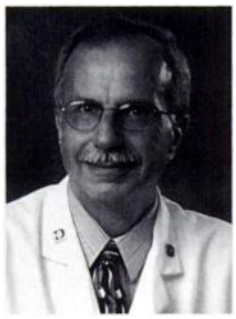

R. Edward Coleman, MD

Henry N. Wagner, Jr., Lecture Clinical PET: Role in Diagnosis and Management

The Henry N. Wagner, Jr., Lecture is presented annually at the meeting of the Society of Nuclear Medicine (SNM). This year's lecture was presented by R. Edward Coleman, MD, Duke University, Durham, North Carolina, at the SNM meeting in June 2000, in St. Louis, Missouri.

This time like all times, is a very good one, if we but know what to do with it.

—Ralph Waldo Emerson

It is a pleasure to give this lecture in honor of Henry Wagner, who has made many significant contributions to the field of nuclear medicine, including the clinical applications of PET. Michael Phelps and colleagues first developed PET at the Mallinckrodt Institute of Radiology in St. Louis, MO, in the early 1970s. MR imaging was developed at about the same time, and it went immediately into commercial development. PET stayed in the research and academic environment for many years, as its clinical applications became apparent. We are now seeing rapid growth in the use of clinical PET. The status of clinical PET as a procedure in nuclear medicine, the reasons for its rapid growth and increased utilization, its use in diagnosis and management of cancer, and the future directions for PET imaging will be discussed.

PET as a Clinical Procedure

Clinical PET imaging is only one of the wide array of uses of PET imaging. PET has been used for almost 30 y to quantify normal physiology and metabolism, to characterize disease, and to evaluate the changes that result from disease processes. The data that have been developed from these research applications have led to the clinical applications. Clinical PET is PET that is used in clinical care and is reimbursed. Clinical PET has only become a reality after widespread reimbursement became available for the procedure.

Clinical PET is having an impact on the distribution of income in a nuclear medicine division. In our division at Duke University, for the month of April 2000, the distribution of revenue for the sections within nuclear medicine included general nuclear medicine at 25%, nuclear cardiology at 34%, PET at 28%, and radiopharmacy at 13% (Table 1). When the fiscal year-to-date revenue through April 2000 is compared with that in April 1999, the increase in revenue for general nuclear medicine is 7%, 25% for nuclear cardiology, 66% for PET, and 41% for radiopharmacy (Table 2). Much of the change in the radiopharmacy revenue relates to PET. Thus, PET has become a major component of the practice of nuclear medicine in our institution, and it is increasing more rapidly than the rest of nuclear medicine and nuclear cardiology. However, nuclear medicine and nuclear cardiology continue to grow at healthy rates.

Don't venture all of your eggs in one basket.

—Samuel Palmer

Put all of your bags in one basket and watch the basket.

—Pudd'n Head Wilson

Regulation and Reimbursement

Rapid growth in the utilization of PET is directly related to changes in radiopharmaceutical regulation and reimbursement. For many years, reimbursement was stifled because of lack of approval of radiopharmaceuticals by the Food and Drug Administration (FDA). In 1997, Congress passed the FDA Modernization and Accountability Act. In this Act, it was stated that PET radiopharmaceuticals have the equivalence of FDA approval until a new process for regulating PET radiopharmaceuticals is developed. The FDA and PET communities are to work in concert for 2 y to develop a mechanism for regulating PET radiopharmaceuticals. After the regulatory mechanism has been developed, the PET community has 2 more years to come into compliance with these guidelines. The FDA and PET communities have been working together for approximately 2 y to develop the mechanism, and the guidelines are to

be published later this summer. The FDA has determined that 3 PET radiopharmaceuticals are considered to be safe and effective: ^{18}F FDG, ^{13}N ammonia, and ^{18}F fluoride. The FDA has an ongoing analysis of ^{15}O water and ^{18}F fluorodopa. It is anticipated that new drug applications (NDAs), abbreviated NDAs, or both, will be submitted for these radiopharmaceuticals.

