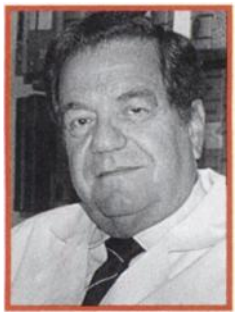

Henry N. Wagner, Jr., MD

SNM 1999

Fused Image Tomography: An Integrating Force

Two characteristics of the Information Age are that (1) communication throughout the world is now free, and (2) everyone can know everything about everything. The internet makes it possible to communicate with each other as if we were in the same room. In this context, I promised to present at the 1999 Society meeting the results of a questionnaire I recently sent to the 1,250 nuclear medicine professionals who made presentations at the 1999 Society meeting. I received over 200 answers. The responses are listed in Table 1.

TABLE 1
Percentages indicate those answering "yes"

1	Will nuclear medicine assume an increasing role in health care?	84%
2	Will there be increasing use of nuclear medicine technology in pharmacology, toxicology, infectious diseases, aging, mental illness and nutritional disorders?	93%
3	Will nuclear medicine imaging become the leader of biomedical imaging?	23%
4	Will nuclear medicine play a major role in "functionalizing" the genome, that is, in defining the messages contained in genes?	59%
5	Will multienergy imaging devices become as common as dedicated PET and SPECT devices?	69%
6	Will the use of positron-emitting tracers equal single photon agents?	42%
7	Will there be a role for specialized devices for breast, brain, and extremity imaging, and small handheld devices for intra-operative applications?	88%
8	Will referring physicians think of nuclear medicine first, rather than last?	35%
9	Will we be able to convince everyone that nuclear medicine decreases, not increases, the overall cost of health care?	57%
10	Will we be able to ensure the availability of nuclear medicine technologists, physicians and scientists?	61%

The results suggest that most persons are optimistic about the continually increasing impact of nuclear medicine on the practice of medicine. Only 23% believe that nuclear medicine imaging will become the leader of biomedical imaging. Fifty-nine percent believe that nuclear medicine technology will help define gene expression, and 69% believe that multienergy imaging with the same instrument will become as common as dedicated PET and SPECT devices. Only 42% believe that positron-emitting tracers will equal those of single photon agents. Eighty-eight percent believe that there will be a role for specialized devices dedicated to breast, brain, and extremity imaging and small, hand held devices for intra-operative applications. Only 35% believe that referring physicians will think of nuclear medicine first, rather than last, and 57% believe that we will be able to convince everyone that nuclear medicine decreases, not increases, the overall cost of health care. Unfortunately, 39% believe that we will not be able to ensure the future availability of nuclear medicine technologists, physicians and scientists. I invite further discussion via the non-commercial web site: www.nuclear.md or via e-mail at hwagner@jhsph.edu The information age now makes it possible for everyone to continue helpful discussions like those that were held in Los Angeles.

Figure 1. A Directory of Nuclear Medicine Professionals.

THE EVOLUTION OF NUCLEAR MEDICINE

The evolution of nuclear medicine can be represented as a circular chain (Figure 2) that began with physics and chemistry shortly before and after World War II. There was progressive development of radiation measurements and imaging devices, moving rapidly into the biomedical fields of endocrinology, pulmonology, cardiology, neurosciences and oncology, and, today, imaging gene expression in vivo. At this meeting, nuclear oncology is at a stage analogous to that of nuclear cardiology in the 1980's and is likely to achieve the same role as nuclear cardiology has today. Nuclear medi-

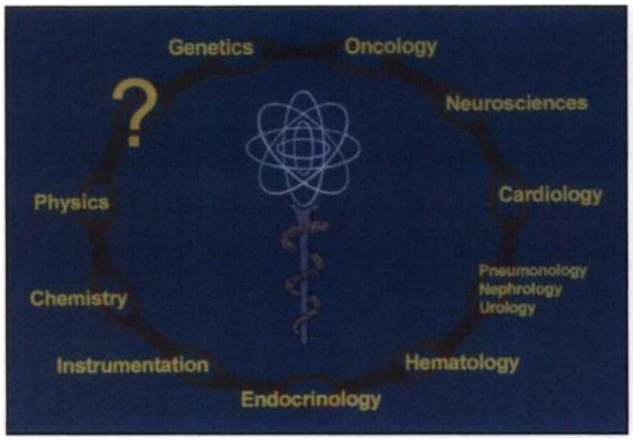

Figure 2: The Evolutionary Circle of Nuclear Medicine.

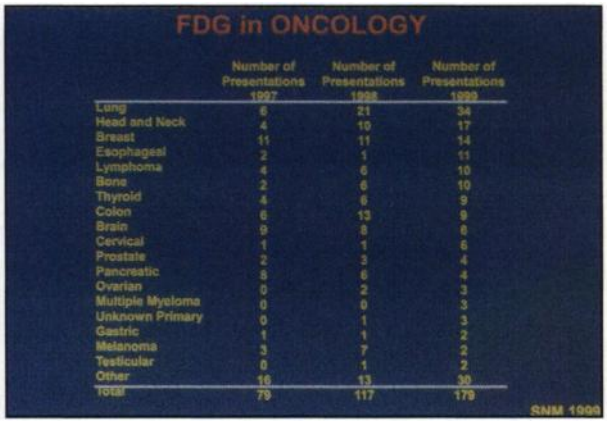

Figure 4: The number of FDG presentations according to the type of cancer.

cine will eventually play a major role in aging, infectious disease and mental illness, with applications that lie just over the horizon as new links in this evolutionary chain. The representation as a circle suggests that advances will continue indefinitely in all of these domains, with continuing advances in physics, chemistry and biology.

