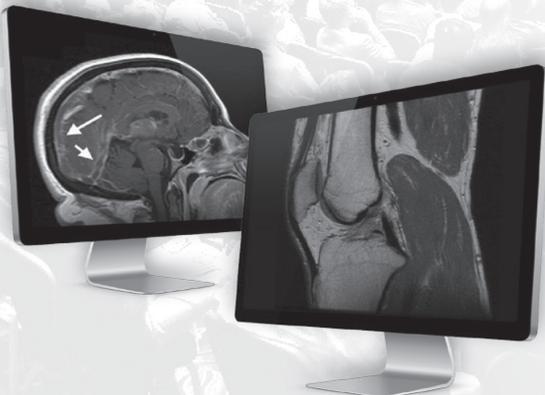


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Summer 2018

A Short History of Nuclear Medicine

by James H. Thrall, MD



James H. Thrall

Laying the Foundations

In 1896, just a few months after Wilhelm Konrad Roentgen's stunning discovery of the x-ray, Henri Becquerel discovered natural radioactivity. It happened in a similar way.

Becquerel had applied uranium paste to a heavy paper covering over a photographic plate, intending to expose the preparation to sunlight in a study of stimulated fluorescence. A cloudy day found the plate left in a drawer but when developed, a clear image was present. Voilà, natural radioactivity. Shortly thereafter, Marie and Pierre Curie discovered radium. Becquerel and the Curies shared the third Nobel Prize in physics.

Unlike x-rays, which were immediately used for imaging, radioisotopes would not be similarly used for another 50 years. Radium was used and misused therapeutically almost from its discovery, but it was not until Georg von Hevesy's experiments assessing water circulation in plants with radioactive lead in 1923 that radiotracers found a role in biology that was directional toward what we think of as nuclear medicine today.

The first medical use of radioisotopes was in studies of the circulation by Hermann Blumgart and Soma Weiss at the Beth Israel Hospital in Boston in 1925. They measured circulation time from arm to arm with Radium C (^{214}Bi) in normal subjects and patients with congestive heart failure. Although very innovative, the procedure did not lead anywhere.

The next pivotal event was the discovery of artificial radioactivity reported in 1934 by Frédéric Joliot and Irène Joliot-Curie. They exposed stable elements to alpha particles to induce radioactivity. Shortly thereafter, Fermi reported the use of neutrons to create radionuclides. This discovery was critical because the use of alpha particles was limited to lower Z elements. Due to their high charge, alpha particles cannot penetrate higher Z nuclei. With neutrons, there were no such limitations.

Two years later in 1936, president Karl Compton of the Massachusetts Institute of Technology (MIT) addressed members of the Harvard Medical School faculty on "What Physics Can Do for Biology and Medicine." Saul Hertz, a young thyroidologist from Massachusetts General Hospital (MGH), asked Compton, "Can Iodine be made radioactive?" A few weeks later, Compton wrote to Hertz affirmatively, leading to a joint venture between MGH and MIT, where scientists at MIT produced ^{128}I and Saul Hertz performed experiments in animals to explore thyroid physiology.

Hertz and colleagues realized that radioactive iodine could be used both diagnostically to measure thyroid gland function and therapeutically. Hertz performed the first radioiodine treatments for Graves disease in 1941 with a mixture of ^{130}I and ^{131}I .

Saul Hertz's work opened the door to clinical nuclear medicine by establishing what proved over the next 75 years to be an enduring therapy.

Our recent ARRS Annual Meeting in Washington, DC, was a great success. Strong turnout numbers plus a record number of virtual attendees via the Internet signaled continued and growing interest in our educational programs as well as the camaraderie that this meeting consistently provides. The virtual meeting option started in 2012 and has steadily increased every year. We saw a 2% increase in overall attendance this spring in Washington, DC, and that represented a 13% increase in attendance over our last meeting in the nation's capital.

The SRS program mirrored the continued success of the annual ARRS gathering. Our annual lecture, the John Tampas Oration, named for the first chair of the SRS, was given by James Thrall, emeritus chair of radiology at Massachusetts General Hospital. Jim is also a past president of ARRS and ARRS Gold Medal recipient. His topic, "A Short History of Nuclear Medicine," is summarized herein.

The SRS docent-led tour of the National Portrait Gallery was marvelous, as was our cocktail reception at the hotel. We are already planning a robust program for the SRS membership attending our next meeting in Hawaii, in spring 2019. Those SRS members who attend the meeting in Oahu will be able to pay a much reduced registration fee while also participating in all SRS activities.

