PET, SPECT, AND NMRI: Competing or Complementary Disciplines?

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In this Second Annual SNM Lectureship, I have chosen to examine whether positron emission tomography (PET), single photon emission tomography (SPECT), and nuclear magnetic resonance imaging (NMRI) are competitive in providing the same, or closely similar, information or whether they should be regarded more as complementary disciplines. I will also attempt to forecast into the reasonably foreseeable future, the roles of these imaging modalities in nuclear medicine.

An analysis of the relative roles of NMR, PET, and SPECT could spur controversy, as strongly expressed opinions are already held in the scientific community about the place, the possible usefulness, the future expectations, and even the disciplinary allegiance of these technologies. A controversial subject can be treated either by attempting to extract a concensus from seemingly divergent opinions or by proposing an analysis of the subject based on the subjective interpretation of scientific evidence. In as much as this lecture is meant to recognize and to honor the pioneering spirit of The Society of Nuclear Medicine, I have chosen the latter approach. Indeed, pioneering spirit is better characterized by personal, sometimes controversial, choices than by the attempt to reach, often artificially, concensus which may not properly identify the issues of the subject analyzed.

NUCLEAR MAGNETIC RESONANCE

The history of the development of nuclear magnetic resonance (NMR) helps us understand the nuclear medicine community's direct interest in NMRI and also the highly optimistic claims which have been made about this modality's role in the in vivo and regional determination of metabolism.

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NMR was invented in the mid 1940s—for this invention Bloch and Purcell were awarded a Nobel Prize in 1952. Between its inception and the early 1970s, NMR was rapidly developed into a highly useful analytical technique providing information about the molecular form of the nuclides capable of producing the proper signals. This technique was, and still is, extensively used by physical and organic chemists. More recently it has been used for the in vivo and in vitro study of biochemical processes essential to life. In many instances tracer methodology was used with NMR analysis, particularly with carbon-13,(^{13}C) but also with fluorine-19 (^{19}F) and other nuclides. In the early 1970s the ability of detecting NMR signals was applied to the imaging in vivo of biological structures and this new imaging procedure was christened "Zeugmatography" by Paul Lauterbur. Today it is probably more generally referred to as nuclear magnetic resonance imaging (NMRI). In light of the wide and effective use of NMR as a tool for the noninvasive study of biochemical processes, particularly of tracer methodology, it was natural for the nuclear medicine community to adopt the new imaging technique of NMRI because its utilization seemed to require the type of competence normally represented in the training and interest of nuclear medicine specialists. The history of NMR as an analytical procedure justified the hope that NMRI would permit the in vivo determination of biochemical processes in a manner similar to that of PET or SPECT. This line of thinking, although logical and founded on solid premises, did not predict well the following trend of NMRI. NMRI today is mostly used as a morphological radiologic imaging technique much closer to computed tomography (CT) than to SPECT or PET; and it is most widely used by radiologists who have rapidly learned to utilize effectively NMRI in conjunction with other radiologic imaging procedures, while so far tracer methodology is playing a negligible role in NMRI. This apparent contradiction between the wide use of NMR as a chemical analytic tool and of NMRI as an imaging procedure providing mostly

TABLE 1
NMR Imaging Variables

Distribution of nuclides which provide NMR signals
Distribution of relaxation times (spin-lattice and spin-spin) of "NMR nuclides"
Frequency shifts of NMR signals
Distribution of "NMR nuclide" tracers, incorporated into selected compounds
Distribution of NMR contrast media
Flow of fluids in and out of the field-of-view

(at least today) morphologic information can be easily traced to: (a) its imaging forming variables; (b) the relatively low signal-to-noise ratio for the NMR signal when used as an imaging variable; and (c) the low concentration in normal tissues of nuclides, other than protons, capable of producing NMR signals.

In assessing from the physical standpoint the position of NMRI with respect to PET and SPECT, two major factors are to be considered: (a) the image-forming variables; and (b) the performance of the systems in imaging these variables. In PET and SPECT, the only image-forming variable is the distribution often varying with time of the systemically administered radionuclide. In NMRI there are six important variables (Table 1) which can be, and already have been, utilized for biomedical imaging applications. The ability of any imaging system including NMRI, PET, and SPECT of displaying the image forming variable can be assessed as the system's resolutions (Fig. 1). A system's resolutions are important in the assessment of its usefulness because, in most instances, they reflect the capabilities and limitations that can be expected, from the system used in displaying the image-forming variables. Indeed, an insufficient spatial or contrast resolution may mask a spatially subtle variable and an insufficient temporal resolution may prevent, through inadequate sampling, the investigation of a phenomenon changing with time.

The overwhelming majority of NMRI examinations to be performed today and, in all probability, to be carried out in the foreseeable future will use hydrogen as the image forming variable, because protons are nuclides which can provide NMR signals easily detectable with a high sensitivity and because their concentration mostly as water in soft tissues is very high (Table 2). The high signal-to-noise ratio yielded by NMRI of hydrogen in soft tissues provides excellent spatial and temporal resolutions (a few percent contrast in a few minutes with a spatial resolution of about 1 mm for a magnetic field of the order of 1 Tesla). It should be emphasized that in NMRI of protons (and other nuclides) the contrast in the image is produced by the density of signal generating nuclei but modulated by physical and chemical variables which affect the relaxation times T_1 and T_2 of the signal. This property can be utilized in emphasizing either T_1 or T_2 in correlating the factors affecting T_1 and T_2 with morphology, tissue composition, and pathology. Figure 2 shows a sagittal tomographic image of the brain obtained at 1.5 Tesla with a spin-echo mode emphasizing T_2 and showing well the distinction of gray and white matters. Another useful variable in NMRI is provided by the differences in the frequency of the NMR signals modulated by the chemical and physical states of the signal producing radionuclide. It is this variable which provides the basis for NMR spectroscopy. Chemical frequency shifts of the NMR signals have been used in imaging with protons. Figure 3 demonstrates the possibility of distinguishing between water and hydrogen bound protons through the use of the differences of the frequencies of the NMR signals from these compounds for a given magnetic field. No nuclear medicine imaging modality competes with NMRI of protons. There are gamma-or positron-emitting

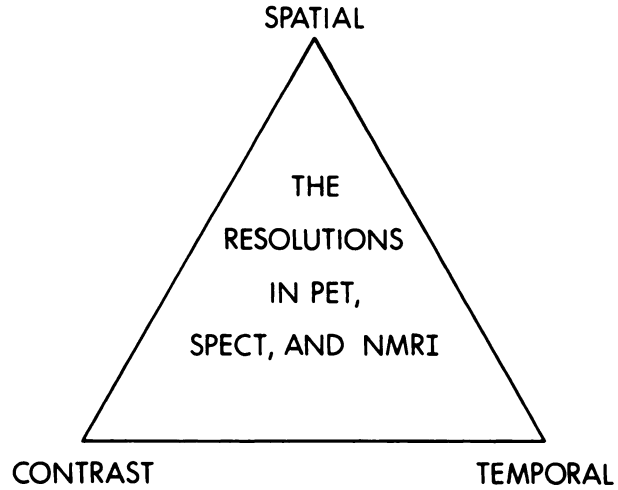

FIGURE 1
Resolutions in PET, SPECT, and NMRI

TABLE 2
Concentrations in Soft Tissues of Nuclides Capable of Providing NMR Signals

Nuclide	Typical concentration in tissue (atoms/g × 10^{20})	Isotopic abundance (%)	NMR sensitivity relative to ^1H at constant field	Imaging* index relative to ^1H
^1H	460	100	1	46,000
^{31}P	0.60	100	0.07	10^{-4}
^{23}Na	0.42	100	0.09	10^{-4}
^{13}C	24	1	0.016	10^{-4}
^{19}F	—	100	0.83	—

Adapted from P. L. McGeer in National Conference on Biological Imaging, National Academy of Sciences, 1983.
*Without consideration of relaxation times.