The action by the Congress, which results in a change in radiopharmaceutical regulation, relieves the hurdle that was inhibiting coverage by the Health Care Financing Administration (HCFA). In January 1998, HCFA began covering FDG PET imaging for the evaluation of indeterminate solitary pulmonary nodules and for the initial staging of lung cancer. After a Town Hall Meeting at HCFA in January 1999, HCFA added the following indications for coverage starting July 1999: detection of recurrent colorectal cancer with rising carcinoembryonic antigens, detection of recurrent malignant melanoma, and staging and restaging of Hodgkin's and non-Hodgkin's lymphomas. The instructions for the coverage included that the coverage was for PET imaging devices, including both dedicated and hybrid systems. The HCFA-approved indications were paid using G codes instead of *Current Procedural Terminology* codes, a policy that is typical for newly approved payments. Beginning August 2000, hospital outpatients will be reimbursed using the new Ambulatory Payment Classification (APC). For PET, we will be using APC 981, new technology level XII, which is reimbursed at $2249.80.

The PET community is requesting a broad coverage policy for PET from HCFA. A document entitled "Report on FDG Positron Emission Tomography for the Health Care Financing Administration" has been prepared by Gambhir, Czernin, Phelps, et al. The document has been organized and produced at the University of California at Los Angeles and contains more than 170 pages of information, including data on 17,000 patients. This document is a submission to the HCFA in support of broad coverage for PET.

Growth of PET

The changes in regulation and reimbursement for PET have resulted in an increased number of FDG studies being performed. These changes have also resulted in improved availability of FDG through commercial distribution. The number of instruments available for PET imaging has increased, and there have been marked improvements in the imaging devices. The estimated number of FDG PET studies was 69,000 for 1998, 106,000 for 1999, and we estimate at least 155,000 studies for this year.

TABLE 1
Distribution of Nuclear Medicine Revenue at Duke University Medical Center

Area	April 2000 (%)	Fiscal year 2000 to date (%)
Nuclear medicine	25	27
Nuclear cardiology	34	33
PET	28	26
Radiopharmacy	13	14

TABLE 2
Increases in Nuclear Medicine Procedure Volum and Revenue at Duke University Medical Center

Area	April 1999–April 2000		Fiscal year 2000 to date	
	Volume (%)	Revenue (%)	Volume (%)	Revenue (%)
Nuclear medicine	4	11	2	7
Nuclear cardiology	32	38	25	25
PET	16	49	42	66
Radiopharmacy	10	20	25	41

In the May 2000 issue of *Diagnostic Imaging*, Bradley M. Tippler wrote an article entitled "No Point Buying Devices that the Buzzard Will Steal from Us." In this article, he goes through the development cycle of new technology from his viewpoint: (1) new technology developed, I read about it; (2) academic centers develop it into potentially useful tool; (3) multiple large centers use and refine; (4) payers reluctantly agree to cover (I do preceptorship and get hospital administration to buy new technology); (5) radiologists incorporate into practice; and (6) other specialists decide they are more qualified to do the procedure.

In the article, Tippler notes that at the last Radiological Society of North America meeting he spent a lot of time reviewing coincidence imaging, primarily for its oncologic applications. He noted that PET is shifting into phases 4 and 5 of his development cycle and notes that it is growing exponentially. "This is hard for me to admit," he writes, "Because just a few years ago, I likened PET scanners to dinosaurs." PET has been considered an expensive,

difficult modality, but the reality is that doing clinical PET is not much different than doing other procedures in nuclear medicine.

Don't try to buy at the bottom and sell at the top. This can't be done except by liars.

—Bernard Baruch

Clinical Applications

PET at Duke University Medical Center is being used in a large number of patients. Approximately 2500 clinical PET scans will be performed this year. A typical schedule for a single day for our dedicated PET scanner is shown in Table 3. On Wednesday, May 24, 2000, we performed 14 studies, including 5 brain imaging studies. The whole-body studies are scheduled for 1 h and the brain imaging studies for 15 min. The whole-body studies are performed in the 2-dimensional acquisition mode for 5 or 6 bed positions. At each bed position, the emission acquisition is for 4 min and the transmission acquisition is for 3 min. At each bed position, the total acquisition time is 7 min. For 5 or 6 bed positions, the actual imaging time is 35–42 min. For the brain imaging studies, a 3-dimensional acquisition is used for a 6-min duration.

