

## Barry L. Zaret, MD and H. William Strauss, MD

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Dr. Barry L. Zaret



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In the early 1970s, management of coronary artery disease (CAD) was changing rapidly. Favaloro performed the first successful coronary artery bypass surgery (CABG) in 1967.<sup>1</sup> Over the next few years, CABG became the standard of care in selected patients with angina pectoris. However, selection of suitable surgical candidates required invasive coronary

angiography. In 1971 and 1973, Zaret and Strauss reported two seminal clinical studies that were timely and relevant for clinical cardiology.<sup>2,3</sup> They demonstrated that using conventional nuclear imaging resting left ventricular function and regional wall motion could be quantified and that myocardial perfusion could be visualized, at rest and after exercise for detection of scar and myocardial ischemia.

The promise of noninvasive evaluation of patients with suspected CAD foreshadowed the beginning of the field of clinical nuclear cardiology. Within a few years, myocardial perfusion imaging with thallium-201, measurement of left ventricular ejection fraction and regional wall motion by first pass and gated blood pool angiography and acute infarct imaging with Tc-99m-pyrophosphate were embraced by cardiologists and nuclear medicine physicians. Drs. Zaret and Strauss are widely acknowledged as establishing the field of non-invasive nuclear cardiology.

### BARRY L. ZARET, MD

Barry Zaret was born on October 3, 1940, in Brooklyn, NY. His father was an immigrant from White Russia (now Belarus), and his mother was the daughter of immigrants from Eastern Europe (Galicia).

After finishing high school, Barry attended Queens College where he met his future spouse, Myrna Zimmerman. In 1961 he earned the honor of Phi Beta Kappa and graduated summa cum laude in 1962. He then enrolled in New York University School of Medicine, where he received the Alpha Omega Alpha Award. In medical school Barry became captivated by scientific medical research, inspired by role models such as 1959 Nobel Laureate Severo Ochoa, MD, internist Saul Farber, MD, and nephrologist Jerome Lowenstein, MD. Zaret decided to become a cardiologist after hearing an inspiring lecture by Dr. Eugene Braunwald, who at that time was at the NIH.

In 1966 Zaret began his internal medicine training at Bellevue Hospital, NYC, where he met and subsequently developed a friendship with H. William (Bill)

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Strauss. In 1969 Zaret was accepted for a Cardiology Fellowship at Johns Hopkins Hospital, Baltimore, MD, and trained under guidance of Drs. Richard Ross and Dick Conti. His research mentors were Cardiologist Dr. Bertram Pitt and Chief of Nuclear Medicine, Dr. Henry Wagner. Fortuitously, Barry Zaret's friend Bill Strauss was at Hopkins at the same time, serving as a Fellow in Training in Nuclear Medicine. Zaret and Strauss collaborated initially on a research project measuring coronary blood flow after the intracoronary injection of radioactive Xenon. While waiting for software to quantify coronary blood flow data, they realized that an ECG gating circuitry used for other purposes would allow for gated cardiac blood pool imaging in diastole and systole, using Tc-99m labeled albumin. This then would permit assessment of regional ventricular wall motion and measurement of global ejection fraction. This new research direction turned out to be fruitful. Regional and global left ventricular blood pool analysis from ECG-gated images was safe and correlated well with invasive contrast ventriculographic measurements. These novel noninvasive findings were published in 1971<sup>2,4</sup> and sparked considerable interest in the embryonic field of noninvasive cardiac imaging.

In 1971 Zaret was drafted for military service and was assigned to the hospital at Travis Air Force base in Sacramento Valley, CA, where Bill Straus had arrived 1 year earlier. They could now continue their collaborative research. Noninvasive radionuclide myocardial perfusion imaging had been explored by others with Cesium-131, Rubidium-86 and Potassium-43, mainly to image myocardial scar after infarction. Zaret was more interested in assessing the functional significance of coronary artery stenoses. As a cardiologist he was trained to perform treadmill exercise testing. Aiming to visualize exertional ischemia, he administered Potassium-43 at peak treadmill exercise, something that had never been attempted before. A total of 43 patients were imaged after radiotracer injection at rest and exercise. Exercise-induced regional myocardial hypoperfusion was thus visualized for the first time. The results of radionuclide imaging studies were published in 1973<sup>3,5</sup> and once again drew considerable attention.