The dominance of oncology at this meeting is documented by the 38.2% of the oral presentations and posters being in oncology.

One hundred and seventy-nine presentations involved F-18 fluorodeoxyglucose, which represents an increase over previous years.

Twenty-eight years ago, I spoke at the dedication of the first cyclotron at UCLA, and made the following prediction: "We have not yet seen the development of a procedure that absolutely requires a cyclotron to solve a medical problem, but I think that the handwriting is on the wall. I predict that within five years a cyclotron-produced radionuclide will provide definitive diagnostic information in some important disease process."

In 1977, Louis Sokoloff carried out his classic studies of the brain with carbon-14 deoxyglucose, and subsequently Giovanni Di Chiro at the NIH recognized the important role that FDG could play in the care of patients with brain tumors.

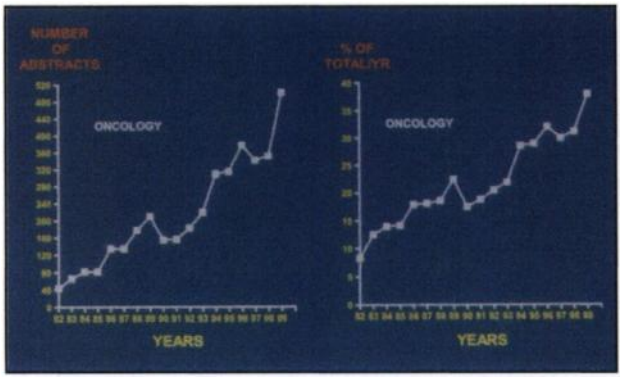

Figure 3: Oral presentations and posters since 1982.

F-18 FDG retains its undisputed role as the molecule of the 20th century in nuclear medicine.

A GOOD YEAR FOR TECHNETIUM-99m

Last year, the number of presentations involving technetium-99m fell to 332 from 430 in 1996. I thought that perhaps the number of technetium-99m presentations had peaked. I was disabused of this idea when, this year, the number of technetium-99m presentations increased to 450.

Among the most important presentations were those from the laboratory of H.F.Kung (abstract numbers #108, 109). Using Tc-99m TRODAT-1, these investigators observed that the dopamine transporter on presynaptic dopaminergic neurons decreased linearly in normal persons until 32 to 42 years of age. It then remained relatively unchanged thereafter, unless the persons suffered from Parkinson's disease, in which case transporter availability was less than in normal persons. The authors suggested that TRODAT/SPECT was useful for the early diagnosis of Parkinson's disease and said that the radiopharmaceutical was in Phase II clinical trials.

Another technetium-99m radiopharmaceutical that is nearly ready for FDA approval is technetium-99m depreotide, a

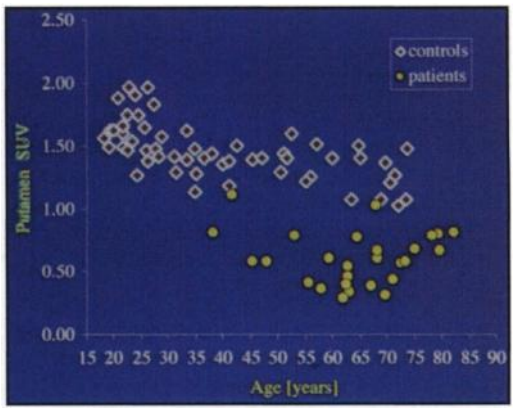

Figure 5: Decrease in dopamine transporter binding by Tc-99m TRODAT as a function of age in normal persons and patients with Parkinson's disease.

somatostatin analog that binds to somatostatin receptors (# 231).

In differentiating benign from malignant solitary pulmonary nodules, imaging with this Tc-99m tracer had a sensitivity of 97% and a specificity of 73%. While the authors presented their results as showing that their agent "outperformed FDG" in terms of cost-effectiveness, this agent should be considered not as a competitor of FDG but as a useful agent for those presently without FDG capabilities. For those now performing FDG studies in oncology, the new Tc-99m tracer for somatostatin receptors can provide additional information, that is, whether somatostatin receptors are present on non-small cell lung cancer lesions. The expression of receptors such as somatostatin on neoplasms is useful in planning treatment. The combined use of F-18 FDG and Tc-99m depreotide provides an argument for multienergy imaging devices that can simultaneously examine bioenergetics and receptor expression. The authors' economic analysis considered the cost of thoracotomy to comprise the bills of the surgeon and the hospital. Morbidity, anxiety, and days lost from work are also important, even though they are not dealt with in most economic analyses.

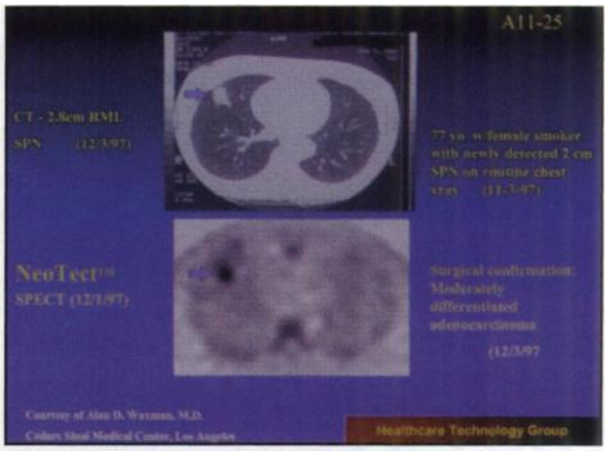

Figure 6: Tc-99m depreotide (NeoTect) in a malignant pulmonary nodule.

