
A Half-Century of Nuclear Medicine

J. Tyler Middlebrooks, CNMT, NMTCB(RS), RT (N)(CT)

CARTI Cancer Center, Little Rock, Arkansas, and Physics, Instrumentation and Data Sciences, Academic Council, and PET Center of Excellence Board of Directors

Dramatic changes have transformed the landscape of nuclear medicine instrumentation over the last 50 y. Since the 1970s, diagnosing and treating diseases have evolved from a best-guess and treatment method to a more science-based test, prove-and-treat method. γ -cameras have evolved from stationary planar imaging to multihead tomographic systems and organ-specific cameras. PET systems have become a clinical reality, and use has exploded. PET has gone from 2D to 3D with time-of-flight, and we are now seeing whole-body imaging systems. New scintillation crystals have been introduced as well as solid-state detectors. Hybrid systems that incorporate CT or MRI are now commonplace. Reconstruction has moved from 2D slice-by-slice filtered backprojection to fully 3D iterative reconstruction that incorporates system modeling and often other prior information or time-of-flight data. Radioisotope therapy has expanded from ^{131}I treatment of the thyroid to receptor-targeted agents and α -particle emitters. The changes are too numerous to detail in a single short article, and so I will focus instead on a few highlights that have affected my own career as a technologist.

In 1971, the Society of Nuclear Medicine created the Technologist Section. Technologists play a crucial role in the advancement of nuclear medicine. They are the front line in the clinical implementation and delivery of new technology, diagnostic tests, and treatments. The continuing advancements in nuclear medicine rely heavily on the technical excellence of technologists. As such, technologists in our era must not only be masters at technical and anatomic knowledge but also continue to learn and advance themselves through continuing education and self-study. Over the past decade, I have seen several new imaging procedures that did not exist when I was in school, not to mention an abundance of new radiopharmaceuticals that are released almost daily. The biggest change, however, in the last 50 y has been with PET.

PET

In the early to mid-1990s PET transitioned from a research tool to a reimbursed clinical reality, which subsequently led to an explosive growth in PET imaging and applications. At the heart of this was a simple radiopharmaceutical produced with the addition of an ^{18}F isotope to a deoxyglucose molecule: FDG. FDG allows visualization of cellular metabolism and is

particularly adept in the detection of cancer. In the beginning, these scans were very lengthy and required an emission and transmission scan. Nevertheless, PET represented a major leap in our ability to detect, diagnose, stage, and restage malignancies.

In the late 1990s and early 2000s, the radioisotope transmission scan was replaced by a CT, creating a new hybrid modality called PET/CT. The low noise and rapid acquisition of CT improved PET image quality and decreased scan times. The excellent spatial resolution of CT allowed precise localization of sites of tracer uptake. Other advances in PET technology are 3D acquisition, the progression toward smaller crystal sizes evolving from ~ 6 mm in the 1990s to ~ 3 mm in top systems now. Also, the advent of Silicon Photomultiplier tubes, which make for faster time of flight, individual crystal read-out (digital PET), more compact light sensors, and MR-compliant machines. These and more have led to a continuous improvement in sensitivity and image quality. Figure 1 (I) presents a PET-only scan done in the 1990s, showing multiple osseous lesions along with a presumed lung mass, and Figure

"In her September 1993 presidential Message, Technologist President Teri Boyce noted that I had appointed more technologists to SNM committees than had been appointed in previous years. Actually, for the first time, a technologist was appointed, without exception, to every SNM committee, not just to demonstrate support for the Tech Section and to promote good communication, but with the hope that this would start a tradition that would be perpetuated. Achieving this goal has given me the most satisfaction of my tenure. Also, I reinitiated a formal liaison with international leaders of non-US societies of nuclear medicine. This has evolved to annual events resulting in ongoing worldwide collaboration in promoting the goals of the SNMMI and the SNMMI-TS."



Richard C. Reba, MD
SNMMI President, 1993-1994
Mid-Eastern Chapter

COPYRIGHT © 2020 by the Society of Nuclear Medicine and Molecular Imaging.



FIGURE 1. Coronal PET imaging 1 h after injection of 10 mCi FDG to a patient with small cell lung cancer. (Reprinted from (1).)

2 (2) shows a hybrid PET/CT, demonstrating a squamous cell carcinoma in the left upper lobe with associated atelectasis.

