benedict Cassen, PhD, was certainly instrumental in advancing the specialty of nuclear medicine. However, perhaps Cassen's greatest legacy rests not in his significant scientific accomplishments but in his contributions to the education of medical and graduate students during and after his lifetime—particularly the $1.25 million endowment donated by the estate of his widow, Mary Wylie Cassen, to the Society of Nuclear Medicine's (SNM's) Education and Research Foundation (ERF), which funds the Cassen Postdoctoral Fellowships as well as the prestigious Cassen Prize.

A Man of Science

Cassen was born in New York City in 1902. He studied physics and mathematics at the Royal College of Science in London, from which he graduated in 1927. He obtained his doctorate from the California Institute of Technology (CIT) in 1930. From 1930 to 1932 he was a National Research Council Fellow at Princeton University, Princeton, NJ, and from 1934 to 1939 he was a physicist at Harper Hospital in Detroit, MI. After a 5-year stint as a research physicist with Westinghouse Research Laboratory, Philadelphia, PA, Cassen returned to CIT in 1944, where he worked on war-related projects. In 1947, Cassen joined the staff of the University of California Los Angeles (UCLA) Laboratory of Nuclear Medicine and Radiation Biology, which at the time was called the UCLA-U.S. Atomic Energy Commission Project, where he continued working until his death in 1972. Additionally, he became a professor of biophysics at UCLA in 1949.

During the 1940s, Cassen began his work on clinical imaging of organs using radiotracer techniques. His first imaging device was the directional scintillation detector that researchers used to obtain ^{131}I images of the thyroid. Imaging with this device was particularly time-consuming, taking 60 to 90 minutes to determine the outline of the thyroid. Cassen decided to automate the device so the thyroid could be scanned more quickly. In 1949, he invented the rectilinear scanner, which obtained data by detecting and analyzing emitted radiation by moving laterally across the body, building the image line by line. According to Cassen's close friend and colleague, William H. Blahd, MD, chief of nuclear medicine service, West Los Angeles Veterans Administration Medical Center, Los Angeles, CA, "Cassen got the idea for the automated readout system from watching the ticker-tape machine and listening to its tapping in his stockbroker's office." Cassen thought a similar principle could be implemented to record radionuclide images of human organs, and the original scanner recording system used a carbon paper strip printer.

Clinical studies using human subjects were performed in 1950, and Cassen reported his results in an issue of *Nucleonics* that year. Two of Cassen's colleagues, Cliff Reed, a biomedical engineer, and Larry Curtis, a technician, undertook commercial production of the scanner—first in Curtis's garage and later at a small southern California plant. The first commercial model was an adaptation of an over-the-bed hospital tray. Over the next 10 years, these instruments were used in many hospitals to image the thyroid. In time, the rectilinear scanner was superseded by photoscanning, which was developed in 1956 by David E. Kuhl, MD (the second recipient of the Cassen Prize), who created a photographic attachment for the rectilinear scanner, thereby improving the scanner's imaging sensitivity and resolution, and eventually by the scintillation camera, developed by Hal O. Anger, BS, DSc, the first Cassen Prize recipient.

In addition to the rectilinear scanner, Cassen's notable scientific accomplishments include studies on the air blast effects on the respiratory, vascular and nervous systems (in conjunction with Blahd), quantitation of total-body potassium and body water in primary muscle diseases, methods to characterize and separate various white blood cells without damaging their physiologic characteristics and development of a large, wide-angle, hydraulic 2000-hole collimator for in-depth imaging of the brain.