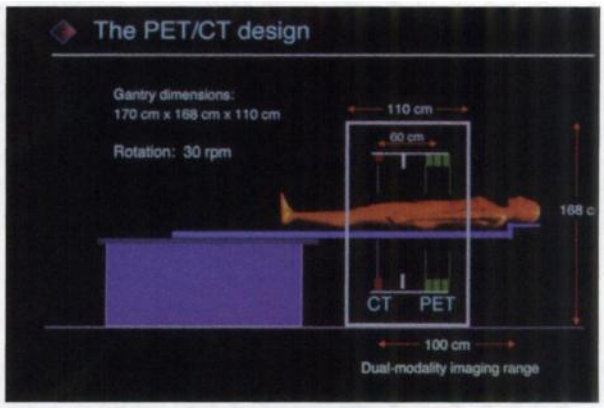

Figure 7: CT and PET scanner mounted on the same gantry so that the patient does not move during the two studies.

FUSED IMAGE TECHNOLOGY (FIT)

Until now, CT or MRI images have been fused with PET or SPECT images using fiduciary markers for alignment of the images. At this meeting, Townsend and colleagues presented whole-body PET scans with F-18 FDG combined with anatomical images obtained with a commercial CT scanner (# 597). Both PET and CT components are mounted on a single gantry that rotates at 30 rpm. In a single scan session without the patient's body moving, CT provides anatomical information accurately aligned with the FDG PET images, as well as a method to correct for attenuation in the PET imaging.

Because these fused images for the first time can be performed with the same gantry without moving the patient, I have chosen an FDG study of a patient with malignant lymph nodes in the neck as the Image of the Year.

The exact portrayal of anatomy and regional biochemistry obtained with the same imaging gantry represents an important integrating force in nuclear medicine. In addition to providing the anatomical information, the CT scanner provides ECT attenuation maps by converting the x-ray CT images to attenuation maps for SPECT and PET. The details of this approach were described by Tang et al. (# 458). Their methods require careful consideration of material properties and photon energy.

For decades, nuclear medicine has striven to improve the spatial resolution of its images in order to provide anatomical as well as biochemical information, while MRI/MRS have striven to mimic the biochemical capabilities of PET. The time has come to combine the best features of the two modalities. Fused Image Tomography (FIT) can provide an important integrating force in imaging sciences, and bring nuclear medicine

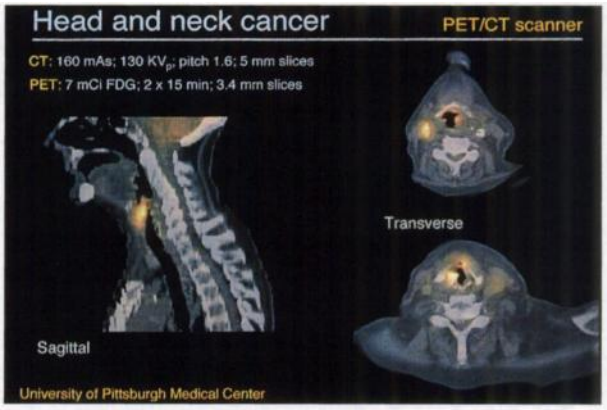

Figure 8: Image of the Year.

and radiology even closer together. Key questions remain, such as what should be the quality of the CT images, keeping in mind economic constraints. The system described by Townsend et al. can yield acceptable and interpretable brain CT images, as well as the PET images.

In a commercial exhibit, a CT capability was added to a hybrid PET/SPECT scanner by attaching an x-ray tube opposite CT detectors on a rotating gamma camera designed for dual-coincidence imaging of F-18 FDG. The x-ray tube and scintillation detectors rotate together and CT images are obtained over a period of about 20 seconds. The excellent fused images are shown in Figure 9B.

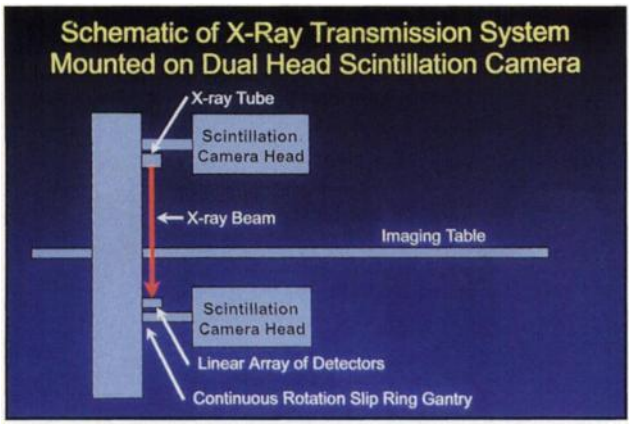

Figure 9A: A fused CT/SPECT imager.

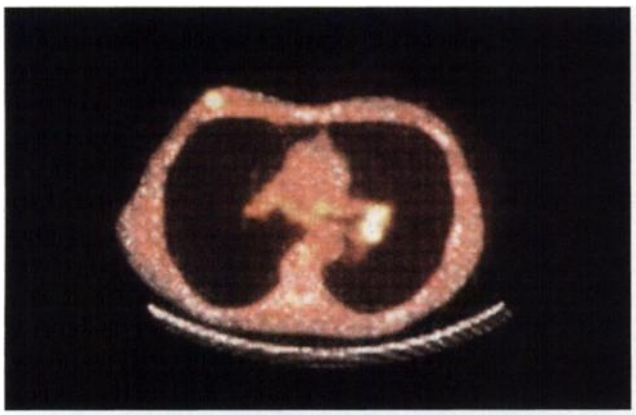

Figure 9B: By means of "Fused Image Tomography" (FIT), the lesion that accumulates FDG can be localized as being in the breast rather than the chest wall or ribs.

