# "Father of Emission Tomography" Receives 1996 Cassen Prize

David E. Kuhl, MD, is a meticulous organizer with indexed files dating back to high school. Everything he has ever worked on or thought of is documented—an example of a true scientist, said Abass Alavi, MD, president of the Society of Nuclear Medicine's Education and Research (E&R) Foundation, who was Kuhl's research fellow in the 1970s at the University of Pennsylvania.

In fact, Dr. Kuhl—recipient of the 1996 Benedict Cassen Prize—had an interest in researching the use of radioactive substances for diagnosing and treating disease even as a teenager. As a junior high school student in the 1940s, he persuaded several friends to combine their chemistry sets with his own and join him in performing experiments.

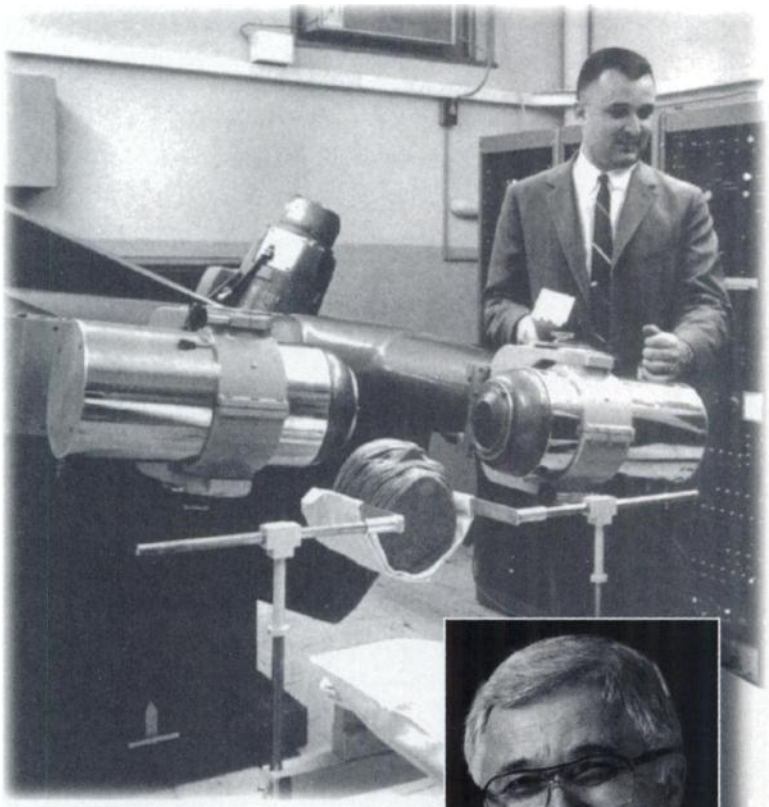
Dr. Kuhl is the second recipient of the Cassen Prize, which is a $25,000 award given by the E&R Foundation to scientists who have made significant contributions to the field of nuclear medicine science. He is best known for introducing tomography into the field of nuclear medicine, leading to the development of SPECT and PET as primary imaging methods. Dr. Kuhl also was a critical member of the team that first researched the use of [$^{18}$F]FDG for the measurement of local cerebral glucose utilization in vivo and opened the door for the widespread use of [$^{18}$F]FDG with PET.

While a medical student at the University of Pennsylvania in Philadelphia in the early 1950s, he scanned his first patient using a photographic recorder that he himself developed. Just a few years after Benedict Cassen, PhD, had invented the rectilinear scanner, Dr. Kuhl realized that a modulated light source projection on photographic film might produce a more controlled image record than a mechanical recorder, which was used in Dr. Cassen's scanner. The photorecorder was attached to the rectilinear scanner, thereby improving the sensitivity and perception of detail in nuclear medicine scans. This recorder became standard on all commercial rectilinear scanners.

In 1958, while a first-year resident at the Hospital of the University of Pennsylvania, Dr. Kuhl conceived of and performed the first emission tomography experiment. He told *Newsline* he invented cross-sectional emission tomography for two reasons: to separate confusing image overlap in scanned pictures and to address the problem of quantifying radiotracers in three dimensions. At the time, accurate maps of cerebral blood flow and neurochemistry could only be obtained by cross-sectional dissections of animal brains—not in living human brain.

From the late 1950s to the mid-1970s, Dr. Kuhl and his colleagues at the University of Pennsylvania invented the Mark II, III and IV series of SPECT scanners and proved their clinical efficacy for image separation in brain tumor and stroke detection. While working on the Mark II scanner in 1965, Dr. Kuhl performed the first transmission transverse section imaging of the living human thorax. This research served as the foundation for the development of x-ray computed tomography.

During that time, Dr. Kuhl also worked with colleagues to develop the Sokoloff autoradiographic method of measuring local cerebral glucose utilization. This required not only research innovation but Dr. Kuhl's methodical management expertise: He needed to coordinate air shipments of cyclotron-produced [$^{18}$F]-FDG from Brookhaven National Laboratory in New York to the Mark IV scanner at the University of Pennsylvania. This activity and others led to the first successful use of this radiotracer in humans.



