Henry N. Wagner, Jr., MD

Highlights 2000 Lecture The Internet: The Road to Smart Nuclear Medicine

The Highlights Lecture is presented annually at the meeting of the Society of Nuclear Medicine (SNM) by Henry N. Wagner, Jr., MD, of the Johns Hopkins School of Public Health, Baltimore, Maryland. This year's lecture was presented at the SNM meeting in June 2000, in St. Louis, Missouri.

Last year, I sent a questionnaire to more than 200 physicians and scientists who presented papers or posters at the 1999 meeting of the Society. In answer to the question "Will nuclear imaging become the leading imaging modality in the future?" 27% of physicians and scientists outside the United States and 23% of the American respondents answered "yes." I hope that after this year's meeting you will communicate with me via the Internet and let me know your opinions. My e-mail and Web page addresses are shown in Figure 1.

Figure 1. Example of a nuclear medicine Web site.

Nuclear medicine has defined itself as the imaging of in vivo physiology and biochemistry, sometimes called functional and molecular imaging, which will interact with genetics and pharmacology to have a major impact on health care over the next decade (Fig. 2). The continuing growth of both PET and SPECT is evident in Figure 3.

The famous internist Francis Peabody wrote: "I believe that the basic tools that we use in the pursuit of scientifically oriented medical practice stand out more vividly when cloaked in the robes of historical origins." Half a century ago, we related function to structure by superimposing nuclear "scans" over radiographs of the region being examined, using small lead disks as fiduciary markers. An example is the localizing of the accumulation of radioiodine in a sublingual thyroid gland.

The dramatic improvements over the ensuing years can be seen in the Image of the Year that I selected last year. It was a fused image of the accumulation of ^{18}F FDG in metastatic nodules in the neck of a patient with head and neck cancer. The delineation of the exact position of the cancerous nodules facilitated their surgical removal.

As shown in Figure 4, the concept of fused image tomography (FIT) has caught on in nuclear medicine. Forty-one presentations covered fusing of many types of imaging, including even magnetoencephalography (MEG). Not included are fusions of images using the same imaging method at different times or different functions obtained with a single modality. An example of the latter (Fig. 5) was presented by Buvat and colleagues from Paris, France, and Bethesda, MD, who

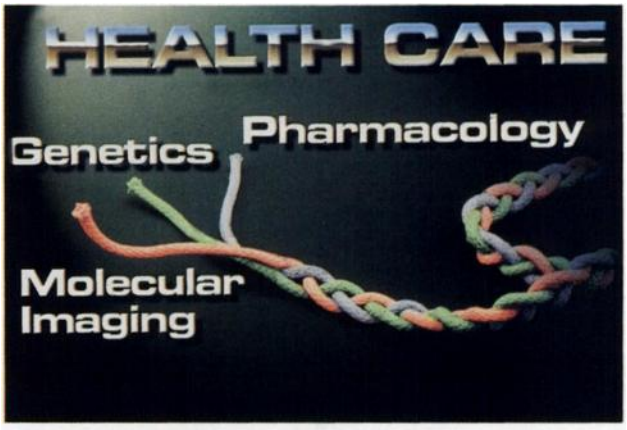

Figure 2. Molecular imaging, genetics, and pharmacology are the 3 strands that will interact to dominate health care over the next decade.

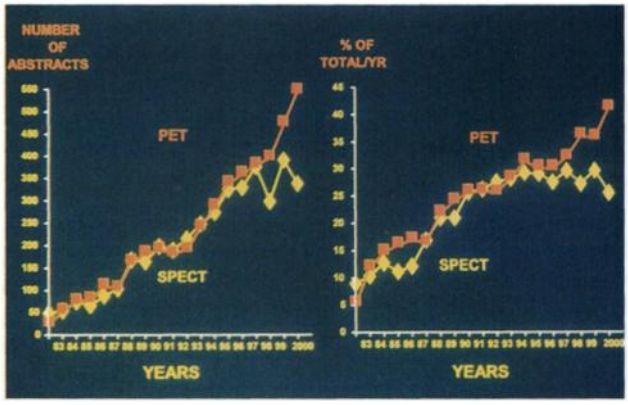

Figure 3. Continuing growth of PET and SPECT in presentations at the annual SNM meeting over the past 2 decades.

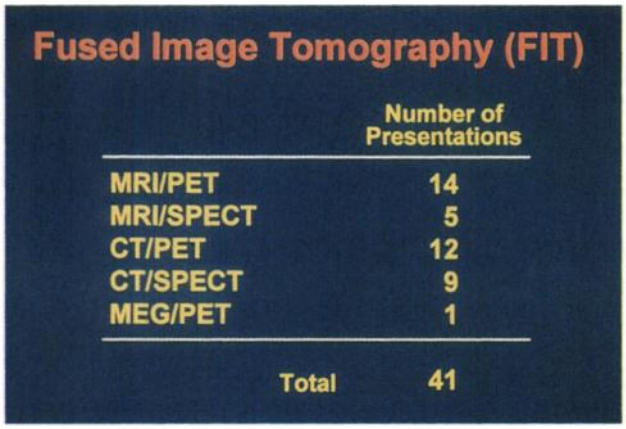

Figure 4. Fused image tomography (FIT).

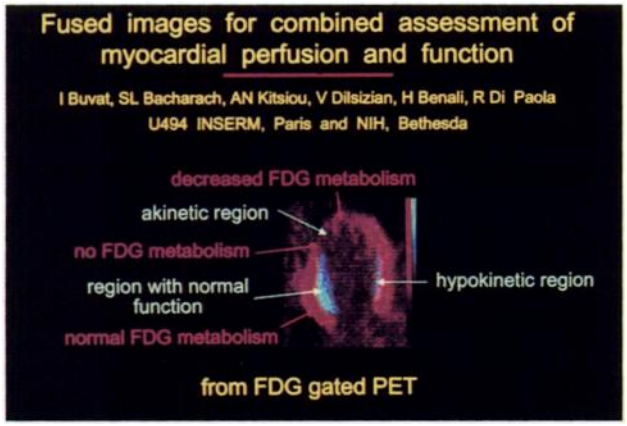

Figure 5. Fused images for combined assessment of myocardial metabolism and ventricular wall motion (#729).

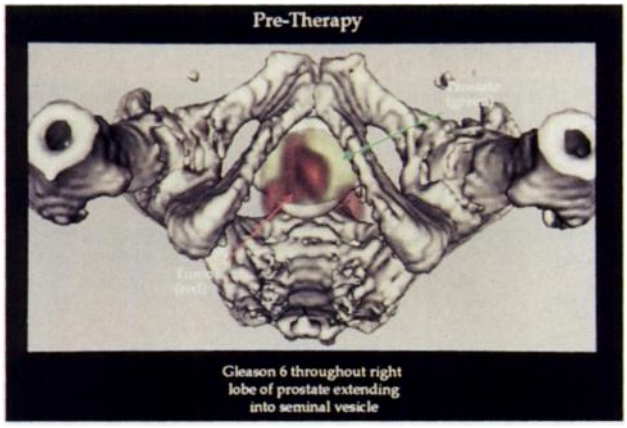

Figure 6. Fused image of ^{111}In prostate monoclonal antibody with an MR image of the pelvis. It can be seen that the cancer, shown in red, extends beyond the capsule of the prostate to involve the seminal vesicles. This tells the urologist that the lesion should be treated with external radiation therapy directed toward the lesions defined in the ^{111}In image, rather than by prostatectomy or radioactive seed implants (#232).

fused FDG accumulation by the heart with gated wall motion images with FDG for the combined assessment of myocardial metabolism and wall motion (presentation #729; all #s in the following text refer to presentations at the SNM meeting).

Image of the Year

This year, Lee and colleagues from University Hospitals of Cleveland, OH, fused a SPECT image of an ^{111}In-labeled monoclonal antibody against prostate cancer with an MR image of the pelvis of a 73-y-old man who presented with a high prostate specific antibody (PSA) test (#232; Fig. 6). The cancer of the prostate, shown in red, extends beyond the capsule of the prostate into the seminal vesicles, which means that the patient is not a candidate for surgery or implantation of radioactive seeds into the cancer but should be treated with external radiation directed toward the lesions shown in the nuclear medicine image.

Because cancer of the prostate is such a widespread disease and because this study represents a fusion of anatomical information with biochemical information in a manner that answers a specific diagnostic and therapeutic question, I have selected this image as the Image of the Year for 2000. This agent, ^{111}In prostate monoclonal antibody, is not popular with some nuclear medicine physicians, because the images are so difficult to interpret by themselves. The diagnostic question, that is, to determine whether the lesion has spread outside of the prostate gland, requires the precise anatomical information provided by the MR image. It is predictable that the use of fused imaging with this radiotracer will greatly increase the usefulness of the procedure.

Fusion of Anatomy, Function, and Biochemistry

Figure 7 is an example of the use of fused imaging to show the effect of laser thermotherapy of a brain tumor (#137). The persistence of part of the tumor can be seen in the follow-up study.

Another example of the value of fused anatomical/molecular information is illustrated in a presentation by Israel and colleagues from Rambam Medical Center in Haifa, Israel (#35). Endocrine neoplasms are difficult to interpret in scintigrams, because anatomical information is needed to answer the clinical questions, such as where parathyroid cancer lesions are located prior to surgery. This is another example in which fused imaging by combined transmission and emission tomgraphy is needed.

Multimodality imaging of hypoxia with ^{60}Cu diacetyl-bis (N4-methylthiosemicarbazone) (ATSM) by the group at Washington University (St. Louis, MO) indicated that the distribution of hypoxia is nonuniform within brain tumors (#1241; Fig. 8). This procedure can assist in demarcating and targeting the resistant hypoxic regions within the tumor.