ATTENUATION CORRECTION

Sixty-nine presentations involved attenuation correction: 21 in ring (dedicated) PET systems, 10 in hybrid (dual coincidence) systems, and 38 in SPECT. Minoshima of the University of Michigan reported (personal communication) that by correcting for attenuation in brain FDG studies, 20% more patients with mild memory loss showed the pattern characteristic of early Alzheimer's disease. In a detailed ROC analysis of lesion detection in whole-body FDG PET , Farquhar et al. examined the effects of acquisition mode, attenuation correction, and reconstruction algorithms (# 130). They found that in the abdomen 2D imaging was preferable to 3D imaging.

NUCLEAR SURGERY

Historically, nuclear medicine has advanced when nuclear physicians established close working relationships with other specialists, such as cardiologists. A promising new relationship should now be developed with surgeons. New imaging devices include an intra-operative compact gamma imager for radiotracer-guided surgery. One imager uses a 2.5cm diameter crystal (# 602), a small gamma camera using parallel-hole and diverging-hole collimators for scintimammography (# 1226). Another imager uses a positron-emission mammography-guided stereotactic breast biopsy system for use with FDG (# 468).

Some surgeons rely primarily on biopsy to determine whether breast lesions are benign or malignant. Hain and colleagues from St. Thomas' and Guy's Hospitals described the results in 32 patients where attempted lung lesion biopsies failed and three patients who were deemed too sick for biopsy. Thirty-one of 35 lesions accumulated FDG, and 31 of these proved to be malignant (# 409).

Another important question in nuclear surgery is the presence of metastatic thyroid cancer when the metastatic lesions are undifferentiated and therefore do not accumulate radioiodine. So and colleagues (# 529) reported that FDG PET detected 20 or 30 cancerous lymph nodes, with a positive predictive value of 88% and a negative predictive value of 69%.

Analysis of the many presentations on detection of axillary lymph node involvement in breast cancer suggests that the combined use of lymphoscintigraphy and direct measurement with probes provides the best patient care (# 1114). Keshtgar et al. emphasized the importance of a team effort among nuclear physicians, surgeons and pathologists (# 1115). Combined use of blue dye, intradermal colloid, and lymphoscintigraphy seemed to be needed for optimum performance in the localization and assessment of sentinel lymph nodes in breast cancer and melanoma (#1123 and 1124).

Metastases to the internal mammary chain occur with such a high frequency that lymphoscintigraphy is indicated in patients with breast cancer. Byrd et al. reported that 21 of 119 patients had internal mammary lymph nodes visualized by lymphoscintigraphy (#557). Drainage was not necessarily as expected on the basis of the location of the primary tumor in the breast. Pace et al. found that of 84 patients, 74 had sentinel nodes successfully identified. Four patients with negative sentinel nodes had axillary metastases, suggesting the need for lymphoscintigraphy (# 559).

Spannu et al. documented the improvement obtained with SPECT over planar imaging in searching for metastatic axillary lymph nodes. There was further improvement with pinhole SPECT (# 1105.)

Kestgar et al. reported cost savings of £273 (British) when axillary lymph node dissection could be avoided (# 560). Again, this does not take into consideration the anxiety and morbidity associated with the unnecessary surgery but only the billable medical costs.

In the future, surgical use of small hand-held imaging devices, such as that described by Menard and colleagues from Villejuif, France (# 602), will become commonplace. The present detector is 2.5 cm in diameter, and one with a 6 cm field of view is under construction. Kim and his Korean colleagues described a small gamma camera designed for breast imaging (# 1226).

Raylman and colleagues from Jefferson Laboratory and the University of West Virginia described a stereotactic breast biopsy device directed to radiotracer-avid lesions (# 468).

COST-EFFECTIVENESS

The value of F-18 FDG imaging was documented in all 179 presentations involving this tracer in oncology. Cost-effectiveness studies provide impressive evidence for third-party payers. Becker and colleagues of Columbia Presbyterian Hospital in New York documented the impact of FDG PET on the care of patients with solitary pulmonary nodules (# 228). They were able to reduce the number of biopsies from 69% of the lesions to 27%. PET findings indicated that immediate biopsy was warranted in 17% of the pre-PET low-probability lesions in 77 patients with pulmonary nodules.

An important question is how such studies regarding the probability of malignancy should be reported. Let us hope we can avoid past problems created by interpreting lung scans as high, intermediate or low probability of pulmonary embolism. Oncology studies should be interpreted in decades of probability of malignancy. The use of likelihood ratios makes it easier to combine multiple probabilities.

Changlai and colleagues examined the impact of whole-body FDG imaging on staging of lung cancer (# 226). In more than 23% of the patients, clinical management of the patients was affected. In a UCLA study (# 225), PET FDG studies led to restaging in half of 25 patients and changed therapy in one-third. Gupta et al. (# 229) reported that PET FDG imaging significantly improved lymph node staging in lung cancer, but pointed out that chronic granulomatous disease can present problems in differential diagnosis.