Bulk Processes to Receptor Imaging

Since the beginning, nuclear medicine and oncology have been intimately connected. In 1937, the first clinical applications used ^{32}P for the treatment of leukemia. In the 1950s, ^{131}I was used to treat thyroid cancer (3). The imaging for these treatments was mostly done using rectilinear scanners seen in Figure 3 (4). In 1970, $^{99\text{m}}\text{Tc}$ generators had just become readily available. $^{99\text{m}}\text{Tc}$ -methylene diphosphate (MDP) imaging of the bones in 1973 (Fig. 4) (5) was a large element in any nuclear medicine department along with $^{99\text{m}}\text{Tc}$ -sulfur colloid imaging of the liver. “In the nuclear medicine clinic at the University of Washington, liver scanning accounted for 30% of total procedures. At M.D. Anderson Hospital in Houston, a more focused cancer center was posted to remind the technologists, *do not schedule more than 40 liver scans per day*” (3).

Phosphate-Labeled Skeletal Imaging. Also, in the 1970s, $^{99\text{m}}\text{Tc}$ -labeled phosphate, most commonly used as MDP, became a game changer with oncologists in evaluating primary and metastatic bone cancer. With this tracer, we moved to the imaging of metabolism. Tc-labeled phosphonates became one of the most popular imaging procedures for surveillance of bone disease. Part of its success was due to the improved image quality available from the γ -camera, which by 1972 was being widely used by the nuclear medicine



FIGURE 2. Coronal PET/CT imaging 1 h after injection on 10 mCi FDG in a non-small cell lung cancer patient. (Reprinted from (2).)



FIGURE 3. Image is a rectilinear scanner used in the 1970s. (Reprinted from (4).)

community (6). $^{99\text{m}}\text{Tc}$ -labeled phosphate increased from approximately 10% of the total department volume to 35%–45% (1).

Somatostatin Receptors. A promising advancement is the radiopharmaceutical ^{111}In -octreotide. This radiopeptide bonds to somatostatin receptors all over the body. Neuroendocrine, carcinoid, gastrinoma, insulinoma, neuroblastoma, and medullary thyroid carcinomas have a very high concentration of these receptors, allowing visualization and localization of these cell types. The use of the new γ -camera allowed for faster imaging along with an increase in image quality (Fig. 5) (7). ^{111}In -octreotide has nowadays been replaced by ^{68}Ga -DOTATATE and PET imaging, which provides images with better resolution and higher contrast. The potential for new radiotracers to be developed using PET imaging will even further improve examination quality.

Expanding Roles in Therapy

Theragnostic Treatments. Like diagnostic imaging, radioisotope therapy has also been influenced by the greater availability of PET/CT. Theragnostic treatments have evolved from the original ^{131}I and ^{32}P to an advanced multidisciplinary treatment process. ^{177}Lu -DOTATATE for neuroendocrine tumors is being used with success across the world currently, and ^{177}Lu -PSMA (prostate-specific membrane antigen) for prostate tumors looks extremely promising. This has the

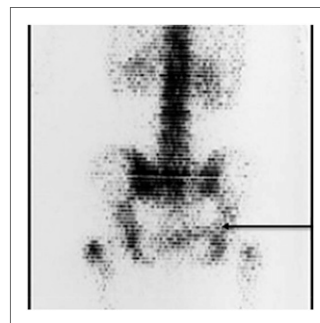


FIGURE 4. (Right) Rectilinear bone scan performed in 1973. (Adapted from (5).)

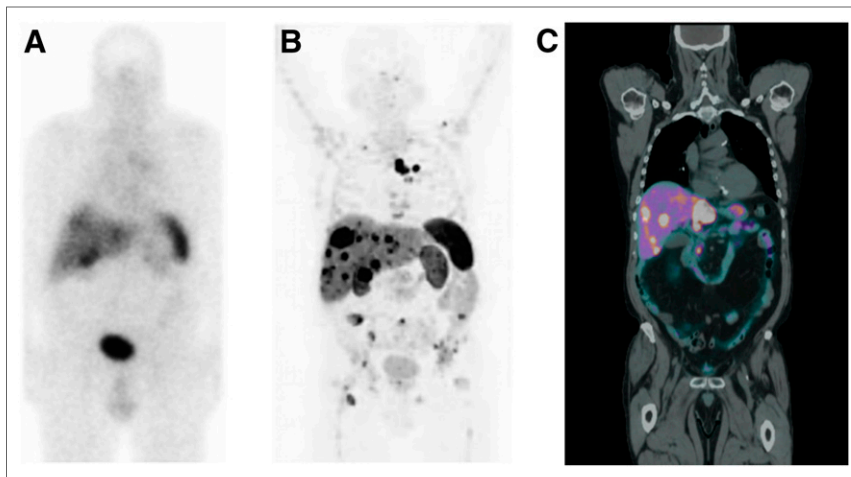


FIGURE 5. (A) Planar ^{111}In -OctreoScan. (B) ^{68}Ga -DOTATATE PET scan; imaging in A and B was obtained 3 wk apart. (C) Coronal fused DOTATATE PET scan. (Image courtesy of CARTI Cancer Center, Little Rock, AR.)