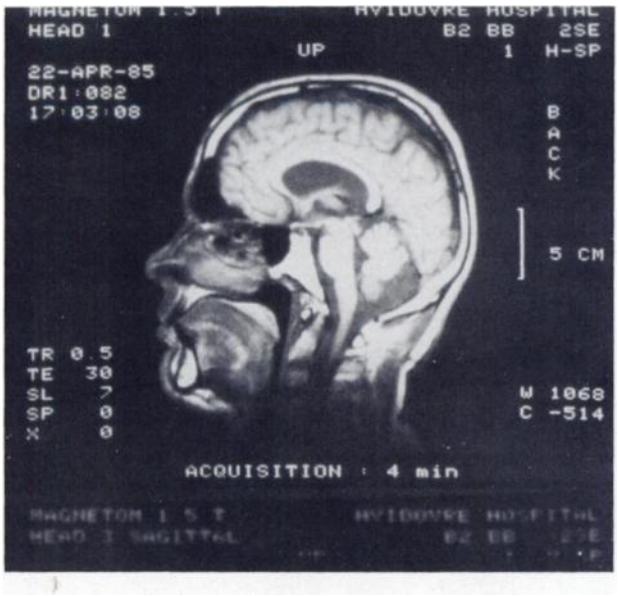

FIGURE 2
Proton NMRI midline sagittal head study acquired with the spin-echo technique. Image parameters were: TR = 0.5 sec, TE = 30 msec, Slice thickness = 7 mm. (Reproduced courtesy of Siemens Medical Systems and Hvidore Hospital Copenhagen)

radionuclides of hydrogen and the splendid NMR morphologic images showing the distribution of hydrogen in various chemical and physical states which are now widely clinically used are the unchallenged domain of NMRI.

The normal composition of living tissues includes, in addition to hydrogen, several other nuclides capable of generating NMR signals. The more abundant of those are listed in Table 2. Unfortunately, because of their low concentration in soft tissues and their lower NMR sensitivity as compared to hydrogen, the imaging of these nuclides yields a dismal signal-to-noise ratio as compared to hydrogen. Nevertheless, highly promising images of the distribution of phosphorus-31 (^{31}P) and sodium-23 (^{23}Na) have already been achieved, albeit with a lower spatial and temporal resolutions than achieveable with protons. A superficial assessment of the spatial resolution that could be achieved on the basis of our present understanding of the physical factors in NMRI, of images reflecting the natural content of ^{31}P in normal living tissues in man is of the order of 2–3 cm with a temporal resolution of several minutes. The NMR imaging of ^{23}Na is much more favorable than that of ^{31}P because of the short relaxation times of ^{23}Na and promising images of that nuclide have been

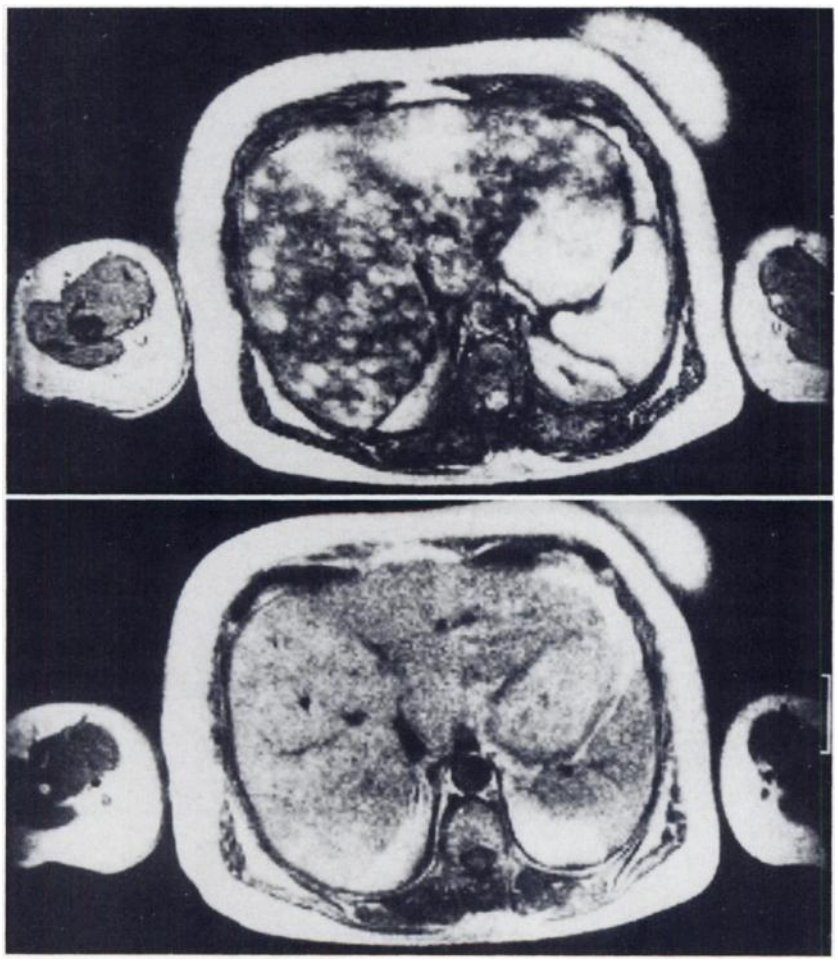

FIGURE 3
Proton NMR images obtained by utilization of difference in frequencies of signal between water and lipid bound protons (Courtesy of T. Dixon, PhD, Washington University School of Medicine, St. Louis, MO)

obtained with a resolution of a few millimeters. It is interesting to note that in the imaging of phosphorus, NMRI provides a considerably poorer resolution than conventional nuclear medicine imaging; however, there is no practical radionuclide which might permit nuclear medicine imaging of the distribution of phosphorus in tissues. The only possible candidate for that role, ^{30}P, decays with a half-life of ~ 2.5 min, and seems to be too short-lived to allow its nuclear medicine imaging after proper equilibration. On the other hand, sodium-24 is a radionuclide which has already been used in nuclear medicine imaging and with the use of SPECT, it potentially might compete, for some applications, with NMRI imaging of this element. It should, however, be kept in mind that NMRI exhibits always the dimension, unchallenged by nuclear medicine imaging, of providing information about the chemical-physical state of the image forming nuclide. In the case of sodium imaging, NMRI permits the distinction between intracellular and extracellular sodium, a useful variable to which nuclear medicine imaging is blind.