Fifty years ago, George Moore at the University of Minnesota used a Geiger-Muller detector to try to locate brain

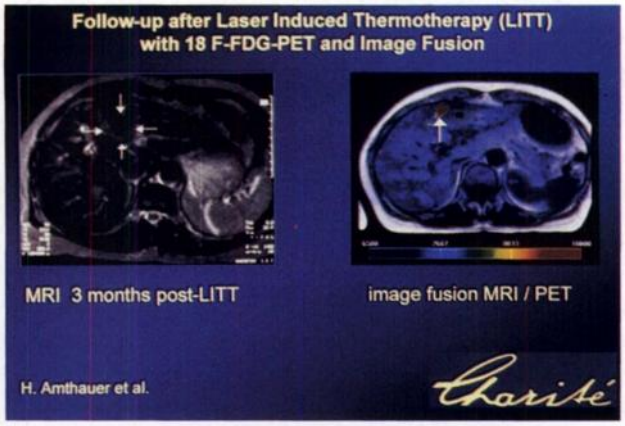

Figure 7. Follow-up of laser therapy by means of fused image tomography (FIT; #137).

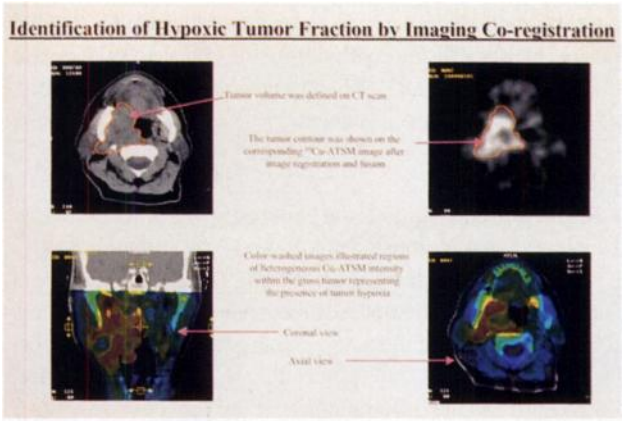

Figure 8. Fused imaging showing the heterogeneous distribution of hypoxia within a brain tumor (#1241).

tumors after the injection of radiolabeled dyes. In the 1960s, brain scans were obtained after the injection of radiotracers that diffused into brain tumors because of absence of the blood–brain barrier. Even in those days, we superimposed the brain scans on skull x-rays, that is, we "fused" the anatomic and functional information.

Foehrenbach and colleagues from HIA Val de Grace in Paris, with colleagues from the Service Hospitalier Frédéric Joliot Atomic Energy Commission, presented the ultimate use of FIT during a neurosurgical procedure (#979). The day before surgery, the patient has an MR study to provide anatomical information, a functional MR study to determine the areas of the brain to be avoided at surgery (activation of sensory, motor, or visual cortex, depending on the site of the surgery), together with nuclear imaging with ^{201}Tl to define the precise site of the cancer. The data are then digitized and analyzed before surgery, with the information portrayed on a screen that the neurosurgeon can see during the operation. The data are also portrayed as contours on the field of view of the neurosurgeon's operating microscope.

Tanaka et al. from Toronto, Canada, reported that coregistration of MEG and FDG PET localized epileptogenic regions in children with cortical dysplasia, again supporting the value of fused tomography (#981). FDG PET was used to guide high-dose conformational radiation therapy for glioblastoma (#269). The regions selected for the most intense radiation therapy ("boost" volumes) were different when defined by FDG PET compared with MR imaging. FDG PET was the most accurate predictor of survival or time to progression of the tumors. Amthauer and colleagues from Charite Hospital in Berlin, Germany, carried out whole-body FDG PET before laser-induced thermotherapy for treatment of hepatic metastases in patients who were not candidates for surgery (#137). The most valuable contribution was the detection of extrahepatic metastases, which excluded the patients from fruitless attempts at laser treatment of the hepatic lesions. After ablative therapy of several types—cryotherapy, laser ablation, or ethanol injection—FDG PET was helpful in assessing whether the therapy had been successful (#1254).

Hypoxia

Nineteen presentations reported on the use of tracers for detecting hypoxia: 11 in oncology, 2 in cardiology, and 6 in other diseases. High degrees of FDG accumulation predicted a poor response to neoadjuvant chemotherapy as assessed in surgical specimens in patients with locally advanced breast cancer after chemotherapy (#442). Some of the lesions were hypoxic, but it was not possible to get an exact indication that hypoxia was driving the increased FDG accumulation. Direct measurement of oxygen partial pressure in neoplasia did not correlate with glucose metabolism, as indicated by FDG PET studies in patients with primary cervical cancer (#458). In the 22 patients studied, staging of the extent of the disease was effective.

Demarcating and targeting more radiation dose to the resistant hypoxic regions within the tumor may be possible with fused imaging of hypoxia (#1241).

Molecule of the Century

A few years ago I nominated ^{18}F FDG as the Molecule of the Century. That was the last century. The continuing growth in the number of presentations at this meeting is seen in Figures 9 and 10 and shows that, at least for the present, FDG retains this title. Of all the presentations involving ^{18}F, 75% were concerned with FDG.

Biological Significance of FDG Accumulation in Oncology

What does FDG accumulation tell us about a cancerous lesion? In many types of cancer, such as hepatocellular cancer, FDG uptake is related to overexpression of hexokinase II, a phosphorylating enzyme present for billions of years in archeobacteria, which existed even before oxygen was on earth. Thus, the observation of FDG uptake can be a reflection of

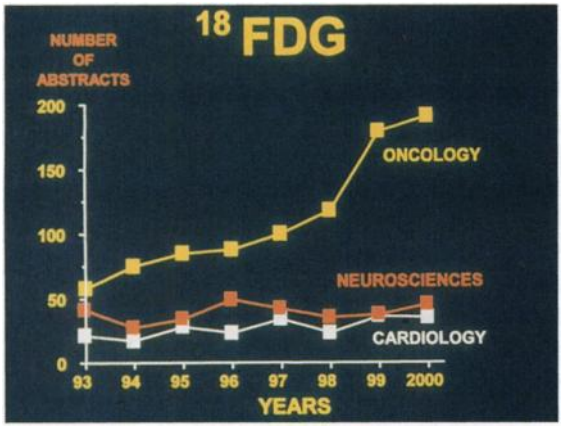

Figure 9. Continuing increase in ^{18}F FDG presentations in oncology.

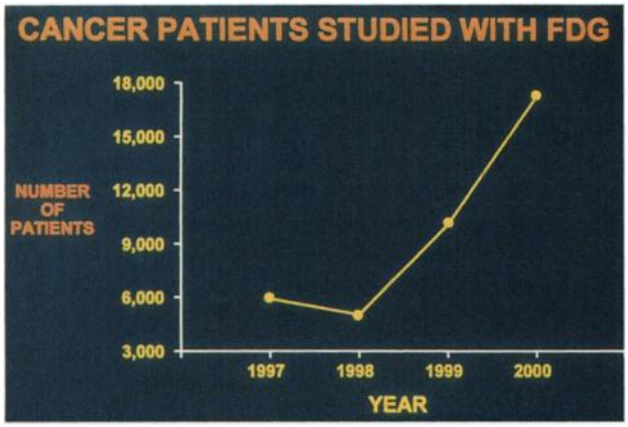

Figure 10. The number of patients with cancer studied with FDG summarized from the presentations at the SNM meeting.

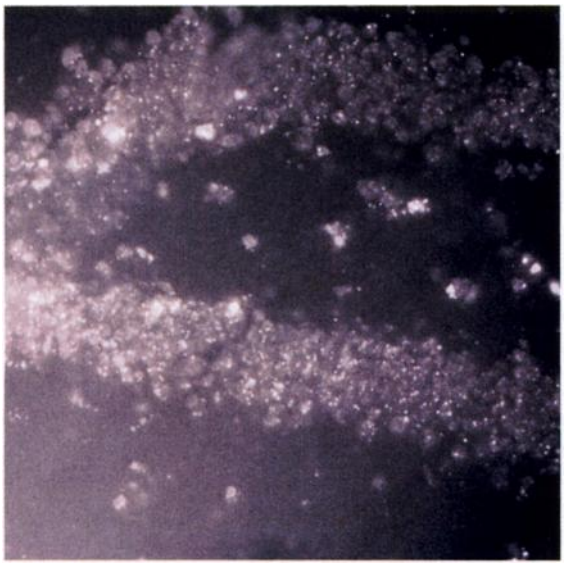

Figure 11. Accumulation of a fluorescent FDG analogue near the nuclei of cells (Mathews W, Baidoo K, and Wagner, HN, Jr., unpublished data).

de-differentiation. Fluorescent imaging of FDG analogues shows the accumulation of this tracer near mitochondria (Fig. 11; from Mathews W, Baidoo K, and Wagner HN, Jr., unpublished data).

Lee and colleagues, in 1 of the 85 presentations from South Korea, provided further evidence that mitochondrial hexokinase is a major factor in FDG uptake (#1132). The same group of investigators showed that both the glucose transporter (Glut 1) and hexokinase contribute to the accumulation of ^{18}F FDG in human cancer cells (#1130). Smith et al. from Royal Marsden Hospital and the Institute of Cancer Research in Sutton, UK, made the important observation that the decrease in the uptake of deoxyglucose by tumor cells receiving chemotherapy depends on the specific chemotherapeutic agent (#1156). This observation indicates the importance of consideration of both tumor type and chemotherapeutic agent in monitoring the response to therapy.