Please encourage your friends and colleagues who may be eligible for SRS membership to join and to attend our meetings. Also, remember to renew your membership and send the appropriate dues payments to the ARRS.

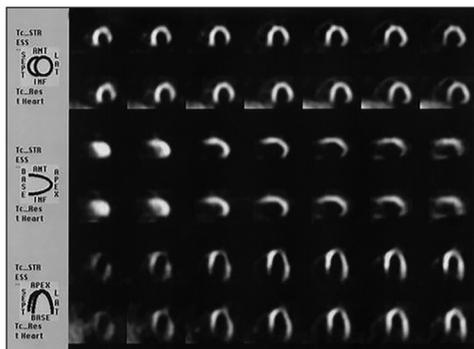


Fig. 1: $^{99\text{m}}\text{Tc}$ Sestamibi myocardial perfusion scan with multiplanar reconstruction (one short axis and two long axis planes) shows a large fixed defect compatible with a myocardial scar in the inferior wall of the left ventricle.

History continues on page 2

History continued from page 1

Initiation of Clinical Applications

After World War II, the U.S. Atomic Energy Commission began making radioisotopes available for medical use, most importantly, ¹³¹I. This led to two decades of remarkable innovation that set the table for the nuclear medicine of today.

People recognized the value of ¹³¹I for assessing thyroid function, known as the radioiodine uptake test, as well as for therapy of hyperthyroidism and thyroid cancer. What was missing was a way to map the distribution of radioiodine within the gland. In 1949, Benedict Cassen invented the rectilinear scanner, which addressed this problem. Nine years later in 1958, Hal Anger invented the gamma scintillation camera. By the 1980s, gamma camera technology had improved to the point of replacing rectilinear scanning.

In parallel with equipment development, there was a series of breakthroughs in development of radiopharmaceuticals. Radioiodine proved to be a versatile agent for labeling useful molecules and materials, such as Hippuran, rose bengal, serum albumin, and macroaggregated albumin, thereby providing a rich armamentarium for clinical applications.

The beta radiation and high gamma energy (364 keV) of ¹³¹I were not ideal for radiation safety or for imaging. In the late 1950s, investigators at the Brookhaven National Laboratory invented the ⁹⁹Mo/^{99m}Tc generator system. In the 50 years since its discovery, ^{99m}Tc has been used as a label for dozens of agents, many of which are in routine use today.

As ^{99m}Tc was finding a dominant role, several other radionuclides gained more niche roles. Among others, these included ¹¹¹In for white blood cell labeling and ⁶⁷Ga citrate

for tumor and abscess imaging. Iodine-123 became used as an alternative for thyroid imaging and as a label for agents like metaiodobenzylguanidine used in the detection of pheochromocytomas and for imaging neuroblastomas.

The Current Era

In the last 30 years, the big story in nuclear medicine has been the ascendancy of tomography—SPECT and PET—along with the development of hybrid SPECT/CT, PET/CT, and PET/MR devices that allow fusion of anatomic information with the physiologic and metabolic information available from radiopharmaceutical localization.

PET/CT with ¹⁸F-FDG has become a standard in cancer imaging for many cancer types and is highly useful in assessing response to treatment, because metabolic changes typically occur ahead of anatomic changes. There are now dozens of other PET radiopharmaceuticals in development.

Even though all radiologists in the United States train in nuclear medicine, it is fair to say that many somehow have not regarded it as part of the specialty of radiology. Going forward, hybrid imaging is helping to “demystify” nuclear medicine by bringing nuclear imaging methods squarely into the mainstream of radiology practice.

The Future

The power of nuclear medicine applications comes in large part from the flexibility in creating radiopharmaceuticals that map important processes in normal and diseased tissues. With innovations in chemistry, it is literally possible to create radiotracers that target any tissue or molecule in the body, define their distribution, and measure different