Moving fluids, particularly blood, can be imaged by NMRI by utilizing the property that NMR excited nuclides in a moving medium may be swept out, or under certain circumstances, swept into, the plane of signal observation. This property has already been shown to offer much promise in NMR angiography.

Another variable which is utilized in NMRI consists of the use of agents administered systemically with the purpose of enhancing contrast. While this approach is similar to the use of contrast media in conventional diagnostic radiology, there are properties of these agents specific to NMRI. Some of the NMRI contrast agents are imaged because they contain a large concentration of nuclides capable of producing specific frequency signals. For example, fluorinated blood substitutes labeled with ^{19}F can be used in angiography. NMRI contrast agents which are excreted by the kidneys or the liver can provide information about renal function or anatomy. Other NMRI contrast agents enhance NMRI signals by altering the local magnetic environment of nuclides normally providing NMRI signals. These usually paramagnetic agents do not provide inherent contrast but they are capable of modifying the NMR signal of indigenous nuclides. Such agents are highly promising for angiography and renal imaging.

Tracer methodology has been used, and is being used, in NMR by the introducing, into the sample analyzed, compounds labeled with nuclides capable of producing NMR signals, such as ^{13}C which naturally exhibits a low natural isotopic abundance as compared to ^{12}C (Table 2) or ^{19}F which has been used in the labeling of analogs such as fluorodeoxyglucose. Thus, it is tempting to extrapolate the use of tracer to NMRI. Unfortunately, the applications of tracer methodology in NMRI are severely impeded by the relatively low signal-to-noise ratio which leads to the requirement of large concentrations of NMR radionuclides to achieve useful resolution in a tolerably short period of time. This condition all but invalidates the use of this methodology in NMRI for the study of metabolic processes because the fundamental premises of tracer use that "abnormalities in metabolism must not be brought about through the action of the isotopic sample on the organism" (M.D. Kamen, In *Isotopic Tracers in Biology* and *Introduction to Tracer Methodology*, New York, Academic Press, Inc., 1957) is, in most instances, violated because the low natural concentrations of molecules important in the investigation of metabolism (Table 3) is dwarfed by the concentrations of NMR nuclides required for effective imaging. The possibility of imaging neuroreceptors through NMRI tracer labeling is even more remote (Table 3). Thus, tracer methodology for NMRI is useable only with the administration of chemically large quantities of tracer materials with the concomitant requirement of the proof that the administration of the tracer material does affect accountably the phenomenon under study. At this time, on the basis of our understanding of well documented physical limitations, it appears that tracer methodology will be useful in the study of metabolism by NMRI under the best circumstances, only in a very limited number of cases. In this, NMRI does not challenge either positron emission tomography or single photon emission tomography which both rely entirely on the use of tracers, usually administered in quantities well below levels which might affect the metabolic process under study.

The present resolution of NMRI for protons is $(3\ mm)^3$ (Table 4) and it is reasonable to speculate that a resolution

TABLE 3
Concentrations of Some Brain Materials and Specific Activities Required of Imaging Ligands

	Specific activity mCi/mmol	Tissue concentration mol/g
Energy intermediates	10^{-1}–1	10^{-6}–10^{5}
Amine neurotransmitters	10^{2} –10^{3}	10^{-9}–10^{-8}
Receptors	10^{5} –10^{7}	10^{-13}–10^{-11}

Adapted from P. L. McGeer in National Conference on Biological Imaging, National Academy of Sciences, 1983.

TABLE 4
Sensitivity and Resolution of NMR and PET

Technique	Approximate sensitivity limits units/g of tissue × 10^{20}	Resolution	
		Present	Estimated achievable
NMR (protons)	4	$(3\ mm)^3$	$(1\ mm)^3$
PET	10^{-12}	$(8\ mm)^3$	$(3\ mm)^3$

Adapted from P. L. McGeer in National Conference on Biological Imaging, National Academy of Sciences, 1983.

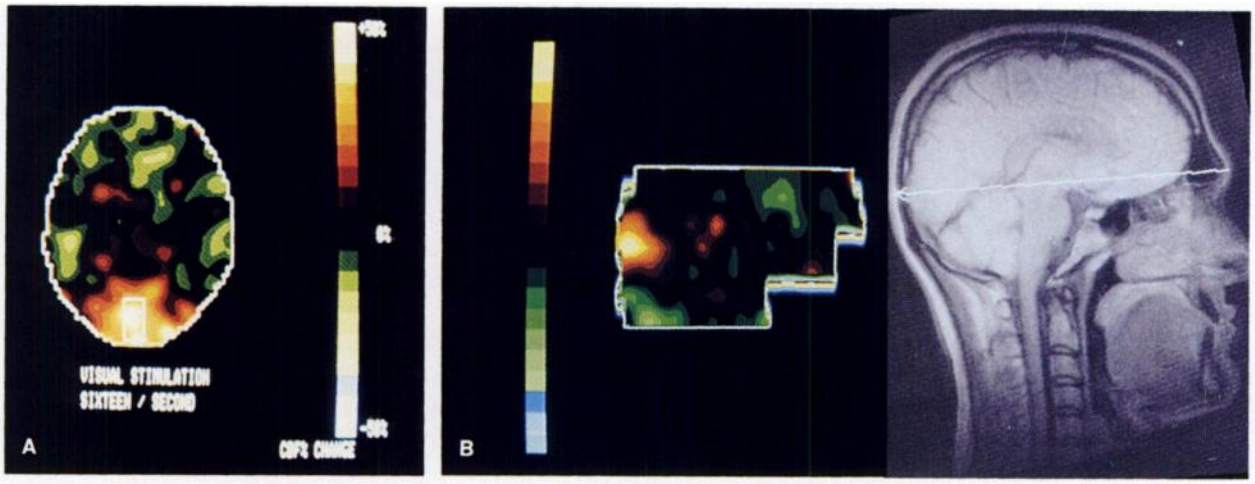

FIGURE 4
PET image of visual stimulation showing increase of blood flow in visual cortex (A: Transverse tomographic section, B: Sagittal section). (Courtesy of P.T. Fox, MD and M.E. Raichle, MD, Washington University School of Medicine, St. Louis, MO)

of 1 mm^3 will probably be achievable in the foreseeable future. In comparison, the present resolution of PET is ~ $(8\ mm)^3$ with an estimated achievable resolution of $(3\ mm)^3$ however, with a sensitivity which is ~ 10^{12} times greater than that of NMR (Table 3). Thus, while PET cannot compete today with the splendid anatomical NMR images, it is reasonable to conclude that NMRI will not image the variables pictured in Figs. 4 and 5, which seem to remain the exclusive domain of PET, and perhaps of SPECT, for the foreseeable future.