It is predictable that within several years, other ^{18}F-labeled tracers, such as ^{18}F fluoroethyl tyrosine (FET), will decrease this dominance by FDG. Other tracers, including ^{11}C acetate, are being used in prostate cancer.

^{11}C Acetate

Seltzer and colleagues at the University of California at Los Angeles (UCLA) compared whole-body ^{11}C acetate and FDG in patients with prostate cancer (#560). ^{11}C acetate improved detection of primary and locally recurrent prostate cancer, and, in the case of distant metastases, there was a marked discordance between FDG and ^{11}C acetate. The lower accumulation of FDG reflects the differentiation of the cancer cells relative to other more aggressive neoplasms. The short half-life of ^{11}C (20 min) makes it difficult to distribute beyond the site of preparation of the tracers.

Liu and colleagues from the Tri-Service General Hospital in Taipai compared FDG and ^{11}C acetate whole-body imaging in patients with lymphoma (#1211). Acetate PET was less sensitive in detecting low-grade and high-grade to indeterminate-grade non-Hodgkin's lymphoma (NHL) but had equal detectability to FDG in high-grade NHL and Hodgkin's disease.

^{18}F Fluoroethyl Tyrosine

For years, it has been recognized that the avid accumulation of FDG by normal brain causes problems in the use of FDG to examine brain tumors. ^{11}C methionine is much preferred for this purpose. Kim et al. from Seoul National University, South Korea, found that ^{11}C methionine was preferable to FDG in patients with brain tumors (#271). Figure 12 is a comparison of FDG with ^{11}C methionine in 1 patient.

Weber and colleagues from the Technical University of Munich, Germany, found a good correlation between ^{11}C methionine and ^{18}F-FET in brain tumors (#272; Fig. 13). ^{18}F-FET is likely to become the second radiopharmaceutical distributed by commercial radiopharmacies.

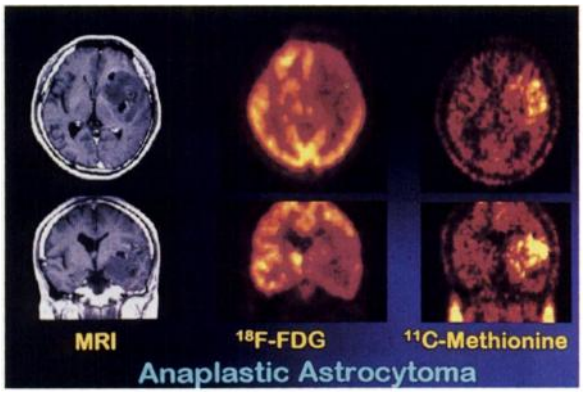

Figure 12. Better visualization of a brain tumor with ^{11}C methionine, compared with FDG, which accumulates in normally functioning brain (#271).

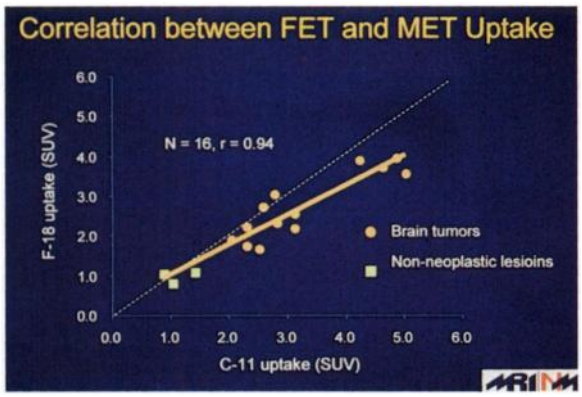

Figure 13. Good correlation between ^{11}C methionine and ^{18}F fluorethyl tyrosine (FET) in brain tumors (#272).

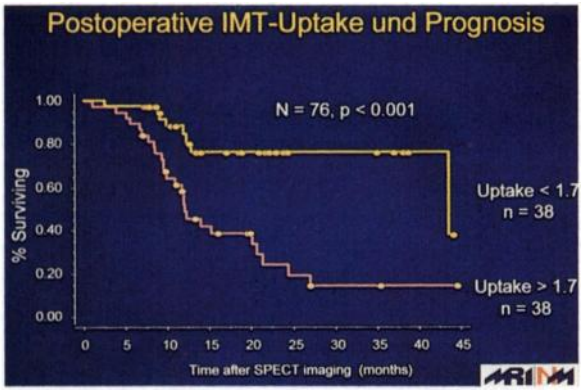

Figure 14. Prognostic value of ^{123}I tyrosine studies in patients with brain tumors (#270).

The residual accumulation of ^{123}I α methyl tyrosine was found to be an important prognostic factor after resection of primary brain tumors. Figure 14 shows the differential survival depending on tyrosine accumulation in brain tumors (#270).

Today we have both single photon (^{123}I) and positron emitting radiotracers for studying amino acid metabolism by neoplasms. The 2-h half-life of ^{18}F-FET will make possible delivery of this tracer for use in the care of patients with brain tumors. Although ^{18}F FDG is what has made nuclear oncology what it is today, it is predictable that multiple tracers will be used to help solve specific problems in patients with specific diseases. For example, Rau and colleagues from the Institute of Pathology of the Technical Institute in Munich found that FET was a specific marker for detection of lymph node metastases in lymphoma. Neither FDG nor ^{11}C methionine was able to differentiate inflammatory from tumor-infiltrated lymph nodes, but FET could do so (#452).

Lung Cancer

Lung cancer remains the number 1 topic of the hundreds of oncology presentations, accounting for 31 presentations. Clearly, FDG PET is playing a major role in clinical decision making in patients with lung cancer, as well as other types of cancer. Schiepers and colleagues from UCLA reported that FDG PET imaging of patients being followed up after treatment for lung cancer resulted in a change of clinical stage in more than half of 71 patients (#295). FDG PET was 25% more accurate than CT. Hicks et al., from the Peter MacCallum Cancer Institute in Melbourne, Australia, found that FDG PET had an important impact in more than 90% of 153 patients with non–small cell lung cancer (#296). The PET results were related prognostically to patient survival. Still another of the numerous presentations supporting the important role of FDG PET imaging in patients with lung cancer was the report of Baum and colleagues from University Hospital, Jena, Germany (#1280). Therapeutic management was changed in 52% of the patients as a result of the FDG PET results. Gupta and Bishop, from the University of West Virginia, found that FDG PET changed the treatment plan in 83% of 77 patients with lung cancer, leading to early surgery in 26% (#299).

How Big Is Your World?

Each of us should extend our world to include the general public, who are becoming more and more involved in their health care (Fig. 15). The distinguished science reporter for *The New York Times*, Lawrence K. Altman, wrote on May 23, 2000: "[There have been] radical changes in the relationship between patients and their doctors. Americans have traded in paternalism for medical consumerism...fighting for a greater voice in making critical decisions about their care."

I have titled my talk this year "The Internet: The Road to 'Smart' Nuclear Medicine." There have been 8 major inventions in the history of nuclear medicine: the cyclotron, nuclear reactor, rectilinear scanner, Anger scintillation camera, computer, PET, SPECT, and now the Internet. I believe that the Internet is the most important new instrument for the growth and further development of nuclear medicine throughout the world today.

Use of the Internet will become an indispensable tool for how we deal with the public, our patients, referring physicians, our suppliers, hospital administrators, and all others who rely on the science and technology of nuclear medicine in

Figure 15. Ask yourself this question.

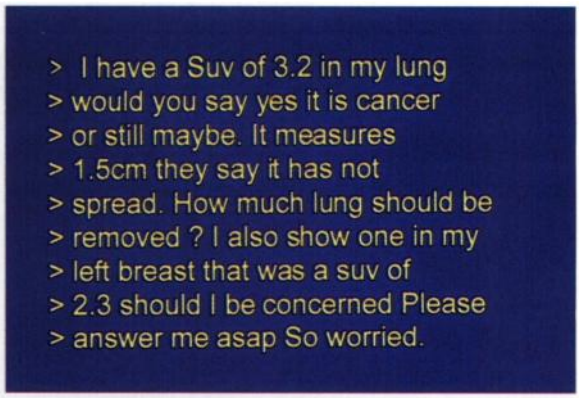

Figure 16. Internet message from a patient.

health care. The time has come to absorb the Internet into everything we do.

To cite an example, I would like to present selected e-mails that I exchanged on the Internet recently with a person whose name I still do not know. Among the messages that I received was the following:

> I am 45 years old. I have smoked for years. I feel because I am young they want to remove to much lung. [Her wording suggests that she is not highly educated, which I believe indicates how widespread is the use of the Internet.] I scared it will really harm me. I don't want a hole lobe removed. Not if it wont make a difference. I also had breast cancer 4 years ago. They say it dose not look like breast cancer. Why cant they just remove the cancer. why do they have to take out so much (on a dont know if it will help)

I answered:

> I believe they will take out only what needs to be taken out. I recommend that you follow their advice, and trust your doctors. I recommend that you have a fluorine-18 FDG study performed before surgery to see if the cancer has spread so far that chemotherapy is the best choice of treatment rather than surgery. Ask your doctors about the FDG study. Tell them that I recommended it and let me know what they say.

The patient responded:

> I will ask about the FDG study, but I would rather remove the lung than do Cemo again. I did cemo for breast cancer. I though a 1.5 cm was small and chances of spread was small also. Why would you do cemo and not surg? The surg. is going to do a needle biopsy on the 28th and see where they are with this.