We have a large number of referrals for brain tumor studies. The primary indication is for the differentiation of recurrent tumor from necrosis after therapy. For our brain tumor studies, we always register the PET images with the MR images. The other studies that were performed on that day are typical for our laboratory: lung cancer is the most common indication, closely followed by lymphoma, melanoma, and colorectal cancer.

TABLE 3
Typical Day's Usage for Dedicated PET Scanner at Duke University Medical Center (Wednesday, May 24, 2000)

Patient no.	Study	Time of injection	Scan time
1	Whole body (lymphoma)	7:00	7:45–8:45
2	Brain	8:15	8:45–9:00
3	Brain	8:30	9:00–9:15
4	Brain	8:45	9:15–9:30
5	Brain	9:00	9:30–9:45
6	Brain	9:15	9:45–10:00
7	Whole body (lung)	9:15	10:00–11:00
8	Whole body (lymphoma)	10:15	11:00–12:00
9	Whole body (SPN)	11:15	12:00–13:00
10	Limited (breast)	12:15	13:00–14:00
11	Whole body (colorectal)	13:15	14:00–15:00
12	Whole body (lymphoma)	14:15	15:00–16:00
13	Whole body (SPN)	15:15	16:00–17:00
14	Whole body (melanoma)	16:15	17:00–18:00

Future of PET

My interest is in the future, because I am going to spend the rest of my life there.

—Charles Kettering

The future of PET imaging is bright. As more PET imaging instrumentation becomes available, issues related to training become more obvious. There is a national shortage of nuclear medicine technologists and certainly a shortage of technologists trained in PET. There is also a shortage of physicians trained to interpret PET scans. PET scans are the most difficult of all nuclear imaging studies to interpret. There is the necessity for correlating with anatomic imaging studies as well as the variability of normal FDG distribution. Physicians need to be trained in FDG PET imaging before interpreting these studies.

I think there is a world market for maybe 5 computers.

—IBM Chairman, Thomas Watson, 1943

We have reached the limits of what is possible with computers.

—John Von Neuman, 1949

640,000 bytes of memory ought to be enough for anybody.

—Bill Gates, 1981

The Internet will catastrophically collapse in 1996.

—Robert Metcalf

The technology of PET will continue to improve, both from the instrumentation and radiopharmaceutical standpoints. From the instrumentation standpoint, CT scanners will be combined with the PET scanners. This combination will permit accurate registration of anatomy and biology, accurate attenuation correction, accurate scatter correction, and information that can be incorporated into the reconstruction algorithms for more accurate PET reconstruction. These combined PET and CT scanners will be available both for dedicated and camera-based PET.

Remarkable improvements in the quality of PET images have been demonstrated through the use of the microPET scanner. This instrument now operates at a resolution of less than 2 mm, and the resolution of the next generation will be at 1 mm. This system uses the new LSO detector material that will be incorporated into clinical PET scanners in the future.

Timothy DeGrado, PhD, at our institution, has developed ^{18}F fluorocholine as an exciting new radiopharmaceutical with a promise for imaging prostate cancer. Choline is transported across the cell membrane by choline transporter and is phosphorylated by choline kinase. The phosphocholine is incorporated into cell membranes. MR spectroscopy studies have shown increased levels of choline and phosphocholine in several malignancies. Studies performed using ^{11}C choline have shown abnormal accumulation in prostate cancer and in brain tumors. The use of ^{18}F fluorocholine will permit wider distribution of the imaging agent. Our preliminary results for both primary and metastatic human prostate cancer and brain tumors are very promising.

Summary

Nuclear medicine imaging is having a major impact on the diagnosis of malignancy and in the determination of therapy of many malignancies. We are in the infancy of the clinical uses of PET, and its applications will continue to grow both through the use of FDG and new radiopharmaceuticals. The instrumentation continues to improve and provide higher resolution resulting in better lesion detection. The combination of PET and CT devices will further improve the information available for improved patient care.