FIGURE 5
Image of distribution of neuroreceptors (Courtesy of Henry N. Wagner, Jr., MD, The Johns Hopkins Medical Institutions, Baltimore, MD)

SINGLE PHOTON EMISSION TOMOGRAPHY AND POSITRON EMISSION TOMOGRAPHY

SPECT and PET have in common the same image reconstruction process which was pioneered by David Kuhl, so it is tempting to regard them as variations of the same nuclear medicine imaging modality. Such characterization is misleading because it obscures fundamental conceptual and technological differences which affect profoundly the applications, the usefulness, and the future of these two approaches. These differences are reflected by the historical development of PET and SPECT.

The fundamental concept which has led to the development of PET and which still represents the major cornerstone of this modality is that a certain number of radionuclides, which happen to decay through the emission of positrons, exhibit chemical properties which render them particularly useful as biological tracers. The most important of these radionuclides are carbon-11, oxygen-15, nitrogen-13, and fluorene-18, the "physiologic" radionuclides. Serendipitously, these radionuclides decay through the emission of positrons a property which considerably facilitates their detection in vivo as demonstrated by Gordon Brownell a number of years ago, and considerably improves the precision and resolution of their tomographic imaging. Thus, the foundations of PET are the utilization of some specific radionuclides in biological tracing with desirable chemical properties considerably facilitated by the fact that their decay through the emission

of positrons; this emission permitting their favorable detection and the tomographic reconstruction of their distribution in vivo. The short half-lives of these nuclides further enhances their usefulness in many instances.

Figure 6 shows what is probably the first applications of ^{15}O in a biological application which demonstrated that this radionuclide, in spite of its very short half-life of about 2 min, could be effectively used in the tracing of metabolic pathway.* Later, ^{15}O and other "physiological" radionuclides were used in various physiological studies including cerebral blood flow and metabolism, various investigations of the functional and metabolic integrity of lungs, and of other organs. These early studies were carried out by means of scintillation probes which were often highly collimated to achieve regional measurements (Figs. 7 and 8). One of the major studies, which was carried out in several centers throughout the world, consisted in the analysis of the data obtained by the use of biological models developed in biochemistry. Often, the interpretation of the data obtained required the proper tailoring of the labeled compound administered, and/or the administration of several compounds, to provide the needed parameters in the model. An example of the latter is the measure of cerebral blood flow by means of probes, such as shown in Fig. 7, through the successive administration, by injection, of ^{15}O-labeled water, oxyhemoglobin, and carboxyhemoglobin into the internal carotid artery.

The reliance of these studies on physiologic modeling and proper labeling attracted a number of physiologists and chemists to this technology whose contributions were vital to the development of PET. In the early 1970s a tomographic reconstruction process provided an added dimension to the use of the "physiological" radionuclides. This reconstruction process followed the SPECT inventions by David Kuhl et al., the construction of a tomographic system utilizing the detection of the annihilation radiation by Robertson et al., and the clear understanding of the mathematical aspects of reconstruction of images from projections developed for computed tomography by Hounsfield and Cormack. These early positron emission tomographs rapidly led, through a series of increasingly sophisticated devices (Figs. 9 and 10), to the type of apparatus presently in use (Fig. 12). It is important to emphasize that the developments in the devices for PET imaging were guided by the demands imposed by the requirements of the physiological processes to be studied and particularly by the type of modeling needed to under-

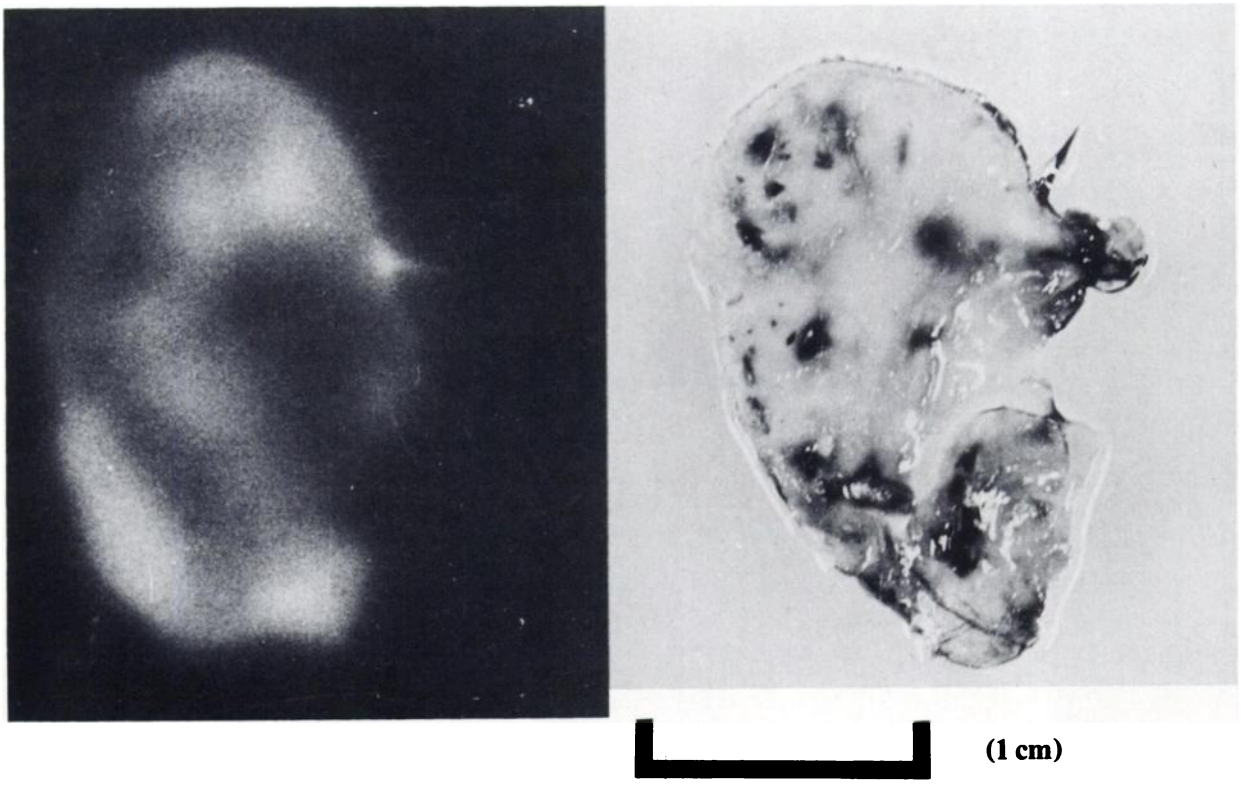

FIGURE 6
Autoradiograph (left) and photograph (right) of section of mouse tumor (mammary adenocarcinoma). Mouse was administered ^{15}O-labeled air by inhalation, before dropping it into liquid nitrogen and sectioning tumor. Autoradiograph shows irregular distribution of ^{15}O in form of metabolically labeled water. This picture represents what is probably the first application of ^{15}O in biology

stand them. For example, the need to increase spatial resolution in many cardiac and cerebral studies led to the gradual improvement of the resolution of the present systems. The requirement for fast data acquisition, particularly in cerebral studies with bolus administration of ^{15}O, led to the development of very fast tomographic systems and to the utilization of time-of-flight in the image reconstruction process. Finally, the multiple sampling in time demanded by some models led to the incorporation of list mode data acquisition in the more modern systems (Fig. 13).