After fulfillment of his military service, Zaret was recruited in 1973 to the Yale University School of Medicine, Section of Cardiology, as an Assistant Professor of Medicine and Diagnostic Radiology. In 1976 he was promoted to Associate Professor, and in 1978, appointed as Chief of the Section of Cardiovascular Medicine. In 1982 he was promoted to Full Professor and in 1984 became the Robert W Berliner Professor of Medicine. To assure continuation of the research in nuclear cardiovascular imaging, he recruited, in 1984,

Dr. Frans Wackers as director of the Yale Nuclear Cardiology Laboratory.

Barry Zaret served as Chief of Cardiology at Yale for 26 years until 2004. He also served as Associate Chair of Clinical Affairs in the Department of Internal Medicine at Yale (1994-2004). Dr. Zaret is recognized as a Gifted Clinician, Teacher, Researcher and Mentor of his Fellows. During this long tenure, Yale Cardiovascular Nuclear Imaging remained preeminent in the field of nuclear cardiology and was at the avant-garde of most new clinical applications. He was a member of the TIMI Executive Committee and Principal-Investigator/Director of the TIMI Radionuclide Core Laboratory (1984-1994). He introduced LVEF-based criteria for doxorubicin cardiotoxicity, he studied the physiologic and functional responses of right and left ventricular function by First Pass Angiocardigraphy under a variety of clinical conditions, including mental stress. He evaluated several of the new Tc-99m-labeled myocardial perfusion imaging agents, such as sestamibi and tetrofosmin.

Dr. Zaret was one of the Co-founders of the American Society of Nuclear Cardiology (1993) and had considerable impact on the development of the field. His influence was further enhanced when he became the Founding Editor-in-Chief of the Journal of Nuclear Cardiology® (JNC) (1993-2003). He used the journal's Editor's Page as a bully pulpit to comment on the state of nuclear cardiology and to express his thoughts about desirable future directions of the field. For instance, he was an early and strong advocate of molecular cardiac radionuclide imaging, which he considered the next important phase in cardiac imaging.

Dr. Barry Zaret published over 300 peer-reviewed scientific articles, chapters and editorials, 9 books (including 4 editions of "Clinical Nuclear Cardiology" with Co-editor George A. Beller, MD) and 58 Editor's Pages in JNC®. In addition he published 2 volumes of his own poetry.

He received numerous honors and awards for his work: Phi Beta Kappa (1961), the Solomon Gertz Award of Queens College (1962), Alpha Omega Alpha (1965), the Sheard-Sanford Award of the American Society of Clinical Pathologists (1966), Alpha Omega Alpha Award, New York University School of Medicine (1966), the Casimir Funk Award, Society of Military Surgeons (1973), Established Investigator Award, American Heart Association (1977-1978), Member American Society of Clinical Investigation (1978), the Herman Blumgart Pioneer Award, New England Chapter Society of Nuclear Medicine (SNM, 1978), Association of University Cardiologists (1980), Master of Arts (Honorary), Yale University (1982), Co-director, Wintergreen Conference on Nuclear Cardiology (1991),

Second President of the Association of Professors of Cardiology (1992-1993), Association of American Physicians (1992), Co-chairman, First International Congress of Nuclear Cardiology, Cannes, France (1992), The Louis Sudler Lecturer Award of Rush-Presbyterian Medical College (1993), The 29th Nathan J. Kiven Orator, Providence, RI (1996), The Solomon A. Berson Medical Alumni Achievement Award in Clinical Science, NYU School of Medicine (1998), The Norman Veall Lecturer Award, Barcelona, Spain (1999), The First Samuel and Patsy Paine Lecturer, University of Texas (2001), The 30th Arvilla Berger Lecturer of the New York Cardiac Society (2003), The 2nd Annual Mario Verani Memorial Lecture, American Society of Nuclear Cardiology (2004), The Ellis Island Medal of Honor (2004), and the Distinguished Service Award, American Society of Nuclear Cardiology (2006).