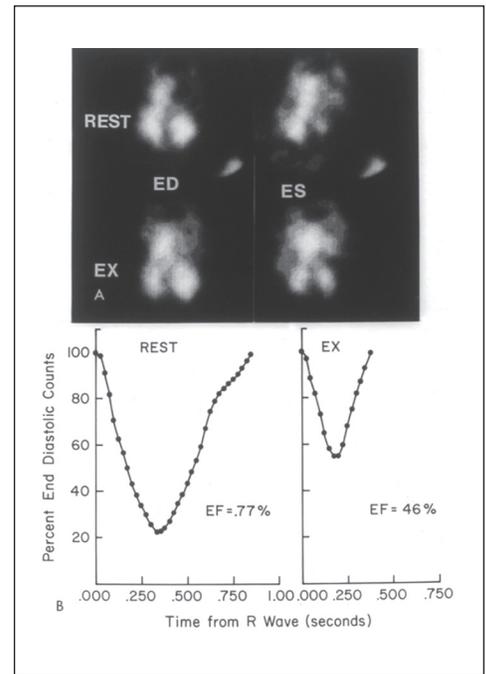


Fig. 2: ^{99m}Tc labeled red blood cell ventriculogram at rest and during exercise stress shows reduced ejection fraction and end diastolic enlargement of the left ventricle indicating stress induced ischemia.

kinds of associated parameters such as glucose metabolism. This flexibility bodes well for the future of the nuclear medicine. Given the extraordinary capabilities of nuclear imaging methods today, it is by equal measures daunting and exciting to imagine where nuclear medicine will be decades hence.

Note

J. H. Thrall is a board member and shareholder of Lantheus Medical Imaging, Inc.; Mobile Aspects; and WorldCare International, Inc. He is also a shareholder in Antares Pharma, Inc.; iBioPharma, Inc.; Avid, Inc.; and Aethlon Medical, Inc.

SRS Birthdays

We wish these SRS members a very happy birthday.

May

- 5 Leonard Berlin
- 6 Lawrence R. Goodman
- 17 Richard G. Fisher
- 19 Zita Baniqued, R. K. Warburton
- 23 Morton G. Glickman
- 25 Michael M. Raskin

June

- 1 Ronald C. Ablow
- 4 Michael J. Bowers
- 5 Mohammed A. Abbas
- 7 Stanley Nakamoto
- 12 Richard Lindgren
- 16 Andrew Osuszek
- 19 Robert Chiteman
- 25 Tearle Meyer
- 27 Chet Baran
- 29 Arnold Kuta
- 30 Jean Cadet

July

- 3 Jonathan Dehner
- 6 David Hunter
- 15 Ralph M. Colburn, Jr.,
- 19 Dieu Pham
- 21 Edwin Goldstein
- 22 Elizabeth Cancroft
- Arthur K. Walter
- 28 Neil Messinger
- Leland Larson

August

- 2 Robert J. Stanley
- 10 Robert D. Steele, Jr., Jay Crittenden
- 11 Philip O. Alderson, Stover Smith
- 15 Mark Kettler
- 19 Richard Sigel
- 20 Richard Daffner
- 21 Marlen Junck
- 26 Edward H. Sessions
- 28 Charles Mueller
- 30 Harry Agress, Jr.
- 31 Richard Haar



Tell your friends...

The ARRS has a special interest group specifically for senior radiologists. “The Senior Radiologists Section (SRS) provides an opportunity and a forum for senior members of the ARRS to be kept informed on the new developments in radiology as well as enjoy the camaraderie of their colleagues,” says John Tampas, former chair of the SRS.

Benefits include:

- SRS newsletter, *SRS Notes*
- Discounted registration fee to ARRS Annual Meeting
- Annual Meeting reception
- SRS Annual Meeting activities (includes sponsored speaker and special tours)

To qualify to join this special interest group within the ARRS membership, you must meet one of the following criteria:

- Be a current emeritus ARRS member (fully retired) age 60 or older
- Be a current ARRS member age 65 or older

SRS dues are in addition to any membership dues that are owed to the ARRS related to an individual’s membership category. Payment of all applicable ARRS dues is required to be a participant of the SRS.

Interested ARRS members may download an SRS application form (http://www.arrs.org/uploadedFiles/ARRS/Membership/srs_app.pdf) and mail it, along with payment, to: ARRS-SRS, 44211 Slatestone Court, Leesburg, VA 20176-5109. Questions regarding this special interest group should be addressed to the ARRS Membership Services Team at membership@arrs.org or at 866-940-2777 or 703-729-3353. If you have not renewed your SRS membership, please contact Sara Leu at sleu@arrs.org or 866-940-2777 to renew today!

Upcoming ARRS Annual Meetings

May 5–10, 2019
Honolulu Convention Center

May 3–8, 2020
Sheraton Grand Chicago

April 18–23, 2021
Marriott Marquis San Diego Marina

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