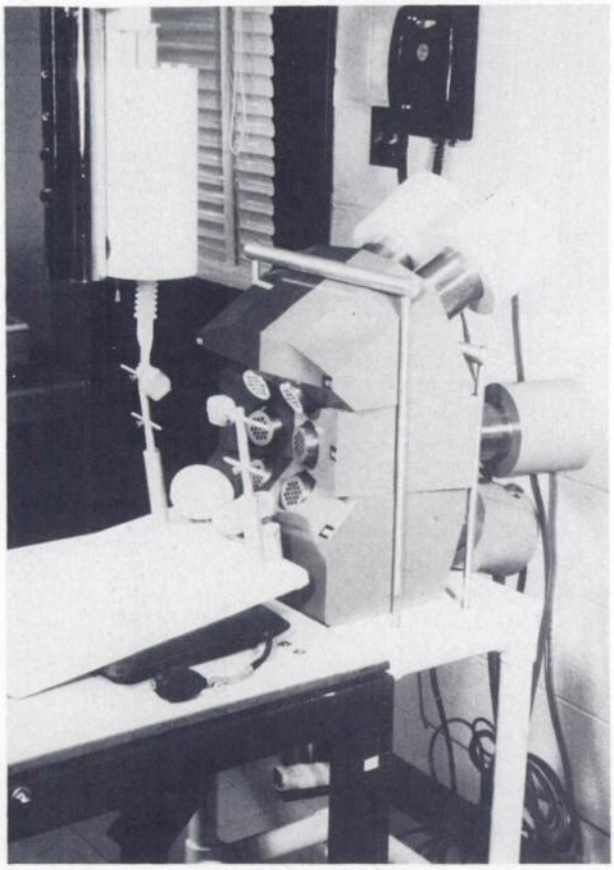

FIGURE 7
Scintillation probes used in regional measurement of cerebral blood flow and oxygen metabolism by means of ^{15}O

An important facet in the improvements of PET imaging devices is that they were guided mostly by the requirements (better quality images, higher spatial contrast, and temporal resolutions) but with relatively little concern to their cost. This resulted in devices challenging to the utmost technology but at a high cost.

Concomitant with the development of PET imaging devices, chemists, guided by the requirements of the physiologists, succeeded in labeling a large number (at the time of this writing over 400) of useful compounds with "physiological" radionuclides and many automated devices were developed to provide routinely used compounds. Today, through the availability of high performance imaging devices, suitably engineered chemical compounds, and well understood physiological models, a number of physiological parameters so far inaccessible by any other means have been unraveled by the application of PET.

The development of SPECT and the general thrust of that modality are different from that of PET. SPECT was developed as an imaging procedure to provide tomographic images with radionuclides used conventionally in nuclear medicine. For a relatively long period of time after the description of this technology in the early 1960s, SPECT, in spite of its promise, was not widely used in nuclear medicine. Within the past decade several academic investigators and industrial concerns recognized the potential usefulness of SPECT. One can speculate that

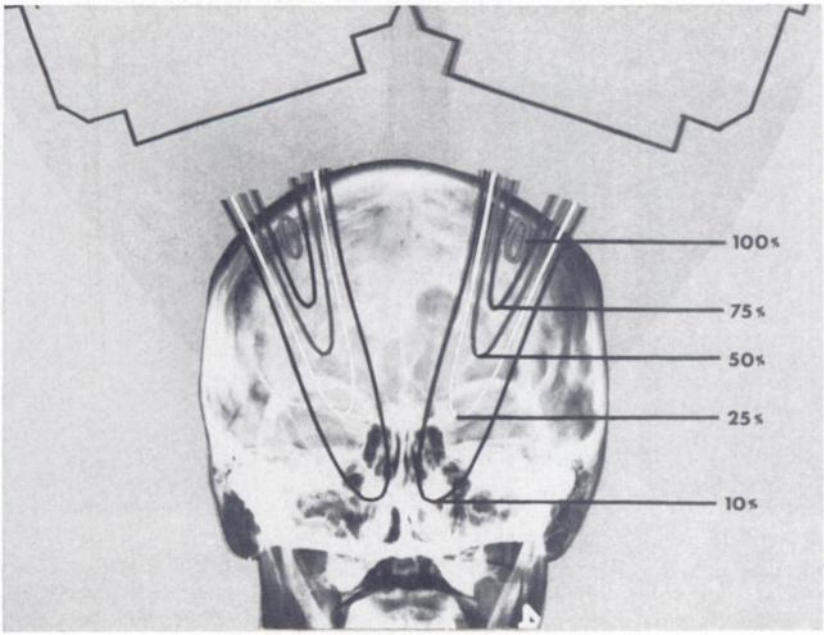

FIGURE 8
Isocount curves for probes shown in Fig. 7

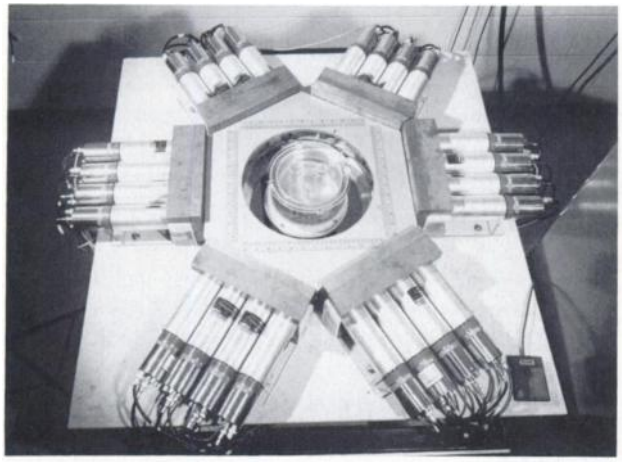

FIGURE 9
Early positron emission tomograph constructed from probes shown in Fig. 7

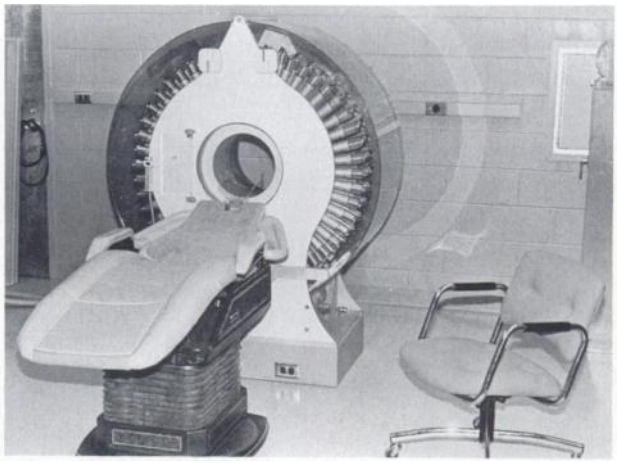

FIGURE 11
PETT V, first positron emission tomograph utilizing wobble motion of detectors to achieve suitable linear sampling

this renaissance was stimulated by the broad use of computer tomography and of the growing interest in PET. The development of SPECT armamentarium followed two different routes.