**Top: David E. Kuhl, MD stands near his Mark II SPECT scanner in 1963. Bottom: David E. Kuhl, MD.**

### Expanding the Research and Clinical Uses of PET

Dr. Kuhl's principal research focus, however, remained on radioactive brain tracers. In 1972, he used three-dimensional imaging to obtain the first quantified radiotracer measurement of blood volume in a localized brain region. This success eventually led to the subsequent use of PET as a major study method of brain physiology, neurochemistry and behavioral activation. Frederick Bonte, MD, a scientist at the University of Texas South-

western Medical Center in Dallas refers to Dr. Kuhl as "the father of emission tomography" since his inventions were the foundation for PET and SPECT.

Proof of this point is illustrated in Dr. Kuhl's founding of a PET Center at University of California at Los Angeles (UCLA) in the late 1970s. His initial work focused on stroke, epilepsy and Alzheimer's disease. For the next ten years at the UCLA, Dr. Kuhl and his colleagues established [$^{18}$F]FDG-PET as a study method vital for differentiating normal brain activity from aging and aging from degenerative brain disease. Cases in point: Dr. Kuhl was the first to demonstrate that temporal lobe hypometabolism in epilepsy is an effective preoperative guide to the site of onset of intractable seizures. He found that local metabolism in stroke is altered by functional de-afferentation as well as by tissue death. He also was the first to document that Huntington's disease causes caudate hypometabolism before either symptoms or atrophy and that demented patients with Alzheimer's and Parkinson's disease share common cerebral metabolic patterns.

Even with his spate of PET discoveries, Dr. Kuhl's interest was not confined to this imaging modality. In 1980, he revisited SPECT after many years and performed the first quantitative measures of local cerebral blood flow determined with the Mark IV scanner using $^{123}$I-IMP and tracer kinetic analysis.

**What the Future Holds**

In his more recent work at the University of Michigan, Dr. Kuhl has concentrated on exploring degenerative brain disorders using both PET and SPECT. He and his colleagues have introduced new radioactive ligands "which should permit a more detailed exploration of neurotransmitter abnormalities in both Parkinson's and Alzheimer's," Dr. Kuhl said.

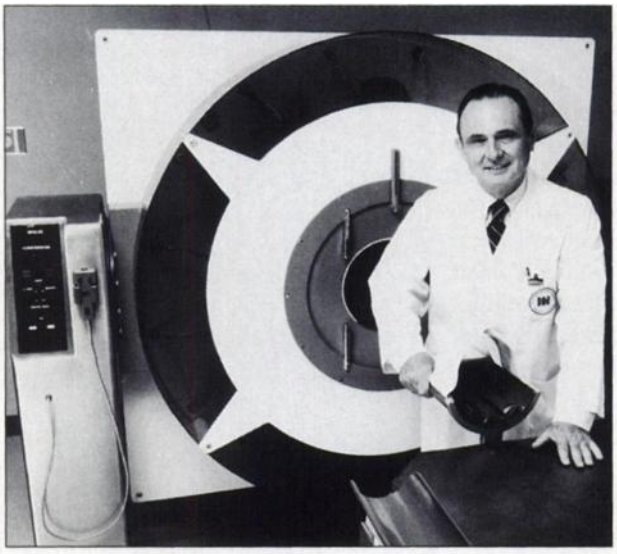
He is convinced that eventually the research will lead to a better classification system for matching patients with the most appropriate therapy. "Since neurotransmitter mapping of the brain can be accomplished in patients only with emission tomography, scientists in nuclear medicine have both a remarkable opportunity and a serious obligation to do the job right," Dr. Kuhl said.

What does Dr. Kuhl view as his greatest accomplishment? His reconstruction tomography which makes it possible to determine quantitative measurements of localized brain regions. "When I started out in the field of nuclear medicine science, my intention was to introduce cross-sectional emission tomography as a means of solving the problem of quantifying radioactive tracers within small volumes of the living human brain," Dr. Kuhl said. Without this foresight, nuclear medicine probably would not have evolved into the specialty it is today.

*—Stacey Silver*

## In Memoriam

Michel M. Ter-Pogossian, PhD, an internationally known pioneer in the use of cyclotron-produced radionuclides in biomedical research, died suddenly of a heart attack on June 19, 1996, while visiting Paris. Dr. Ter-Pogossian, 71, was emeritus professor of radiology at Washington University's Mallinckrodt Institute of Radiology in St. Louis.



Michel M. Ter-Pogossian, PhD

Among his many accomplishments, Dr. Ter-Pogossian will be remembered foremost for helping to develop the PET scanner into a practical diagnostic tool. In the early 1970s, he was a leader in the collaborative research team of physical scientists, chemists and nuclear physicians who developed the concept of PET. He played a major role in developing short-lived radionuclides and developed the first PET scanner and the first multislice PET scanner as well as the first time-of-flight PET scanner.

During a career which spanned more than four decades, Dr. Ter-Pogossian earned numerous accolades for his achievements in nuclear science, including both the Paul C. Aebersold Award and the Georg Charles de Hevesy Nuclear Medicine Pioneer Award of the Society of Nuclear Medicine (SNM), France's Gold Medal Award of the French Society of Nuclear Medicine and Biophysics, and Canada's Gairdner Award. He was a member of many professional societies including SNM. He was elected to the Institute of Medicine, National Academy of Sciences in 1987 and served on the editorial boards of major scientific journals including *The Journal of Nuclear Medicine*.

Dr. Ter-Pogossian was a prolific author with more than 250 scientific articles and book chapters to his credit. In addition, he served as a member of several Department of Energy and National Institutes of Health committees. He is survived by his wife Ann, three children and five grandchildren.