Serum markers, such as CEA, are used to determine the status of patients with cancer, such as colorectal cancer. Moretti et al. found that three serum markers for the presence of lung cancer had a sensitivity of 80%, compared to 92% for FDG PET (# 1092). It would seem that both procedures should be performed, since the goal is not to use the most accurate test but to use both to achieve a nearly 100% accuracy. In this case, if both the serum markers and FDG PET were negative, this risk of malignancy would be 1:36.

CANCER OF THE ESOPHAGUS

In 151 studies of 109 patients, FDG PET had a sensitivity of 80% and a specificity of 86% (# 95). The FDG studies were more accurate than CT, detecting 22 confirmed lesions not seen on CT. Care was affected in 14% of the patients. Hubner et al. found that FDG studies saved more than $ 200,000 in staging 19 patients with cancer of the esophagus (# 96).

NEOADJUVANT THERAPY

Among the most valuable uses of FDG PET studies in oncology is the assessment of the patient's probable and actual response to chemotherapy. Neoadjuvant chemotherapy consists of administering the chemotherapeutic regimen for two weeks prior to surgery and then correlating the change in FDG accumulation with the histopathological characteristics of the lesions biopsied at surgery. When FDG accumulation falls as a result of the neoadjuvant therapy, there is quantitatively related evidence of histopathological changes indicating that the tumor has responsed favorably to therapy (# 547). In studies from Munich, Weber et al. found that a decrease in FDG after neoadjuvant therapy had a sensitivity of 80% and a specificity of 100% in indicating subsequent histopathological evidence of tumor responsiveness. The authors concluded that FDG PET can have a major impact on patient management (# 550). Mankoff et al. from the University of Washington observed that a positive response to neoadjuvant therapy was indicated by a fall in the accumulation of FDG and a decrease in lesion blood flow (# 551). Smith et al. from the United Kingdom reported that PET was able to predict the pathological response with a sensitivity of 75% and a specificity of 100% (# 552).

ASSESSMENT OF CELL PROLIFERATION

At any time, about 10% of neoplastic cells are dividing while nearly all of them are accumulating glucose as a result of

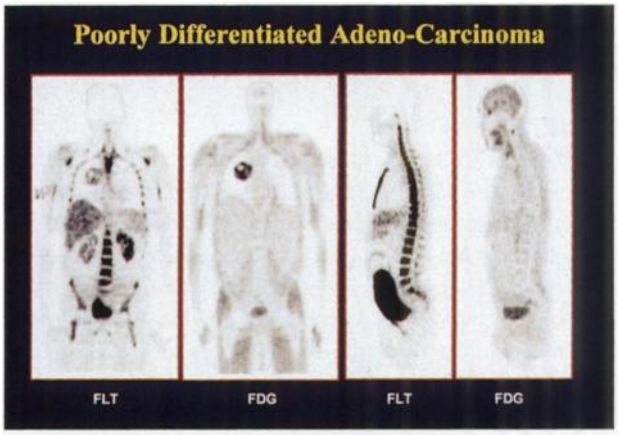

Figure 10: FDG and F-18 fluorodeoxythymidine imaging in poorly differentiated adenocarcinoma .

hexokinase expression. It is still not clear whether cell proliferation studies of DNA precursors or FDG measurement of the energy supply to tumors is most effective in assessing or predicting the response to chemotherapy.

Hammersley compared various tracers for measuring nucleic acid incorporation into experimental tumors (# 99). Rasey et al. from the University of Washington reported that measurement of thymidine kinase 1 activity was better than using C-11 thymidine to assess cell division (# 100). Shields et al. (Fig. 10) presented their extension into human studies of the use of fluorine-18 fluorodeoxythymidine to assess cell proliferation (# 101).

AMINO ACID TRANSPORT IN CANCER

Iodine-123 methyl tyrosine is widely used in oncology in Europe. Dierickx and Belgian colleagues showed that very high-quality images could be obtained with this tracer in patients with head and neck cancer (# 256).

RECEPTORS IN ONCOLOGY

Of the 54 presentations concerned with receptors expressed by neoplasia, 28 concerned somatostatin receptors, five estrogen receptors, four each of bombesin and sigma receptors, and three vasoactive intestinal peptide receptors. John et al. reported the first human studies of a new tracer for imaging sigma receptors in patients with melanoma (# 486, 488). Thacker et al. from Thomas Jefferson University and UCLA labeled vasoactive intestinal peptide with Tc-99m and carried out successful studies in patients with breast cancer (# 1088). Virgolini et al. from the University of Vienna also reported the use of a Tc-99m tracer for VIP-expressing neoplasms (# 1081).

HYBRID PET/SPECT

Fifty-five presentations documented the value of dual-coincidence PET studies of FDG in patients with cancer. Four hundred and thirty two of all the FDG presentations at the meeting involved ring (dedicated) PET, while 301 involved SPECT, all representing considerable increases in numbers over previous years. Thus, hybrid PET seems to have established its value, although its lesser sensitivity than ring PET in the case of lesions less than 1 cm continues to be documented.

NUCLEAR GENETICS

The microPET scanner played a major role in a study designed to illustrate the concept of gene therapy. An adenovirus was used as a vector to make possible the insertion of two genes into a tumor. One of the genes expressed the enzyme thymidine kinase. The other gene expressed dopamine receptors. Each of these two genes was connected to the same promoter gene that would activate the expression of each of the genes. The expression of dopamine receptors by the tumor could be detected by the accumulation of F-18 fluorospiperone, which binds to dopamine receptors. The expression of the thymidine kinase gene could be detected by the binding of F-18 antiviral antibiotic phosphorylated by thymidine kinase and thereby remaining trapped in the tumor cells, in a manner similar to the trapping of FDG by hexokinase phosphorylation.