Later she wrote (Fig. 16):

> I have a Suv of 3.2 in my lung would you say it is cancer or still maybe. It measures 1.5 cm they say it has not spread. How much lung should be removed? I also show one in my left breast that was a suv of 2.3. Should I be concerned. Please answer ASAP. So worried.

This exchange illustrates what will be more and more commonplace in medicine. Not only must we make ourselves readily available to the public and our patients and referring physicians, but we must also have our science and technology widely distributed on the Internet and referenced in our Web sites. There are at least 15 major cancer-related Web sites. I looked at cancerfacts.gov, a site sponsored by the National Institutes of Health, and found it to contain very little about nuclear medicine. Personally and collectively, we need to do something to correct this.

Planning and Monitoring Treatment

As in the case of most so-called "diagnostic" tests, molecular imaging studies are performed to plan and monitor treatment in patients for whom the diagnosis is already known. At this meeting, 41 presentations involved treatment planning, whereas 43 involved monitoring the response to treatment.

Investigators from Guy's and St. Thomas's, and the Royal Free Hospital in London, UK, described what is needed for serial assessment of the response to anticancer drugs for both dedicated (ring) PET and hybrid (dual coincidence) PET (#830). The following are necessary to achieve optimum results: (1) Faithful attention to acquisition protocols; (2) attenuation correction using ordered-subset expectation maximum (OSEM); (3) accurate coregistration with anatomic imaging; (4) use of normal regions for comparison; (5) creation of functional (parametric) images; and (6) operator-independent quantification of the results.

After showing that FDG PET is as helpful in staging patients with other cancers as it is in lung cancer, the UCLA group carried out a prospective survey of referring physicians to determine the impact of whole-body FDG PET imaging in the care of patients with cancer (#428). The decision not to operate or perform radiation therapy occurred in 17% of the patients, whereas a new decision to operate or perform radiation therapy occurred in 14% of the patients. A major focus of the meeting was the documentation for all to see of the enormous value of FDG PET in the care and most effective decision making in patients with most types of cancer. Few could leave the meeting without resolving to incorporate FDG PET into their nuclear medicine practices.

It is unlikely that FDG PET will remain the only radiotracer agent used to monitor treatment. Dohmen and colleagues from Tubingen, Germany; Detroit, MI; and Seattle, WA, showed

how brain tumors, visible with high contrast with ^{18}F fluorothymidine (FLT), had a decrease in tracer accumulation with treatment (#966). FLT accumulation decreased with treatment in breast cancer as well (#290; Fig. 17).

Rasey et al. from the University of Washington showed that the accumulation of FLT reflected the level of thymidine kinase (TK), the phosphorylating enzyme, but that TK was not the whole story (#142).

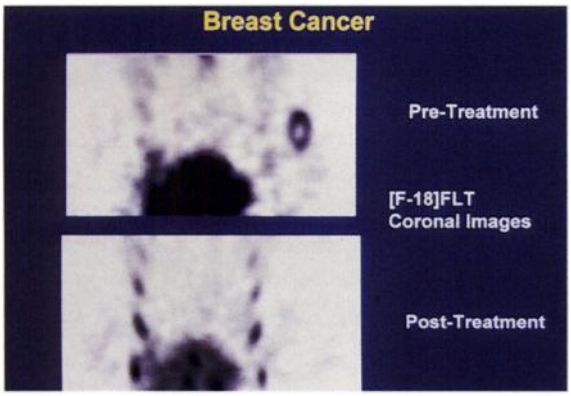

Figure 17. Decrease in ^{18}F fluorothymidine (FLT) after treatment of a breast tumor (#290).

Prognosis

Even survival could be predicted from the results of the FDG studies. Iwata and colleagues from Osaka University Medical School, Japan, showed the great difference in survival of patients with hepatocellular carcinoma, depending on whether the standardized uptake value (SUV) was greater or less than 1.5, again supporting the concept that FDG accumulation indicates the degree of malignancy of cancer (#1298).

Importance of Whole-Body Studies

A major characteristic of functional and molecular imaging is that the entire body can be examined at 1 time. Martin and colleagues from St. Louis University Hospital emphasized the importance of interpreting mediastinal and hilar accumulations of FDG in patients with extrathoracic malignancy as metastases, not as incidental findings (#126). Eighteen percent of their patients with this finding were shown to have mediastinal/hilar metastatic disease.

Another "clinical pearl" was to administer insulin at least 1 h before FDG in diabetic patients being examined for cancer (#1238).

p-Glycoprotein Assessment and Apoptosis

Henze et al., from Heidelberg, Germany, found that the sensitivities of FDG PET and the amino acid ^{123}I α methyl tyrosine were the same (88% and 85%), but the target/nontarget ratios were 6.7 and 3.0, respectively, in patients with hypopharyneal/larynx carcinoma (#559). They found that only 71% of the lesions were found with ^{99m}Tc sestamibi (MIBI). Although it is clear that both FDG and radiolabeled tyrosine are more sensitive, ^{99m}Tc-MIBI plays an important role. As discovered by D. Piwnica-Worms, ^{99m}Tc-MIBI accumulation and excretion from cancerous lesions can be used to reflect the status of p-glycoprotein, which facilitates the excretion of toxic substances, such as cancer chemotherapeutic agents, from many types of cancer and normal cells in the brain and liver.

The efflux rate of ^{99m}Tc-MIBI from breast cancer lesions in untreated patients could not be related to prognostic factors (#1264) but was related to an increase in the apoptotic (programmed cell death) pathway (#1261, #1264). Thus, this tracer might prove useful in monitoring apoptosis in therapeutic attempts to modulate it. Aloj et al. showed that rapid clearance of ^{99m}Tc-MIBI was associated with a high proliferative rate of the tumor and an underexpression of the tumor suppressor gene, p53 (#1264). Expression of the p53 gene in tumors can be assessed with PET using ^{124}I-FIAU, a positron emitting analogue of thymidine (#1158; Fig. 18).

Apoptosis can be assessed with the new radiotracer ^{99m}Tc annexin V in order to obtain objective evidence of the effectiveness of chemotherapy soon after administration of the first

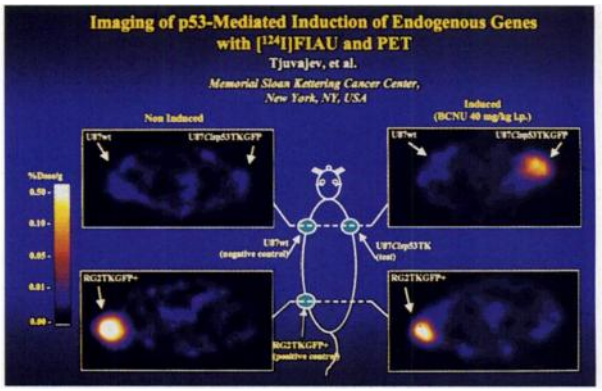

Figure 18. Measuring expression of the p53 gene promoter with the positron-emitting tracer ^{124}I thymidine analogue FIAU (#1158).

dose (#1154). This agent was first used to assess heart transplants but is now being extended to oncology.

To make PET studies of the p-glycoprotein system possible, the Washington University group has developed ^{67}Ga-labeled agents that will be useful in quantifying the functional activity of p-glycoprotein in tumors and normal tissues in vivo (#164).

Hybrid (Dual Coincidence) PET

Many came to the meeting to learn how hybrid PET, that is, PET/SPECT or transmission emission tomography, had performed over the past year. The short answer is "very well, thank you." Fifty-seven presentations were concerned with hybrid PET, many comparing its performance with dedicated or ring PET. Hybrid PET did not have an inhibiting effect

on dedicated PET, as evidenced by the increase in dedicated PET studies from 432 in 1999 to 513 in 2000.

In the preoperative staging of patients with non–small cell lung cancer, Rakotonirina and colleagues from Orsay, France, and Paris found that ring- and hybrid-PET instruments gave concordant results with respect to the question of nodal involvement and distant metastases in 91% of their patients (#1274). Among the presentations providing overwhelming evidence of the value of FDG PET in staging patients with lung cancer was the study of Rao and colleagues from California. They reported that their studies revealed nonresectable lesions in 16% and resectable lesions in 65%, the remaining 19% being candidates for surgery after neoadjuvant therapy (#297).

Bongers et al. from Utrecht, The Netherlands, reported their excellent results with dual-coincidence hybrid PET in 75 patients with recurrent laryngeal cancer (#1252). In 10 patients with initially negative biopsy after positive FDG PET, the negative biopsies became positive for tumor in follow-up biopsies 6–12 mo later. Grahek et al. from the Hospital Tenon in Paris found dual-coincidence PET was 96% accurate in detecting recurrence of breast cancer (#1267). In pretreatment staging of lymphoma patients, Lin and colleagues from Liverpool Hospital in Australia reported a nodal site sensitivity of 97% and an extranodal site sensitivity of 93% (#467). Similarly, excellent results in lymphoma were reported by Kostakoglu and colleagues from the Center for Lymphoma and Myeloma in New York, NY (#466). In imaging lymphoma prior to treatment, FDG PET using dual-coincidence PET with attenuation-correction FDG PET detected significantly more disease sites than ^{67}Ga SPECT, which affects the staging of the patients for subsequent treatment.

Receptors in Oncology

Although FDG PET has revolutionized oncological diagnosis and the planning and monitoring of therapy, the existence of molecular recognition sites, chiefly receptors, provides the greatest opportunity for expansion of radionuclide therapy. The ^{131}I metaiodobenzlyguanidine (MIBG) story is perhaps the best example. Chmielowiec and colleagues from the Cross Cancer Institute in Edmonton, Canada, described the protocols for optimum treatment of patients with pheochromocytoma with MIBG (#581). In many patients, FDG PET is used to diagnose cancer, which is then examined with other tracers to determine whether somatostatin, dopamine, adrenergic, or bombesin receptors are present.