One consisted in optimizing the imaging devices for the tomographic reconstruction process; the other utilized existing imaging devices, usually Anger cameras (Fig. 14, 15), and adapted them through the incorporation of motion and computer hardware and software to tomography. Many of the early adaptations of Anger cameras to SPECT yielded images of poor quality because their design overlooked some of the stringent requirements for tomographic reconstruction such as high mechanical stability in the system's motions and high constancy of the detectors' sensitivity for different angles of data acquisition. This deficiency was, however, recognized by the manufacturers and they have been eliminated in many state-of-the-art systems presently offered but at a cost of considerably increased price over the earlier designs. SPECT devices specifically designed for the application of this modality are usually well engineered and by and large yield better quality images (Fig. 16) than SPECT devices based on the adaptation of the Anger camera.

CONCLUSION

PET, SPECT, and NMRI have now reached a degree of maturity where it is possible to assess, with an acceptable degree of certainty, whether these technologies exhibit areas of overlap in their usefulness, whether one of the modalities may be competitive with another, or whether the usefulness of one technique is enhanced by the availability of the others. The foundations of the above three disciplines are sufficiently well understood that an assess-

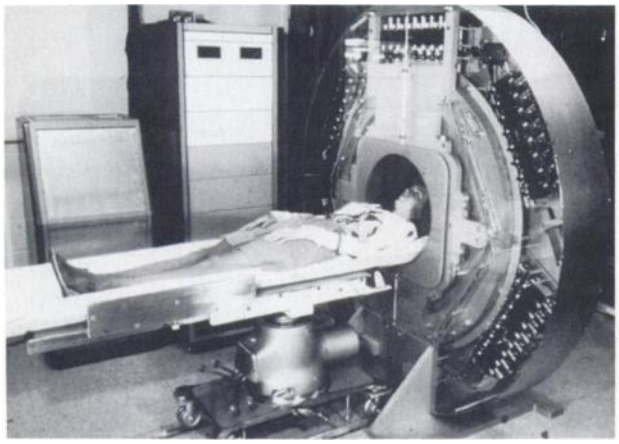

FIGURE 10
PETT III, positron emission tomograph developed from pı totype in Fig. 9, which was, and still is extensively used PET studies in human subjects

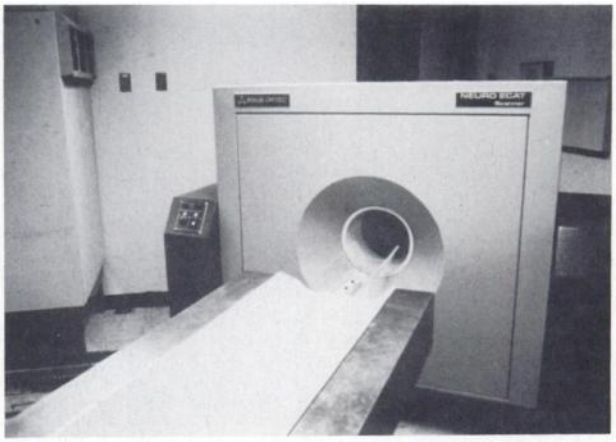

FIGURE 12
Neuro-ECAT, positron emission tomograph specifically designed for cerebral studies. (Courtesy of Henry N. Wagner, Jr., MD, The Johns Hopkins Medical Institutions, Baltimore, MD)

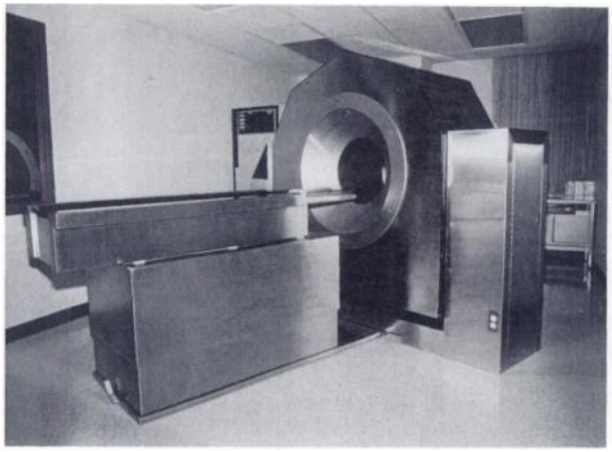

FIGURE 13
Super PETT I, positron emission tomograph utilizing photon time-of-flight information in image reconstruction process. This device also incorporates list mode data acquisition.

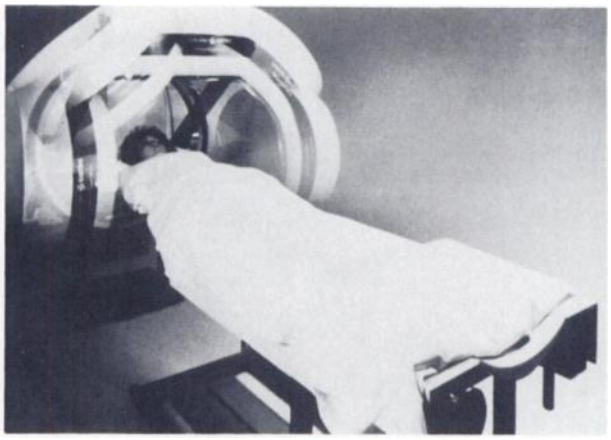

FIGURE 14
SPECT camera utilizing single Anger scintillation camera fitted with suitable gantry to provide tomographic imaging capability. (Courtesy of General Electric Company, Milwaukee, WI)

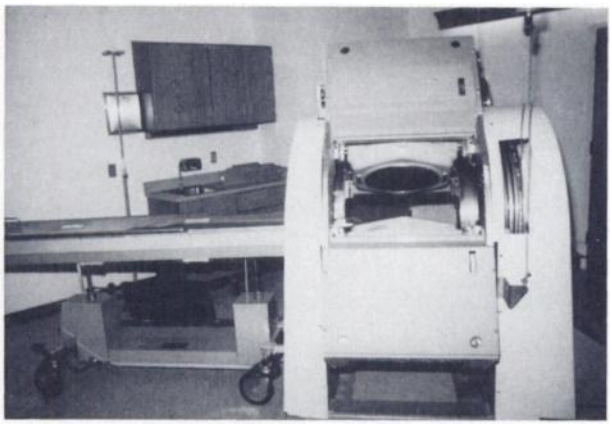

FIGURE 15
SPECT camera incorporating two Anger scintillation cameras (Courtesy of R.E. Coleman, MD, Duke University Medical Center, Durham, NC)

ment of their relationships is valid for the present and for the near future.