Dr. Barry Zaret became Emeritus Professor of Yale University in 2010. He continued to work as a Senior Research Scientist till his full retirement in 2018. In retirement he continues to write poetry, paints oil landscapes, reads voraciously and likes to travel.

#### **H. WILLIAM STRAUSS, MD**

Dr. William (Bill) Strauss was born on April 29, 1941, in Brooklyn, NY. His father, a first-generation American, was in the printing business. His mother was a second-generation American and a housewife. Bill went to public elementary schools and attended the Bronx High School of Science. In 1958 he matriculated into Yeshiva College in New York City. In his third year of College (1961), he was accepted at Downstate Medical College, from which he graduated in 1965.

During his internship in internal medicine at the Downstate Medical Center he became interested in nuclear medicine, through his interactions with Nuclear Physician, Dr. Larry Silver. The combination of technology and medicine inspired Bill to choose Nuclear Medicine as a career. In 1966 he applied and was accepted for a Fellowship in Nuclear Medicine at Johns Hopkins Hospital. However, Dr. Henry Wagner, the Chairman of the Nuclear Medicine Department, insisted that Bill first take a second year of internal medicine residency. In 1967 Bill was accepted as an Assistant Resident in Medicine at Bellevue Hospital, New York, NY. Working on the wards of Bellevue Hospital late at night, while working on a very ill cardiac patient, he met Barry Zaret.

In 1968, Bill Strauss started a 2-year Fellowship in Nuclear Medicine with Dr. Henry Wagner at Johns Hopkins Hospital. One year later Dr. Zaret arrived for his cardiology training at Johns Hopkins. As part of their training programs, Bill Strauss and Barry Zaret were

required to spend time in a research laboratory. They worked together with cardiologist, Dr. Bertram Pitt on experimental studies in dogs with coronary occlusion, and measuring Xenon-133 washout after intracoronary injection. These experiments brought Bill and Barry together, and was the start of a very successful collaboration at Hopkins and later in military service.<sup>2-5</sup>

In 1970, the idea of ECG-gated blood pool imaging was inspired by the discovery of an unused gating device in the basement of John Hopkins Hospital.<sup>2,4</sup> The idea of exploring radioisotope exercise myocardial perfusion imaging<sup>3,5</sup> came up in 1972 at Travis Air Force Base during discussions about the issue of asymptomatic air force pilots with (false) positive exercise ECGs, needing proof of normal coronary arteries, which could only be demonstrated at that time by invasive coronary angiography. Strauss and Zaret acquired potassium-43 for myocardial perfusion imaging from Medi-physics in nearby Berkeley, CA. This began the practice of using stress perfusion imaging to distinguish between true and false positive ECG responses to exercise stress.

After completion of his military service in 1972 Bill Strauss was recruited back to Johns Hopkins University School of Medicine as Assistant Professor of Medicine and Environmental Health and was in 1975 promoted to Associate Professor.

In 1976, he was recruited by Harvard Medical School with the rank of Associate Professor of Radiology at Massachusetts General Hospital. He was promoted to full Professor of Radiology in 1984. From 1992 to 1994 he served as Vice-President of Diagnostic Drug Discovery at Bristol-Myers Squibb, Princeton, NJ. Dr. Strauss was recruited in 1994 to Stanford University School of Medicine as Professor of Radiology. In 2001, he moved back to New York to the Memorial Sloan-Kettering Cancer Center as Attending Physician in Nuclear Medicine and Professor of Radiology and Nuclear Medicine, Weill Cornell Medical School, where he remained until 2018.