Sixty-one presentations were concerned with receptors in oncology. The greatest number (33) involved somatostatin receptors. The next highest number was folate receptors, with 5 presentations. The presence of these plasma membrane receptors provides therapeutic possibilities. The receptors on tumors can first be detected by radiotracer methods, and then a radionuclide can provide a means of delivering a therapeutic radiation dose to the molecular target. I refer to the diagnostic tracers as nanoDx tracers, and the therapeutic agents as nanoRx agents, the prefix nano referring to the nanomolar concentrations of both types of agents.

Radionuclide Therapy

Those old enough to remember the immediate post–World War II period will recall that what made atomic medicine (as nuclear medicine was then called) so popular was the treatment of thyroid cancer and hyperthyroidism with radioactive iodine. There followed a search among other elements, such as zinc, for similar benefits, but none was found. It took the advances in molecular medicine to bring about functional and molecular nuclear medicine as we know it today. The encouraging results that are finally being obtained in radionuclide therapy are beginning to attract the attention of other physicians, the public, and the media. This bodes well for the renaissance in appreciation of nuclear medicine that is now becoming evident. The increase in the number of presentations concerning radionuclide therapy can be seen in Figure 19.

The presentation of Jonard and colleagues in a multiinstitutional study from Brussels, Belgium; Rotterdam, The Netherlands; Florida, and New Jersey provides an excellent example. The PET tracer ^{86}Y dodecane tetraacetic

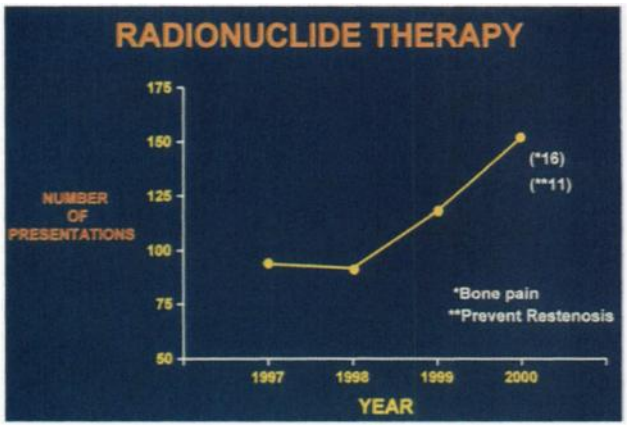

Figure 19. The number of presentations dealing with radionuclide therapy is increasing.

acid (DOTA) octreotide was used together with CT for radiation dosimetry, and then the patients with cancer expressing somatostatin receptors (such as carcinoid) were treated with ^{90}Y octreotide (#437; Fig. 20). There was a decrease in tumor volume that was related to the increase in the dose of radiation to the tumors.

In a phase I clinical trial of ^{111}In octreotide therapy in patients with neuroendocrine tumors, McEwan and colleagues from the Cross Cancer Institute found symptom control and no renal toxicity in most of the patients, but only a few had a decrease in tumor size (#1170).

Gulec and colleagues from Tulane University in New Orleans, LA, utilized the fact that proliferating human vascular endothelium expresses somatostatin receptor type 2. They used an ^{111}In somatostatin analogue as an antiangiogenic therapeutic

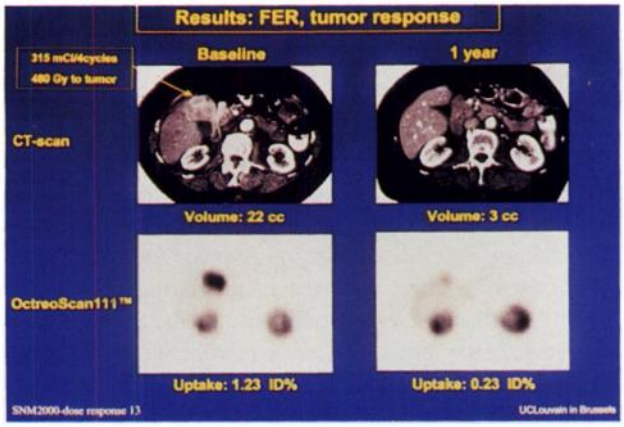

Figure 20. Reduction in tumor size and decreased accumulation of a somatostatin receptor-binding tracer (^{86}Y DOTA octreotide for dosimetry) after treatment with ^{90}Y DOTA octreotide (#437).

agent to induce cell death (#133). The tracer inhibited both the initiation and promotional phases of angiogenesis. Emitting Auger electrons, the tracer has a direct effect on DNA.

The presence of estrogen receptors in breast cancer is of both prognostic and therapeutic importance. Mankoff and colleagues from the University of Washington found a heterogeneous distribution to be of both prognostic and therapeutic importance (#108).

^{131}I-MIBG therapy depends on the presence of adrenergic receptors on the tumor. Papavasileiou and colleagues from the Royal Marsden Hospital have developed a fully automated image registration method for fusion of CT and SPECT that facilitates 3-dimensional dosimetry (#825).

Pain is a frequent symptom in patients with cancer, and, here again, radionuclide therapy is more and more being shown to be effective. Throughout the history of nuclear medicine, the International Atomic Energy Agency (IAEA) has played a major role in extending the use of radioactive tracers. An example of a recent multi-institutional study conducted under IAEA auspices is a report by Olea and colleagues, in which 417 patients from Chile, Austria, China, Thailand, Argentina, and the Philippines were treated for painful skeletal metastases with ^{153}Sm ethylene diamine tetramethylene phosphate (EDTPM) (#575). Seventy-three percent of the patients had significant improvement. Wyndaele and colleagues from Belgium reported that radionuclide therapy for bone pain with ^{186}Re hydroxethylidine diphosphonate (HEDP) was less expensive and the treatment of choice when compared with external radiation therapy (#1168).

In addition to ^{186}Re, ^{188}Re is likely to become very important in the future. It is available as the 17-h daughter of ^{188}W, which has a half-life of 69 d. The cost of the ^{188}W generator is low enough to make possible extensive use of ^{188}Re as a therapeutic radionuclide, especially because of its chemical similarity to ^{99m}Tc. Over the next few decades. it is likely to become the therapeutic radionuclide of choice. The sources of ^{188}W are limited, but the generators can be obtained today in the United States, Europe, and India. Fifteen presentations employed this tracer.

^{188}Re-labeled antibodies were used in radioimmunotherapy prior to stem cell transplantation by investigators from the University of Ulm, Germany (#1058). Individual dosimetry is a prerequisite for this therapy and was obtained by imaging at multiple times during the first 2 d after injection. High doses of ^{166}Ho DOTMP were used prior to stem cell transplantation by investigators at the University of Washington, and NeoRx was used in myeloablative treatment of multiple myeloma (#576). The short 27-h half-life simplifies the need for radiation isolation and bladder catheterization.

^{131}I monoclonal antibody radioimmunotherapy was used by investigators at the University of Michigan to treat patients with untreated follicular lymphoma (#309). Seventy-six percent of the patients had complete responses, whereas 21% had partial responses.

Other positron emitting radionuclides of interest for radionuclide therapy include ^{64}Cu, ^{61}Cu, ^{60}Cu, ^{68}Ga, ^{66}Br, ^{67}Br, ^{124}I, ^{99m}Tc, and ^{90}Y. Reischl et al. described the use of a low-energy cyclotron for making ^{124}I (#1110).

Focus on Breast Cancer

Unlike the case with solitary pulmonary nodules, oncological surgeons are less concerned when the results of surgical removal reveal that breast lesions are benign. Lumpectomy is far less traumatic than thoracotomy. Considerable attention is being given to the question of how to examine the axilla. Dwamena and Wahl of the University of Michigan carried out an economic analysis of their data that showed the impact on survival and economic advantages of FDG PET in eliminating the need for axillary exploration in patients with breast cancer (#1269). One of the essential prognostic factors in breast cancer and of decisive importance in regard to adjuvant chemotherapy is the question of involvement of axillary lymph nodes. Joerg and colleagues from Linz, Austria, reported the results of sentinel node studies in 150 patients (#308). The study was successful in localization and assessment of the involvement of sentinel nodes in 79% of the patients, which indicated that many patients do not require dissection of the axilla for staging purposes.

FDG PET is very helpful in identifying patients with internal mammary lymph node involvement in locally advanced breast cancer (#574). Standard imaging with CT is not sensitive for detecting internal mammary metastases.

A remarkable study was carried out by Fujii and colleagues from the HIMEDIC Imaging Center in Japan (#1268). Between September 1994 and March 1999, 1148 asymptomatic women were screened with whole-body FDG PET. Six patients were found to have unsuspected breast cancer, which was cured by surgery. This is higher than the expected incidence of breast cancer in the United States, which is 110 cases/100,000 women. It is likely that in the future the most commonly screened patients

will be those who have specific genetic abnormalities, such as BRCA1 and 2. These patients will be analogous to those asymptomatic men who have abnormal PSA levels on routine screening. The key role of nuclear medicine in these patients at higher than normal risk will be to determine when, where, and how phenotypic manifestations of the genetic abnormalities occur.

Although x-ray mammography is likely to remain the chief means to screen women for breast cancer, the diagnosis of recurrence of breast cancer is a different story. Kolasinska and colleagues from the Royal Free Hospital in London found that scintimammography correctly detected 26 out of 33 patients with recurrence, whereas x-ray mammography detected only 12 of 26 (#110).