NMRI has, within the past few years, achieved a well-deserved recognition as a useful clinical tool. The research potential of NMRI is vigorously exploited by many investigators. The early expectations that NMRI would provide the same, or similar, information as SPECT or PET, in measuring regional metabolic processes have, so far, not been justified. While the possibility of imaging phosphorus and performing phosphorus spectroscopy by NMRI is unmatched by either SPECT or PET, tracer methodology, which is the mainstay of SPECT and PET, seems to be denied to NMRI at useful spatial and temporal resolutions. NMRI has already proven to be useful as a complementary modality to SPECT and PET in establishing, particularly in the brain, an anatomical map for the biochemical information which they supply. NMRI, at this time at least, appears to supply mostly morphological information with additional valuable information provided mostly by T_1 and T_2 about the chemical bonds of the image forming protons. So far, NMRI is much closer in its use to diagnostic radiology than to nuclear medicine. Indeed, most radiologists are well prepared, usually from their training in computed tomography and from their direct NMRI training, to interpret NMRI images; whereas the particular skill of nuclear medicine diagnostic physicians in utilizing tracer methodology and physiological modeling does not seem to be directly applicable in NMRI. Many interested nuclear medicine specialists have acquired through training the needed skill for interpreting NMRI images just as diagnostic radiologists have developed suitable competence in nuclear medicine imaging.

The present position of PET in nuclear medicine and its future are relatively easy to assess. PET can be regarded as a textbook example of tracer methodology applied to the in vivo assessment of regional metabolism associated parameters and drug distribution. So far, PET has been mostly used in basic physiological investigations and it is safe to speculate that investigation of normal physiology and pathophysiology will remain the important application of this methodology. A certain number of clinical applications of PET have already been identified and are being applied, albeit in a small number of medical centers. The number of PET units in the world at the time of this writing is ~ 50 and their number is increasing roughly at the rate of 10% per year. It is safe to speculate that the applications will grow and therefore stimulate greater use of this imaging modality. The type of information supplied by PET, either in basic research or in clinical applications, is not provided by NMRI or by SPECT. The single most important factor that severely slows down the application of PET in nuclear medicine is the necessity of generating the "physiological" radionuclides, usually by means of a cyclotron in the immediate vicinity of the site where they are to be used and in labeling the needed radiopharmaceuticals. These operations are costly and re-

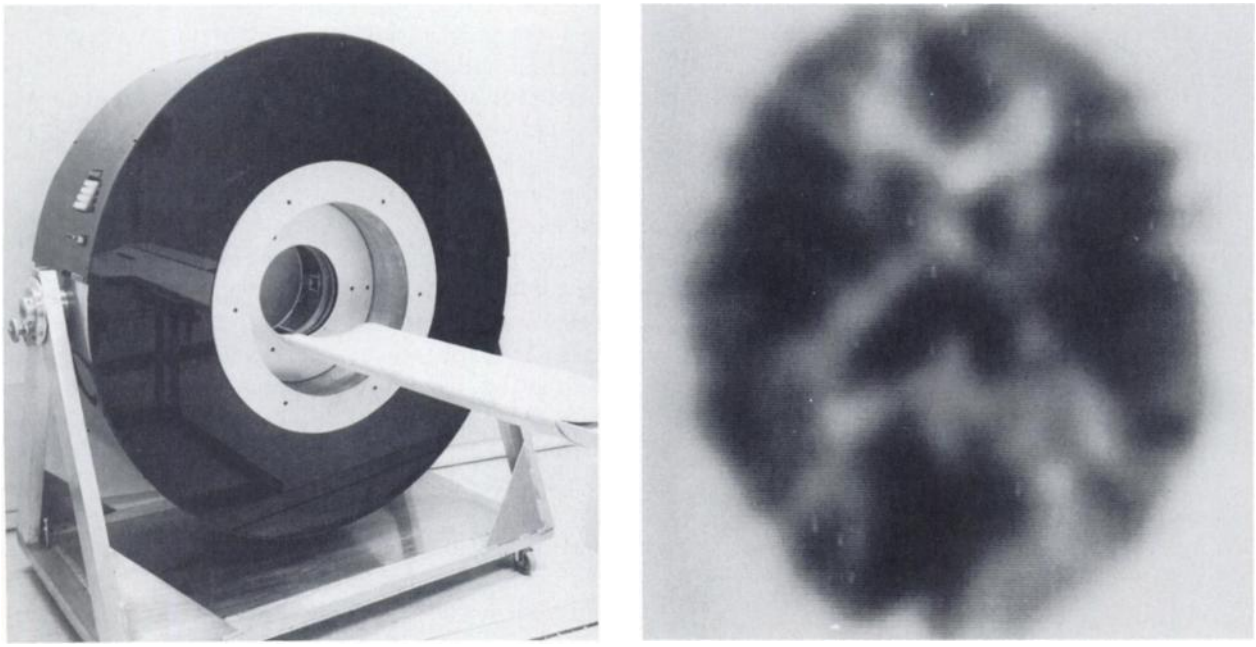

FIGURE 16
SPRINT, stationary detector single photon tomograph for cerebral studies. Photon collimation is achieved by means of rotating slit system. Transverse resolution of this system in 8 mm FWHM for central located source (Courtesy of W. Leslie Rogers, MD, *IEEE Trans Med Imaging* MI-1:63–68, 1982). Image of brain obtained by SPRINT. Radiopharmaceutical: 8 mCi of [^{123}I] HIPDM (Courtesy of W. Leslie Rogers, PhD, *The Journal of Nuclear Medicine* 25:1013–1018, 1985)

quire expensive highly trained personnel. However, the gradual decrease in the cost of PET armamentarium coupled with the availability of automated systems for the labeling of clinically useful radiopharmaceuticals is reducing the cost of the use of PET for clinical purposes. A reasonable extrapolation, from well documented cost figures, shows that, with a sufficiently large patient population, a PET unit can be operated clinically at a cost per patient comparable to that of the more expensive nuclear medicine examinations.

The present place of SPECT and its future in nuclear medicine are difficult to gauge. The progress of SPECT is hindered by three weaknesses.

1. The sensitivity of SPECT expressed as counts recorded for a given image spatial resolution for a given dose of radiation delivered to the patient is considerably lower than for PET. The reason for this difference lies mainly in the methods used in the collimation of the photons in these two technologies but also in the short half-lives of PET "physiological" nuclides.

2. Most of the SPECT devices, with few exceptions (Figure 16), presently utilized in nuclear medicine have not been sufficiently optimized for tomography. While the cost of less than optimal SPECT devices is moderate, their performance does not do justice to the SPECT tomographic reconstruction process.