After the seminal research on gated blood pool imaging and exercise myocardial perfusion imaging,<sup>2-5</sup> Bill Strauss focused his research on the application of radiotracers for the diagnosis and characterization of inflammation and atherosclerosis. He worked with a team of radiochemists, immunologists and clinicians to develop radiopharmaceuticals for imaging of myocardial fatty acid utilization (beta-methyl fatty acids), the detection of acute myocardial necrosis (anti-myosin and glucarate), the use of radiolabeled polyclonal IgG to detect chronic inflammation/infection and atherosclerosis, the use of radiolabeled Annexin for in vivo detection of apoptosis, new techniques for labeling red blood cells, wearable instrumentation to measure cardiac function in

ambulatory subjects and novel catheters to detect vascular inflammation.

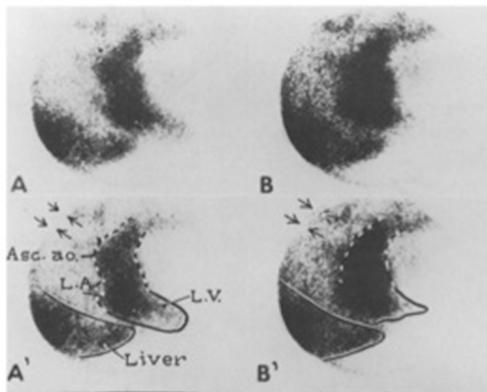
Dr. William Strauss played an important role in the Society of Nuclear Medicine (SNM). He was Vice President, President-Elect and President of the SNM from 1990 to 1998. He served also as Editor-in Chief of the *Journal of Nuclear Medicine* (1989-1993). Dr. Strauss published over 500 peer-reviewed original articles, 9 books and 72 book chapters. In addition he holds 19 USA patents.

Dr. Strauss received numerous honors and recognitions during his career: the Casimir Funk Award of the Association of Air Force Physicians (1973). He was elected to the American Society of Clinical Investigation (1974), delivered the New Horizons Lecture of the Radiological Society of North America in 1975, received the William Beaumont Award in Medicine of the American Medical Association (1979), he received the Hermann Blumgart Pioneer Award of the New England Chapter of the SNM (1982). He was the recipient of the Distinguished Alumnus Award of the

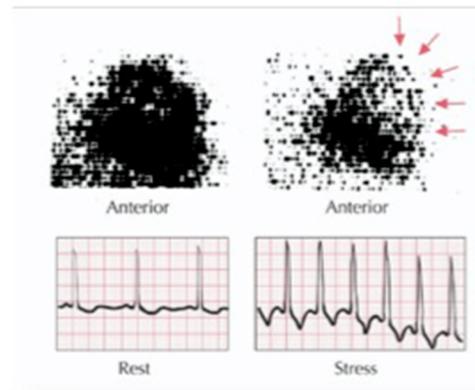
Johns Hopkins Nuclear Medicine Department in 1986, Master of Arts (Honorary) of Harvard University (1989), and received the SNM Distinguished Service Award (1993). He became Doctor Honoris Causa at the Autonomous University of Barcelona, Spain in 1995, received the George DeHevesy Nuclear Pioneer Award of the SNM in 2002, and was the Holman-Kaplan Memorial Lecturer of the New England Chapter, SNM in 2008. He was honored as a Distinguished Alumnus of the Massachusetts General Hospital, Department of Radiology in 2015. He became Honorary Member of the Japanese Society of Radiology in 2016, and received the Benedict Cassen Prize, Education and Research Foundation, SNM and Molecular Imaging also in 2016.

Dr. Strauss semi-retired from the Sloan Kettering Cancer Center in 2013, where he is still active as an Ad Hoc Consultant. In 2014 he joined the Faculty of Icahn School of Medicine at Mount Sinai, New York, NY, as Professor of Medicine and Cardiology and continues to serve as a Research Mentor to young investigators.

### Iconic Nuclear Cardiology Images



**Rest ECG-Gated Blood Pool**



**Rest –Exercise Potassium-43**

## Acknowledgements

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## Disclosure

*The author declares that he has no conflict of interest.*

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