Infection and Inflammation

The Georg Charles de Hevesy Award was presented at the opening ceremony of the SNM meeting to Mathew Thakur for his lifetime achievements in labeling white blood cells with ^{111}In oxine and, more recently, for his development of a ^{99m}Tc antibody directed against the plasma membrane antigen CD15 on leukocytes. Kipper et al., in a multi-institutional trial of this latter agent, described its safety, efficacy, and cost effectiveness in studies of adults and children suspected of having appendicitis (#36). In a comparison with ^{99m}Tc-labeled leukocytes, Kipper and Rypins found that the results with the anti-CD15 tracer were equally good and pointed out that the latter procedure was faster and improved patient throughput in emergency studies (#38).

Of the 51 presentations on infection and inflammation, 14 employed FDG PET. In a direct comparison of ^{111}In-labeled leukocytes with FDG PET in diagnosing infected hip prostheses, Love and colleagues from the Long Island Jewish Medical Center, NY, found that FDG, although sensitive, was less specific than leukocyte labeling and concluded that FDG cannot replace labeled leukocytes for this purpose (#60). In bone infections, Prandine and colleagues from Italy and the UK reported that a labeled antibiotic ^{99m}Tc ciprofloxacin was comparable to labeled leukocytes in diagnosing peripheral osteomyelitis, but the labeled antibiotic was more effective in central bone infections (#62).

The ^{99m}Tc ciprofloxacin represents an important new approach to differentiating infection from inflammation. Surprisingly, when labeled tetracycline was introduced decades ago it was used as a myocardial perfusion agent. No one thought to see whether it accumulated in bacterial infections. Britton and colleagues from London, Chile, India, Greece, Egypt, Argentina, and Austria, in a multi-institutional study supported by the IAEA, found that in a wide variety of bacterial infections the labeled antibiotic was more specific than labeled leukocytes (#40).

Sentinel Nodes

As mentioned previously, the concept of sentinel node detection of metastatic cancer is not widely known throughout the medical community and warrants our greatest efforts to educate referring physicians and the public. Jana et al. from St. Vincent's Hospital in New York found that in breast cancer, radiocolloid localization of sentinel nodes was more successful than the use of blue dye alone but that the use of both agents simultaneously provided the best success rate (#1230). We all must deal every day with colleagues who have an exaggerated fear of low-level radiation. Brenner and colleagues from Christ-Albrechts University in Kiel, Germany, provided data to show that in sentinel node detection the radiation risk to staff is very low and there need be no concern for radiation risks. According to German radiation safety standards, persons involved do not need to be classified as occupationally exposed radiation workers. No special radiation protection measure or personal dosimetry is required (#1042).

Jacobs and others from Kettering Medical Center in Dayton, OH, found that, in patients with breast cancer, FDG PET was not able to detect axillary node metastases smaller than 1 cm in size (#573). Failure to detect other lesions with FDG does not rule out involvement of other lymph nodes when the sentinel node is positive. FDG PET improves the detection of metastases in internal mammary and mediastinal lymph nodes in patients with breast cancer (#109; Fig. 21).

The practice of searching for metastases in sentinel nodes began with melanoma and soon progressed to breast cancer. Fujii and colleagues from Keio University School of Medicine in Tokyo, Japan, imaged sentinel nodes in patients with esophageal cancer (#1222).

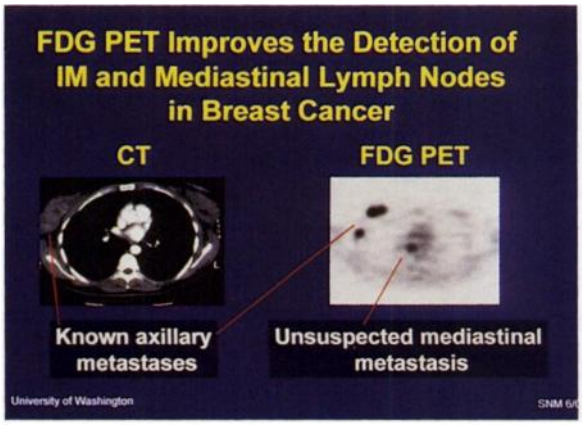

Figure 21. Unsuspected mediastinal lymph node metastasis in a patient with breast cancer (#109).

Intraoperative Studies

Sentinel node studies and the explosive growth of nuclear oncology has increased the attention of surgeons to nuclear medicine technology. Raylman reported his recent studies with a β-probe system for use with ^{18}F and the conversion electrons of ^{111}In (#221). Essner and colleagues described a system that consists of 2 separate detectors connected to a single operating system. The surgeon can easily switch back and forth with

a foot switch from a 511-keV γ detector for locating deep cancerous lesions identified with ^{18}F FDG, to a β-plus detector to examine the site from which the cancer has been removed, in order to see if the edges of the removal site have extended beyond the cancer into normal tissue (#1239).

Solid State Imagers

Instrument manufacturers have long been interested in the use of solid state detectors to facilitate the construction of small to large imagers. Iwata and colleagues from Watertown, ME, described a prototype system that employs a 1-cm^2 4 x 4 pixellated semiconductor cadmium zinc telluride (CZT) detector (#218). Phantom studies from a combined x-ray CT and SPECT system were presented.

Nakamura and colleagues from Toshiba presented their results with a cadmium telluride (CdTe) semiconductor module with an intrinsic energy resolution of 5% full width at half maximum for 140 keV photons (#805). Contrast and sharpness were significantly better than the images from a scintillation camera.

Karp from the University of Pennsylvania summarized the relative characteristics of various scintillators used in recently constructed scintillation-based imagers (#81; Fig. 22).

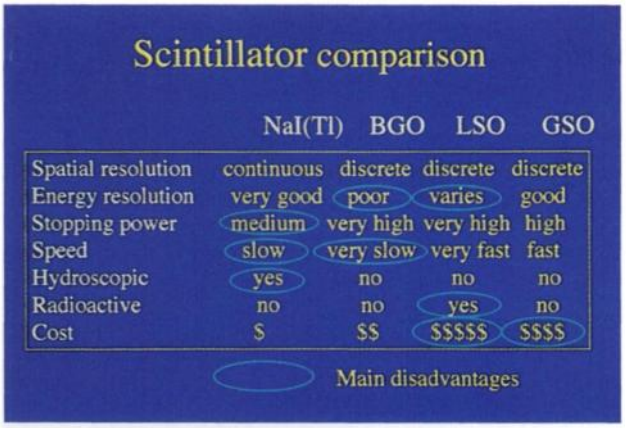

Figure 22. Comparison of several types of scintillation detectors used in imagers (#81).

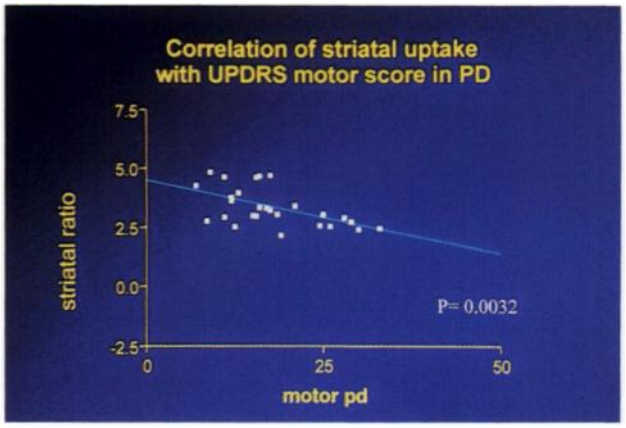

Figure 23. Relationship between decline in motor abilities and decline in dopamine transporter availability in the basal ganglia (#543).

Neurosciences

Discoveries made over the past quarter of a century concerning the chemical correlates of mental functions are as revolutionary as those of atomic physics at the turn of the 20th century or genetics over the last half century. The use of radioactive tracers has been essential for these discoveries, including the use of ^{32}P in discovering that genetic information is encoded in DNA.

An example of the advances being made is the steady growth in the number of presentations on the dopaminergic system since 1983, when the system was first imaged in human beings, to the 75 presentations at this meeting. Twenty-six presentations dealt with the dopamine transporter on presynaptic neurons, 22 with dopamine D_2 receptors, 5 with D_1 receptors; and 5 with dopamine release.

Twenty-four presentations were concerned with movement disorders, 20 with substance abuse, 15 with depression, and 10 with schizophrenia.

Multiple system atrophy (MSA) includes striatal-nigral degeneration (SND), autonomic insufficiency, and olivopontocerebellar atrophy. ^{123}I β CIT was not able to differentiate these diseases from idiopathic Parkinson's disease with respect to decreased binding to the dopamine transporter (#544). In studies of 78 patients, Seibyl and colleagues from Yale University (New Haven, CT) showed a decline of accumulation of this tracer in the basal ganglia related to the increase in motor disability (#543; Fig. 23).

The paradigm for the development of radiotracers is illustrated by the example of the imaging of the dopamine transporter. Because of the natural occurrence of carbon, the first tracer was ^{11}C, which does not change the identity of the putative binding agent. Buoyed by the success of the positron emitting tracers, chemists developed ^{123}I tracers, which became commercially available, and subsequently, the more difficult task of developing a ^{99m}Tc tracer was accomplished (#541). Tzen and colleagues from Taiwan, Republic of China, used the agent developed by Hank Kung at the University of Pennsylvania, Trodat-1, a ^{99m}Tc tropane, to differentiate patients with idiopathic Parkinson's disease from those patients with tremor and other symptoms resembling Parkinson's disease but resulting from vascular disease (#426; Fig. 24).