3. Most importantly the majority of the radiopharmaceuticals available for SPECT, at this time, were developed for more conventional nuclear medicine imaging and they do not compete well with the rich pharmacopoeia developed for PET.

Some of the shortcomings of SPECT, as compared to PET, are difficult, some impossible, to overcome. It is quite probable that the quality of the images obtained with PET will remain appreciably superior to those obtained with SPECT. Nevertheless, in spite of the poorer image quality, SPECT may, in many cases provide the needed information without requiring additional spatial or contrast resolution. The instrumentation for SPECT is continuously being improved, albeit at increased cost. While at this time there is a considerable difference in the cost of a PET and SPECT device (over $1 million for a PET device, and ~ $200,000 for a SPECT device), the optimization of SPECT devices and the lowering of PET costs is leading to the narrowing of this gap. From technological considerations, an optimized SPECT device should not be any cheaper than a PET device similarly optimized. There is little doubt that the number of radiopharmaceuticals which can be effectively utilized in conjunction with SPECT is growing. Indeed, many highly imaginative chemists are working on structuring radiopharmaceuticals to compete with those utilized with PET but labeled with SPECT useable radionuclides such as technetium-99m, iodine-123.(^{123}I) It is probable that some of the information acquired about biochemical processes by means of PET can be transferred to the tailoring of suitable ra-

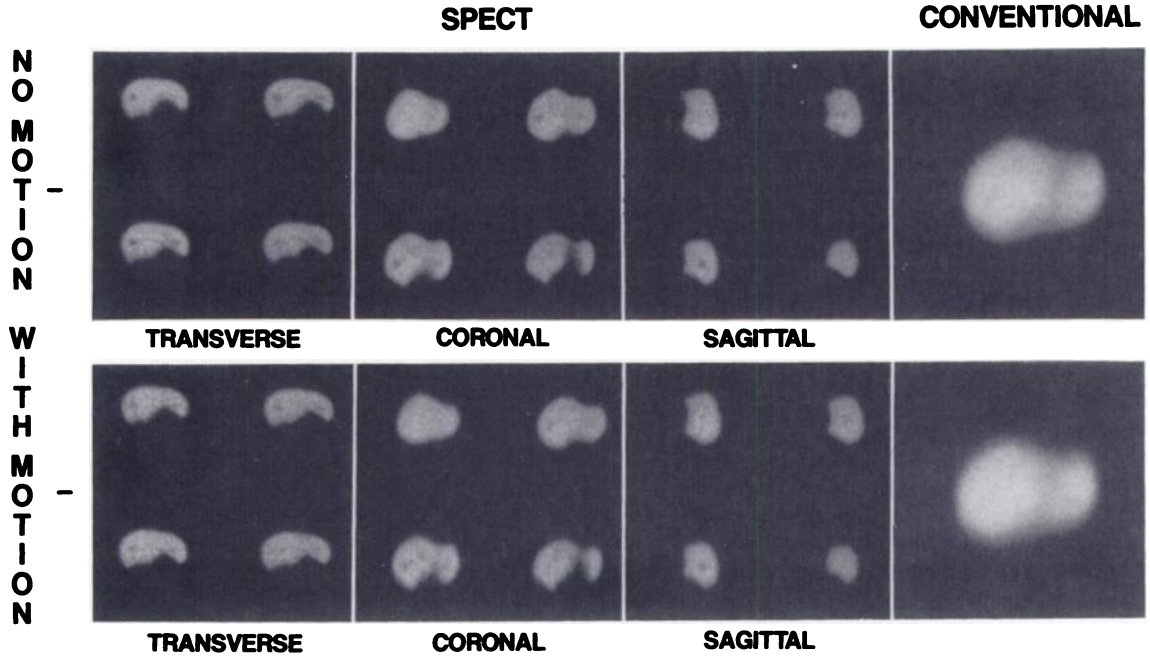

FIGURE 17
Conventional gamma camera and SPECT images of patient's liver. Note that SPECT images reveal metastases invisible by conventional examination. SPECT study was obtained with camera shown in Fig. 15. (Courtesy of R.E. Coleman, MD, Duke University Medical Center, Durham, NC)

diopharmaceuticals compatible with SPECT imaging, but only time will tell to what extent such transfer of technology will become clinically effective. SPECT does not compete effectively with PET in basic studies of physiology and pathophysiology. In these areas the much more performant imaging devices and the flexibility provided by radiopharmaceuticals labeled with "physiological" radionuclides permits well modeled and clearly understood studies which so far are unmatched by SPECT. In many clinical studies, SPECT is no match for PET either, mostly because of the unavailability of suitably labeled radiopharmaceuticals, but also because of the lesser performance of SPECT imaging devices. Such applications include metabolic studies of oxygen, glucose, and fatty acids metabolism and, in the future, will probably include the assessment of neuroreceptor integrity. In general, but with exceptions, any study that can be carried out by PET, provided a suitable radiopharmaceutical is available, yields better quality results for a lower dose of radiation than with SPECT. In clinical applications, SPECT offers, over PET, the considerable advantage of the availability of radiopharmaceuticals from commerical suppliers without the need of the operation of a costly and complex cyclotron with the associated instrumentation and personnel needed for the labeling and quality control of radiopharmaceuticals.

The strength of SPECT stands out not with respect of PET, but with respect to conventional nuclear medicine imaging. Indeed, it is now well established that many clinical studies carried out by SPECT yield superior results than obtainable with conventional nuclear medicine imaging procedures (Fig. 17). This recognition of the usefulness of SPECT has led to a rekindled interest in this modality leading to the installation, in the recent past, of ~400–500 SPECT units worldwide. Parenthetically, the success of PET has probably contributed to a revival of interest in SPECT. Perhaps in return, the acceptance of SPECT will diminish the fear of PET complexity. It is reasonable to expect that more clinical applications will be found for SPECT because the higher contrast achieved with SPECT as compared to conventional nuclear medicine imaging, allows strategies inaccessible to the latter. In spite of its successes, it appears at this time, that the broader dissemination of SPECT in nuclear medicine will depend on the rate of development of newer clinically useful radiopharmaceuticals and also the availability of instrumentation optimized for SPECT, which, in all probability, will be more expensive than many of the present devices. The ultimate future of SPECT must await the results of the most valid touchstone test in medicine, that is, clinical usefulness.

In conclusion, there does not seem to be any appreciable competition between PET, SPECT, and NMR in the type of information that these modalities yield. They compete only in utilizing the different types of information which they provide in answering some biomedical problems. NMRI adds to PET and SPECT superb morphological information for the anatomical localization of the nuclear medicine studies. The only real competition between these technologies is for financial and human resources.

FOOTNOTE

*This picture was shown during a conference on the peaceful applications of radioisotopes organized by UNESCO and held in Paris in 1957. The chairman of the session during the presentation was Dr. Frederic Joliet Curie, a recipient of the Nuclear Medicine Pioneer Award who, at the time, expressed the opinion that very short-lived radionuclides could indeed be used effectively in biological investigation.

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