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Government Relations Update

FDA Holds Public Workshop on Radiopharmaceutical Approval Regulations

The Food and Drug Administration (FDA), complying with the FDA reform bill passed last year, held a workshop on the approval process for radiopharmaceuticals on February 27, 1998. The workshop was moderated by George Mills, MD, of the FDA Office of Biologics, and the staff panel was headed by Patricia Love, MD, Jane A. Axelrad, JD, and David Lee. There were four questions posed by the FDA:

1. How should the proposed use of a radiopharmaceutical in the practice of medicine determine the nature and extent of safety and effectiveness evaluations?
2. What general characteristics should be considered in the preclinical and clinical pharmacological and toxicological evaluations of a radiopharmaceutical (including the radionuclide as well as the ligand and carrier components; i.e., nonradioactive components)?
3. How should the estimated absorbed dose in humans be determined and considered?
4. Under what circumstances might an approved indication for marketing refer to manifestations of disease (biochemical, physiological, anatomic or pathological processes) common to, or present in, one or more disease states?

Presentations addressing these questions were made by representatives of several organizations, including the Council on Radionuclides and Radiopharmaceuticals (CORAR). Mark Tulchinsky, MD, represented the American College of Nuclear Physicians and the Society of Nuclear Medicine (ACNP/SNM). Radiation dosimetry was addressed by Barry Wessels, PhD, a radiation biologist from George Washington University, Washington, DC, and a member of SNM's MIRD committee, and Richard E. Toohey, PhD, CHP. Richard L. Wahl, MD, spoke on behalf of the American College of Radiology.

The panel's initial tone was skeptical and inquisitive. As the presentations progressed, however, the tone became interested and collaborative. At the end of the meeting, the FDA panel and the participants were comfortable discussants, and there was a positive atmosphere. The workshop discussions led to tentative agreements with the FDA regarding the approval of radiopharmaceuticals. The following are the major agreements attained in negotiations with the FDA regarding regulation of diagnostic radiopharmaceuticals:

- The FDA agreed to acknowledge the concept of "Class 1 radiopharmaceuticals" (i.e., tracers) and, further, that flexible safety requirements would apply.
- The FDA agreed to further define "Class 1 radiopharmaceuticals" in the preamble to the forthcoming regulation and in a guidance document to accompany the regulation.
- The FDA assured workshop participants that a guidance document would be proposed soon after the regulation (approximately May 20, 1998).
- The FDA agreed to include language in the preamble of the regulation making it clear that the Nuclear Regulatory Commission's occupational radiation limits (5 rem) are not an appropriate benchmark for establishing the radiation dose of a radiopharmaceutical.
- The FDA stated that the proposed regulation language would be similar to the position taken by CORAR and ACNP/SNM regarding both indications for diagnostic radiopharmaceuticals (multiple indications) and the evaluation of effectiveness.
- The FDA also agreed to the concept of granting early meetings with sponsors both before and during the preclinical phase of a trial to determine the level of safety studies required.

According to Tulchinsky's comments on the workshop, it appears that ACNP/SNM and CORAR achieved major gains in the FDA's approach to the regulation of radiopharmaceuticals. While the outcome of the process will not be determined until the release of the proposed rule, ACNP/SNM representatives feel confident about the content of the rule. Under Tulchinsky's direction, ACNP/SNM and CORAR will comment on the proposed rule when it is published.

—David Nichols is the director of the ACNP/SNM government relations office.

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Cassen was the author of numerous journal articles and book chapters, including, as coauthor with Drs. Blahd and Bauer, the highly regarded 1958 text, *The Practice of Nuclear Medicine*. He also served for many years as a trustee of SNM, from which he received its first Distinguished Scientist Award in 1970. He was honored again by SNM in 1978 when he was cited as a Nuclear Medicine Pioneer.

Nuclear Medicine's Prestigious Cassen Prize

In 1982, Cassen's widow, Mary Wylie Cassen, made a bequest to the ERF to establish a major scientific award to honor the contributions of a living scientist or physician-scientist to nuclear medicine. As a tribute to the man who dedicated his life to research, the Cassen Prize, which is referred to as the " Nobel Prize of nuclear medicine," is a testament to Cassen's contributions to nuclear medicine and to his enduring legacy.

—Eleanore Tapscott