Little is known about the regulation of neuroreceptors. Nader and others from Wake Forest University School of Medicine (Winston-Salem, NC) showed that down-regulation of the D_2 dopamine receptor in monkeys results from the administration of cocaine, which increases synaptic dopamine, and that these changes persist for months (#413).

Another dopamine transport system involved in Parkinson's disease is the vesicular monoamine transporter type 2 (VMAT2), which transports dopamine into the presynaptic vesicles, where

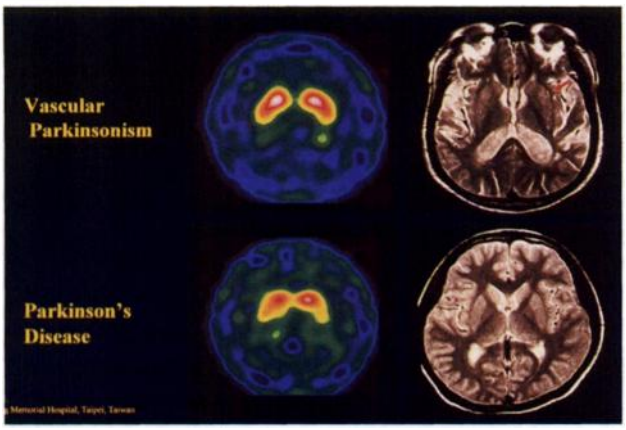

Figure 24. High-quality images of the dopamine transporter imaged with ^{99m}Tc tropane-1 (#426).

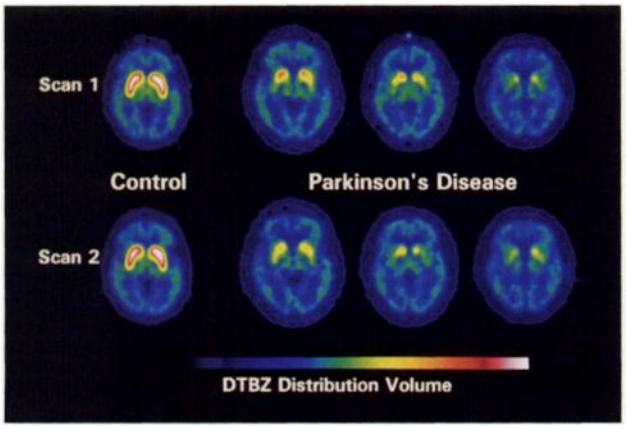

Figure 25. Progression of Parkinson's disease imaged with DTBZ (#542).

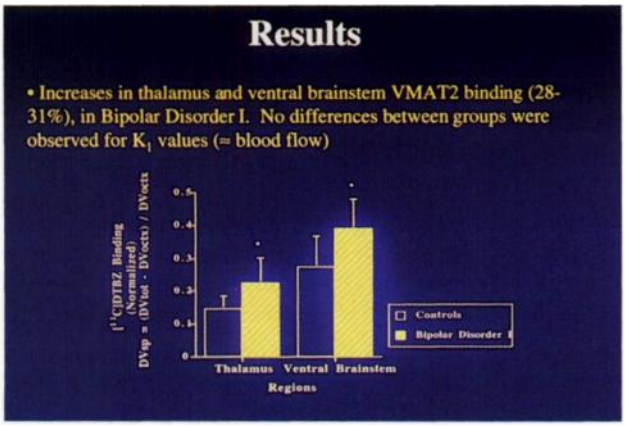

Figure 26. Increased availability of monoamine vesicular transporter in patients with bipolar disorder (#535).

it is stored prior to release. Frey and colleagues have introduced ^{11}C dihydrotetrabenazine (DTBZ) as a positron emitting ligand for measuring the availability of this transporter (#542; Fig. 25). They find that it is a useful marker for assessing progression of idiopathic Parkinson's disease. Zubieta and others from this group of investigators at the University of Michigan also find an increase in the availability of this vesicular transporter in certain brain regions of patients with bipolar disorder (#535; Fig. 26).

In a retrospective study, Bonte et al. found diminished occipital perfusion in children with major depressive disorder (#901).

The Serotogenic System

Forty-one presentations dealt with serotonin. Twenty-three were concerned with serotonin receptors and 17 with the serotonin transporter. As in the case of the dopamine transporter, we have progression to ^{99m}Tc tracers. Acton and others from Dr. Kung's group at the University of Pennsylvania have developed 3 selective transporter radioligands for SPECT (#150). ^{123}I-ADAM gave the most favorable results.

Patel and colleagues from Yale University were unable to find any differences in serotonin transporters in the midbrain of patients with Parkinson's disease compared with controls, based on ^{123}I β CIT, which binds to both the serotonin and dopamine transporter (#985). Preliminary unpublished data by others suggest that there are detectable abnormalities in the basal ganglia.

Van Laere and colleagues from Ghent University in Belgium found reduced availability of serotonin receptors in the frontal regions of persons attempting suicide compared with normal control subjects (#534). This group of investigators also found focal reductions of serotonin receptors in the frontal regions in patients with anorexia nervosa (#908).

Memory Disorders

Brain abnormalities are becoming detectable earlier and earlier in persons with memory disorders. The UCLA group found distinct evidence of abnormal cerebral FDG accumulation in brains characteristic of SDAT in 60% of persons with mild cognitive disorder (MCD) (#248). Thirty percent had mild abnormalities of the Alzheimer type. Extrapolation of the decline with age suggests that some abnormalities may be present even during the educational stages of personal development. Initial FDG PET predicted subsequent development of Alzheimer's disease in patients with minor memory deficits (#250; Fig. 27).

Imabayashi et al. from Kodaira, Japan, showed how important it is to apply the same rigor and technology to brain SPECT as is applied to brain PET (#963). They showed how 3-dimensional stereotactic surface projection (3DSSP) makes it possible to correctly diagnose more than 90% of patients with senile dementia of the Alzheimer type, even at a very early stage. Hutton et al. from Royal Prince Alfred Hospital in Sydney, Australia, presented a method for correction of SPECT for head motion during brain studies (#239).

Small Animal Imaging

Twenty-one presentations concerned animal PET, 2 concerned animal SPECT, and 1 combined both. The group

at University of California San Francisco, led by Wu, used a conventional SPECT camera with a specially constructed pinhole collimator to again show how high-quality, high-resolution gated blood-pool studies could be carried out in living mice with ^{99m}Tc-MIBI (#75). They propose the use of this method for transgenic experiments in mice.

Specially designed small animal PET instruments included Tierpet from Julich, Germany (#64), and MADPET from Munich (#77). The latter was based on LSO detectors and is used for imaging gene therapy in rats. Clinthorne et al. from Switzerland and Norway presented very high-resolution animal PET using solid state detectors (#76). Bentourkia et al. from Sherbrooke, Canada, showed how it is possible to generate kinetic data in rat PET studies based on the use of the sinogram (#227). Investigators from Ferrara and Pisa, Italy, have developed a hybrid PET SPECT system for small animals, with a spatial resolution of 3.5 mm (#71).

An example of the usefulness of small animal imagers is the study by Brownell et al. from Harvard Medical School (Cambridge, MA), which showed that brain damage from the neurotoxin 6-OH dopamine caused an increased binding of the peripheral benzodiazapine receptor ligand, C-11 PK 11195, in the striatum of rats, suggestive of microglial activation by the toxin (#407; Fig. 28).

The Lung

Among the oldest surviving procedures in nuclear medicine are the ventilation/perfusion studies with radiolabeled particles and gases. In a comparison with electron beam CT, there was a discordance with V/Q results in 203 pulmonary segments compared with 301 concordant. Because of the known sensitivity of V/Q studies for detecting segmental artery defects, it is likely that the V/Q scan will remain the most definite predictor of the results of subsequent pulmonary angiography (#47). So it looks as if lung scanning still lives! Holst et al. from Lund, Sweden, described an automated method for interpreting lung scans that was a good as experienced physicians (#49).

The peptide ^{99m}Tc-DMP performed better than ultrasound in detecting deep venous thrombosis (#44). This is but 1 of 420 presentations that show that ^{99m}Tc is living and well in nuclear medicine. Some have said that the best thing that ever happened to ^{99m}Tc is PET, providing firm evidence of the potential usefulness of new ^{99m}Tc-labeled radiopharmaceuticals.

The Heart

Two presentations stood out because they illustrate important principles. The first is the development of a ^{99m}Tc tracer for imaging hypoxia with a ^{99m}Tc analogue of metronidazole (#1245). This tracer can reveal hypoxia in the heart as well as in oncology. The authors bound the fluorometronidazole with the N2/S2 EC chelate (Fig. 29).

The second is the development of ^{99m}Tc aprotinin, which makes it possible to image amyloid in the heart (#464; Fig. 30).

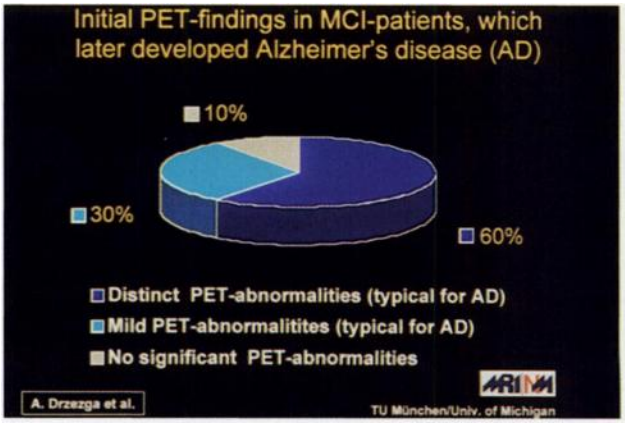

Figure 27. Initial FDG PET predicted subsequent development of Alzheimer's disease in patients with minor memory deficits (#250).