This experiment was a demonstration. In the actual practice of gene therapy, one of the transfected genes would be the therapeutic gene, the other the "reporter" gene, each with the same promoter gene. Gambhir et al. presented evidence that the expression of the one gene could be measured by the expression of the other (# 102). Again we can see the interactions of the sister sciences of molecular nuclear medicine, genetics and pharmacology (Fig. 15).

SMALL-ANIMAL SCANNERS

The newly developed microPET small animal scanner developed at UCLA by Kudo et al. was used to image F-18 FDG accumulation in the rat myocardium. The images were comparable to those obtained in human beings (# 20). Lapointe and colleagues from the University of Sherbrooke (# 832) also showed FDG images of exquisite quality of myocardial FDG accumulation in the rat.

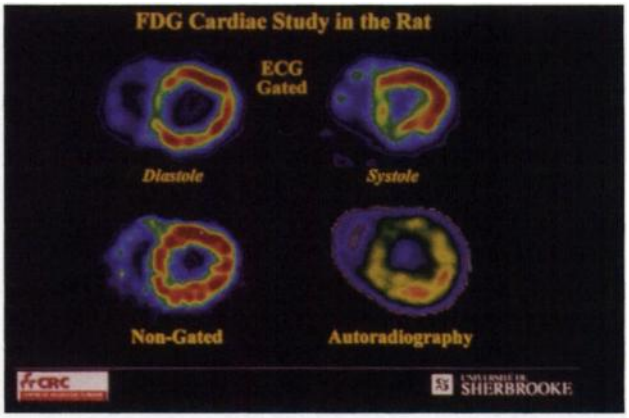

Figure 11: Gated and ungated images of cardiac metabolism with F-18 FDG.

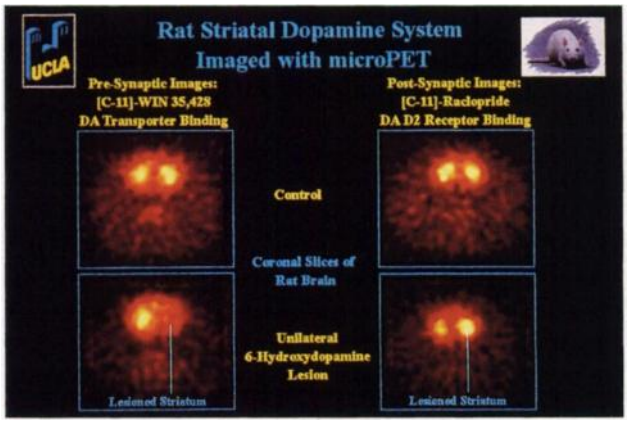

Figure 12: Animal Image of the Year. MicroPET studies of dopamine receptors and transporters in the rat. The receptors are intact. The transporters on the left side have been damaged by a neurotoxin.

Wu and colleagues from the University of California at San Francisco obtained similarly high-quality pinhole SPECT imaging in a 23-gram mouse (# 1249). These important advances in the quality of small-animal scanners promise to greatly contribute to pharmacology and genetics, two special fields closely related to nuclear medicine.

Figure 12 shows the binding of a C-11WIN tracer to dopamine receptors in the basal ganglia of rat where a neurotoxin had been injected into the left carotid artery. The dopamine receptors are not affected, but the dopamine transporters, imaged with C-11 flurospiperone is damaged on the injected side. This image has been selected as the Animal Image of the Year.

NUCLEAR PHARMACOLOGY

Gatley and colleagues from Brookhaven National Laboratory, in studies of mice, found that the occupancy of cocaine in the presynaptic dopaminergic neurons by a given amount of methylphenidate was similar to that found in baboons and human beings (#440). His studies further support the relevance of studies in lower-animal species, where the results are often directly applicable to human studies. Today the mouse is perhaps the most important experimental animal, particularly in view of the advances in mouse genetics.

In a study by Yokoyama at Tokyo University, myocardial FDG accumulation was stimulated in patients with noninsulin-dependent diabetes mellitus by the administration of the drug troglytazone, which decreases insulin resistance (# 939). Choi and colleagues from Sungkyunkwan University in Korea used I-123 MIBG imaging to assess the effects of the third generation beta blocking drug, carvedilol, in patients with heart failure (# 736). Not only was there improvement in left ventricular ejection fraction, but this improvement was related to the washout of MIBG, reflecting sympathetic innervation. That regional myocardial blood flow measured with Tc-99m sestamibi was improved in patients with coronary heart disease was shown by direct injection of genes expressing vascular endothelial growth factor (VEGF) directly into the myocardium. There was an associated decrease in angina. Hendel reported similar studies with genes expressing vascular growth factor injected into the myocardium of patients with coronary heart disease (# 342). The beneficial effect seems to last only about a month, presumably the result of immunological processes directed against the vector adenovirus.

MULTIENERGY IMAGING

Measurement with a single tracer is often not sufficient. For example, tracers such as F-18 FDG are used to measure the hexokinase concentration in tissues . Buck and colleagues used immunohistopathology to reveal that 41% of all pancreatic cancer cells are proliferating, that is, synthesizing DNA, while 4% of the cells in chronic pancreatitis are doing so.

Thus measurement of hexokinase activity, proliferation, receptor expression and other biochemical processes may often be necessary. This will require tracers emitting different energies so that they can be differentiated. Nuñez and colleagues at Memorial-Sloan Kettering Cancer Center presented examples of the value of multiple tracers (# 912).