FIGURE 6. Patients treated with ^{90}Y resin microspheres followed by a PET/CT for coverage verification and dosimetry calculation.

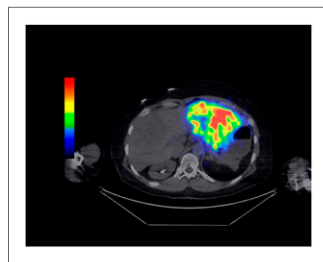
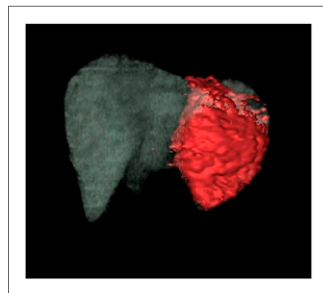


FIGURE 7. Rendered 3D volume of ^{90}Y PET/CT in treated left hepatic lobe. Notice the red area is the treatment area. (Images in Figures 6 and 7 are compliments of CARTI Cancer Center, Little Rock, AR.)



potential to reform prostate cancer treatments and dramatically improve survival rates and quality of life.

^{90}Y selective internal radiation therapy (SIRT) radioembolization has grown in popularity over the past couple of years. The use of ^{90}Y SIRT enables physicians to deliver a high absorbed dose directly to the tumor with a precisely placed catheter (8). This allows for selective radiation therapy. I have seen great results using this treatment that has extended lifespans, and I hope for its continued success. Figure 6 shows an axial fused ^{90}Y PET/CT scan demonstrating left hepatic localization, and Figure 7 is a 3D volume rendering showing treated liver tissue in red (images compliments of CARTI Cancer Center in Little Rock, AR). I

asked Dr. Edgar St. Amour, interventional radiologist at CARTI, why he thought CARTI Cancer Center's ^{90}Y program has seen such success. He said "I think we are successful for several reasons. First, we are a multidisciplinary group with medical, radiation and interventional oncology all under one roof. Therefore, our patients can be treated quickly while minimizing interruptions to treatment. Finally, we have an excellent support staff who are committed to making our ^{90}Y program the gold standard" (Edgar St. Amour, MD, written personal interview, February 28, 2020).

WHAT IS AHEAD?

The practice of nuclear medicine has changed significantly over the past 50 y, but what will it look like in the future? The use of PET/CT, MRI, and CT will continue to be the leaders in diagnostic imaging, but the major changes, I believe, will be with the addition of artificial intelligence (AI) applications and new radiopharmaceuticals. AI will add a level of confidence by providing a more systematic approach in processing data at all levels of an examination. The ability to have computer-aided lesion detection will improve image quality and increase more detailed reporting. New PET/CT radiopharmaceuticals continue to be introduced which better differentiate disease processes and allow new theragnostic treatments. Most recently, there has been the introduction of novel tracers for detecting neurologic diseases such as Alzheimer, Parkinson, and dementia, which will further expand the field of applications. These dramatic changes will continue to take huge strides in the direction of curing diseases through clinical research. We will see substantial technologic advancements in our lifetime, and I am honored to be in the forefront of the field of nuclear medicine.

REFERENCES

1. Nelp WB. Nuclear oncology. *J Nucl Med Technol.* 1995;23(4, suppl):2S-7S.
2. Lee P, Kupelian P, Czernin J, Ghosh P. Current concepts in F18 FDG PET/CT-based radiation therapy planning for lung cancer. *Front Oncol.* 2012;2:71.
3. Wagner HN Jr. 25 years of progress. *J Nucl Med Technol.* 1995;23:S1.
4. Kulshrestha RK, Vinjamuri S, England A, Nightingale J, Hogg P. The role of ^{18}F -sodium fluoride PET/CT bone scans in the diagnosis of metastatic bone disease from breast and prostate cancer. *J Nucl Med Technol.* 2016;44:217-222.
5. Cook G Jr, Maisey MN, Britton KE, Chengazi V, eds. *Clinical Nuclear Medicine.* 4th ed. Boca Raton, FL: CRC Press; 1998:332
6. Stefanović L. The beginnings and development of diagnostic imaging in nuclear medicine [in Croatian]. *Med Pregl.* 2001;54(5-6):289-296.
7. Ambrosini V, Fanti M, Forrer F, Maecke HR. Radiolabeled peptide imaging and therapy in Europe. *J Nucl Med.* 2011;52(suppl 2):42S-55S.
8. SIRTEX. SIR-spheres microspheres [package insert]. Section 5.2. SIRTEX website. <https://www.sirtex.com/media/155127/pi-ec-12.pdf>. Accessed April 21, 2020.