For example, a patient with neuroblastoma showed avid accumulation of FDG in a lesion that did not express somatostatin receptors (In-111 pentreotide imaging), but did accumulate the norepinephrine analog, I-131 MIBG.

Physicists are now able to separate the 140 keV photons of technetium from the 640 keV photons of iodine 131 and from the 511 keV photons of a positron-emitting tracer (#480).

An example of the immediate usefulness of multienergy imaging is separation of Tc-99m MIBI from fluorine-18 FDG in cardiac studies (# 132).

A uranium pinhole collimator provided a much better contrast in a system designed to facilitate imaging in patients receiving iodine-131 radiotracer therapy (# 138).

Iodine-123 methyltyrosine can be used to differentiate lung cancer from sarcoidosis (#878). In studies from Gunma Universty, Oriuchi and colleagues showed that while F-18 FDG accumulated in both neoplasia and sarcoidosis, methyl tyrosine did not, a helpful way to increase specificity in detecting malignancy.

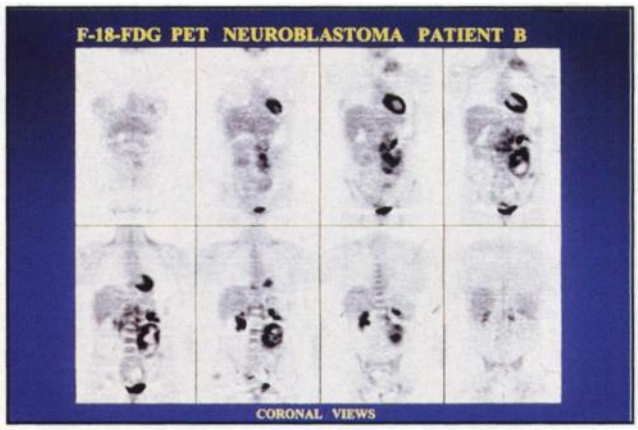

Figure 13A: The lesion accumulates FDG.

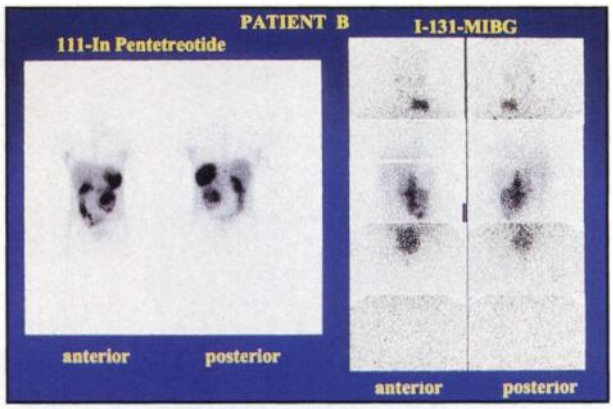

Figure 13B: The lesion does not express somatostatin **receptors but does express norepinephrine receptors.**

RADIOIMMUNOTHERAPY

The treatment of thyroid cancer and hyperthyroidism with radioiodine shortly after World War II gave birth to nuclear medicine. Encouraging results are now being obtained in radioimmunotherapy of lymphoma, ovarian and colon cancer, neuroblastoma, and melanoma. Wahl of the University of Michigan reported that approval of radio-LL2 in the treatment of B-cell lymphoma will almost certainly occur this year. His group was able to treat patients in the early as well as later stages of disease (# 77). There was a 97% response rate with a 53% complete response in 34 patients treated early in the disease. No longer do we have to be limited to the treatment of advanced disease where everything else has failed.

Lamonica and colleagues from the University of Buffalo showed excellent quality imaging that is now being obtained by radioimmunodiagnosis with SPECT (# 949).

PREVENTING RESTENOSIS

Radionuclides are also being used in efforts to prevent restenosis of coronary arteries after angioplasty. Korean physicians use solutions of rhenium-188 in balloons (# 819). Thirteen presentations involved this radionuclide.

DRUG DESIGN AND DEVELOPMENT

It behooves us to try to relate ever more closely with the pharmaceutical industry. For example, a study from Cleveland used PET to examine the distributions of aerosols as a method of drug delivery (# 383).

Perkins and colleagues examined the fate of different oral dosage forms by means of oropharyngeal scintigraphy (# 365). Belgian investigators measured the residence time of drugs deposited in the nasal mucosa (# 610). These are but a few examples.

NUCLEAR CARDIOLOGY

I searched the program for studies of cardiac metabolism, since studies of the pumping function of the heart and regional myocardial blood flow are now well-established in modern cardiology, and the presentations represent refinements. One example of a metabolic study is that by Johnson and colleagues from Tulsa, OK, who used Tc-99m glucarate to assess the location and degree of myocardial ischemia (# 815). Glucarate binds to intracellular histone when cells are necrotic.

MIND/BRAIN DISEASE

Among these presentations 15 were concerned with substance abuse. Brain tumors are still the number one topic, with 20 presentations, movement disorders with 19, epilepsy and dementia with 15 each, depression nine, and schizophrenia eight.

Kogure and colleagues from Tokyo showed that the exquisite technology that was developed primarily by PET is now being applied to SPECT, including the use of statistical parametric mapping, volume rendering and image fusion (# 1192). Barrio and colleagues have developed a fluorescent tracer that they believe binds to amyloid in plaques and tangles in the brain of patients with Alzheimer's disease.

Fluorescent tracers have not previously been used much in nuclear medicine because the emitted fluorescent photons cannot penetrate the body. The higher energy of near-infrared makes this possible in the living mouse, and therefore one can carry out whole-body imaging with fluorescent tracers in this animal. The most fundamental principle of nuclear medicine is the tracer principle, going back to de Hevesy. The field is not limited to radioactive tracers but to all kinds of tracers, including fluorescent tracers.

PARKINSON'S DISEASE

Seibyl and colleagues from Yale have data to support the hypothesis that Parkinson's disease is caused by progressive accumulation of neurotoxins via the opamine transporter on presynaptic neurons in the basal ganglia (# 197). They found that the progression of the disease was fastest in those patients who, in the early stages of the disease, have the highest capacity of the transporter and would presumably more avidly accumulate toxins. There is no greater incidence of Parkinson's disease in an identical twin of a patient with Parkinson's disease, further supporting environmental etiology of the disease.

Radau and colleagues showed that the selection of the region of interest in the basal ganglia could be selected accurately and automatically, which will greatly improve serial studies in the same patients (# 110).

SCHIZOPHRENIA

Higher levels of synaptic dopamine and D2 dopamine receptors than those of normal persons lend further support to the important role that the dopaminergic system plays in schizophrenia (# 121). In schizophrenic patients there is a decrease in dopamine transporter binding, which may be due to down-regulation as a result of increased synaptic dopamine levels in this disease (#126).

SUBSTANCE ABUSE

Rarely can a single parameter solve a complex medical or research problem. One needs to develop multiple measurements and relate them to one another. Heintz et al. from the NIH found increased orbitofrontal glucose utilization was associated with low serotonin metabolism as indicated by measurements of metabolites of serotonin in the cerebrospinal fluid (# 1219). There was also a relationship to alcoholism.

Nora Volkow was honored by her neuroscience colleagues because of her many contributions to the study of substance abuse. She and her colleagues reported that persons who abuse methamphetamine have impairment of presynaptic dopaminergic neurons comparable to that observed in Parkinson's disease (# 443). There was a correlation of the biochemical findings with the degree of impairment in a motor and memory task.

ing closely with basic scientists and clinicians," Lim said, "dedicating a year to this fellowship will prepare me for the teamwork skills needed for a career in academic medicine."

The longstanding Annual Mallinckrodt Fellowship Program was established to facilitate original research in nuclear medicine. The award is aimed at furthering research involving the development of single photon radiopharmaceuticals or beta emitters to be used in nuclear medicine oncology.

Both the Mallinckrodt and Dupont fellowships were announced at the Society's Annual Business Meeting. Other award recipients at the meeting included Carol Marcus, PhD, MD, who received the 1999 SNM Distinguished Service Award, and Mark Rotman, PhD, National Institutes of Health, and Kenneth McKusick, MD, who received SNM Presidential Distinguished Service Awards.

Rotman and McKusick were recognized for their contributions to coding and reimbursement issues and government relations, respectively. Similarly, Marcus received the Distinguished Service Award, said SNM President James Fletcher, for her "continuous support of the SNM Government Relations Committee in its efforts to deal with regulations promulgated by numerous government agencies."

Education & Research Foundation of Society of Nuclear Medicine

For the second time in four years, Abass Alavi, MD, chair, Department of Nuclear Medicine at the University of Pennsylvania Hospital and past president of the Education and Research Foundation of the Society of Nuclear Medicine, has made a large donation to the Education and Research Foundation (ERF). At the recent Annual Meeting of the Society of Nuclear Medicine, Alavi presented Conrad Nagle, MD, president of ERF, with a check for $30,000 to additionally fund the Alavi/Mandell Fund. Income generated by the Fund will provide future awards within the Education and Research Foundation.

Kenneth McKusick, MD, treasurer of the ERF has been elected by its board as president-elect, to assume office following the Society's Annual Meeting in the year 2000.

Other actions by the Education and Research Foundation include the creation of the Joseph Ross, MD, TraineeAward. Currently, a $25,000 fund created by the Board is expected to generate income of $500-$1,000 which the ERF will then donate to the Society of Nuclear Medicine to allow the Awards Committee of SNM to select trainees to receive the award for presentations at the Annual Scientific Meeting. These awards will likely begin at the Annual Scientific Meeting of 2001 and will be announced by the Society at the time the awards are instituted.

SNM 1999

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and atoms, circulating, bumping into each other, fitting and sticking, controlling processes at the local level rather than at some master control center in the brain. For example, if herpes simplex virus, aflatoxin, arsenic, and iron all happen to meet in one's liver, one is likely to develop liver cancer.

This Annual Meeting provides evidence that people are now integrating and collaborating rather than competing with others in different fields of medicine. But we still have problems. The number of approved NDAs by the FDA is too low. Perhaps we can piggyback radionuclide studies that are being used in Phase I, II, and III studies of stable drugs in order to obtain information relative to the radionuclide as well as to the stable drug. It is permissible under FDA regulations to use radiotracers that have INDs in studies of stable drugs. For example, beta CIT is being used as part of drug trials designed to measure the effectiveness of stable drugs in Parkinson's disease.

Another problem that has been around for half a century and is getting worse is that the phrase "nuclear medicine" conjures up horrific science-fiction-inspired images of grave, dangerous procedures. The time has come to bring hormesis to the attention of the public. Progress is made only when purposeful and determined persons are relentlessly guiding it. At every crossing on the road to the future, every leader is opposed by thousands of persons who relentlessly guard the past. Always remember, as Dag Hammarskjold said, "Only he who keeps his eye fixed on the far horizon will find his right road."