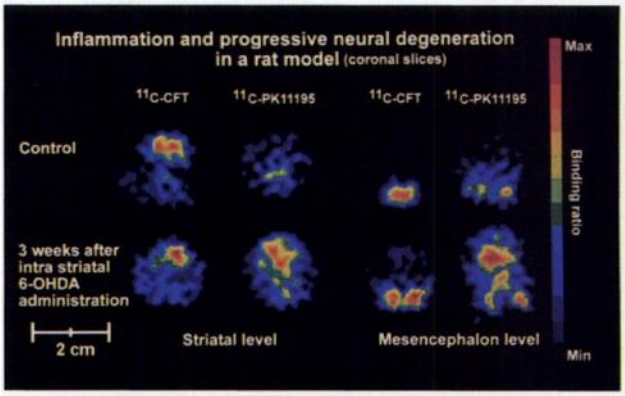

Figure 28. Example of small animal scanning (#407).

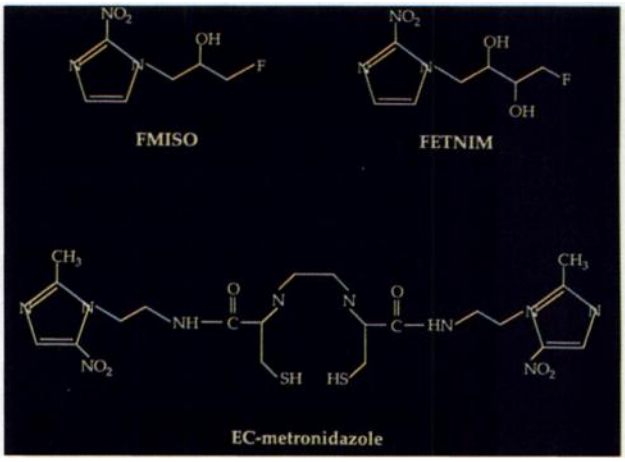

Figure 29. Structure of the chelate that binds the metronidazole groups for imaging hypoxia (#1245).

Two inadequately implemented opportunities present themselves in nuclear cardiology. First is the increasing use of functional and molecular imaging in the care of patients coming to emergency rooms with chest pain. In the United States, this accounts for more than 5 million visits per year.

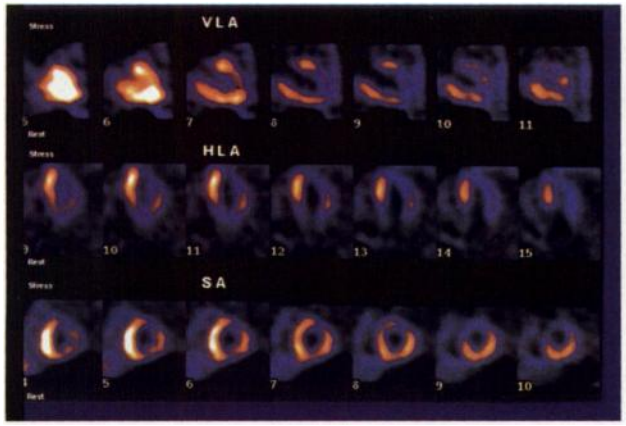

Figure 30. Amyloid involvement of the heart revealed directly with ^{99m}Tc aprotinin (#464).

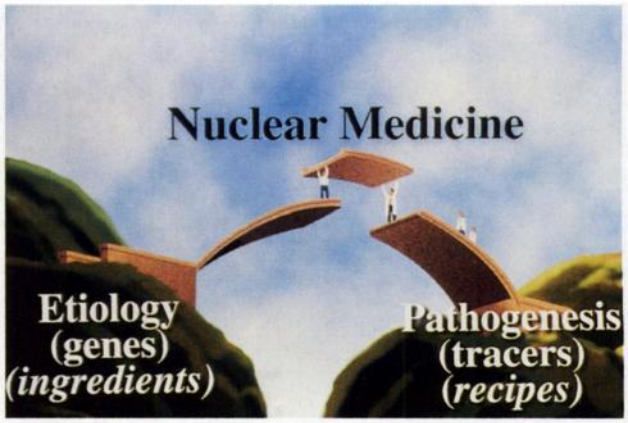

Figure 31. Abnormal genes can cause disease (etiology). Abnormal processes comprise pathogenesis, which can be examined by functional and molecular imaging. Genes can be thought of as the ingredients of disease; pathogenesis can be thought of as the recipe for disease. A 2-way bridge connects them.

More than a third of the patients with chest pain admitted to coronary care units do not have coronary artery disease. Of the 7% who are sent home with undetected coronary artery disease, many suffer severe consequences. Singh et al. from Hahnemann University, Philadelphia, reported the excellent prognosis of patients shown to have normal perfusion scans after hospitalization for chest pain (#724). Although many hospitals have protocols for chest pain patients that include nuclear cardiology, most do not. Yoon, from Korea, reminds us that we are still doctors and should not hesitate to perform physical examinations of our patients. He reported that the presence of diabetic retinopathy doubles the chances of an abnormal ^{201}Tl study (#6).

Another area of increasing interest is assessment of the sympathetic innervation of the heart, which bears on both early detection of ventricular disease and the problem of sudden death. Taki et al., from Kanasawa, Japan, detected cardiac sympathetic denervation with ^{123}I-MIBG imaging in patients with Parkinson's disease who had no cardiac symptoms and normal cardiac function (#193). Gokcora et al. from Ankara, Turkey, examined patients with orthostatic hypotension and found differences in MIBG uptake in patients suffering from vasovagal syncope compared with controls, who did not develop orthostatic hypotension when tilted (#191). Matheja et al., from Munster, Germany, examined patients with ST segment elevations despite having apparently normal hearts (Brugada syndrome), who were at risk of life-threatening arrhythmias (#190). They found local regions with uptake of MIBG, again suggesting focal autonomic dysfunction. Agostini et al., from Caen, France, observed reduced MIBG uptake in all myocardial walls except the septum, in patients with myotonic dystrophy (#194). Further investigation of cardiac innervation clearly seems indicated.

Coronary Artery Restenosis

More than 500,000 coronary angioplasty procedures are performed in the United States every year. About 40% of them result in subsequent restenosis, which costs more than $1 billion every year, to say nothing of the associated morbidity. Evidence indicates that radiation to the arterial wall at a dose between 2000 and 3000 rads can reduce the restenosis rate to less than 5%. Until now, ^{186}Re has been used, either as a solution in intracoronary balloons or incorporated into stents (#27). Other methods include ^{192}Ir ribbon seeds and ^{32}P stents. An attractive candidate is ^{188}Re, which, as stated previously, can be obtained from a generator with a 69-d half-life and is therefore relatively inexpensive.

Molecular Genetics

Molecular genetics is a whole new way of looking at medicine. Functional and molecular imaging is a whole new way to look at genetics (Fig. 31).

Most diseases, for example, Parkinson's and Alzheimer's disease, are heterogeneous. Molecular characterization, such as measurement of the dopamine transporter or the distribution of hexokinase in the brain, can be used to produce more homogeneous groups of patients, which can form the basis for hunting for abnormal genes.

The famous geneticist, Sidney Brenner, has stated, "We have now accumulated a large number of sequences from a variety of organism. The problem is, nobody knows what they do." Functional and molecular imaging can help determine what specific genes and networks of genes do.

The Age of Communication

We frequently read how expensive picture archiving (PAC) systems are and conclude that they are not for us. Truong and colleagues from UCLA provide a model for all of us, illustrating what should be implemented immediately by every nuclear medicine department (#867). A diagram of the components of

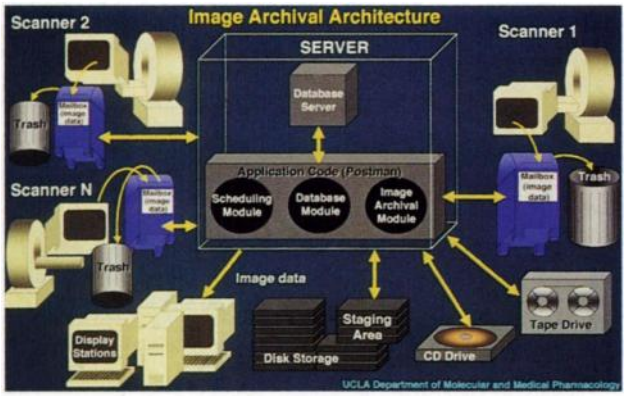

Figure 32. The exemplary imaging data storage and distribution system at the University of California at Los Angeles based on the Internet (#867).

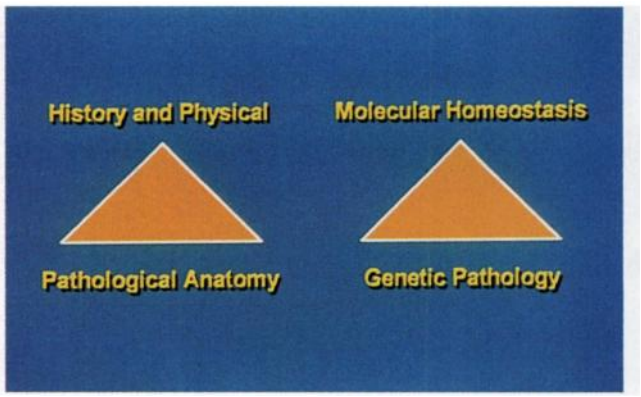

Figure 33. These 2 triangles are combining to form a new paradigm for the practice of medicine.

their system is shown in Figure 32. Using the Internet (JAVA), they have developed an automated computer system that extends from acquisition of the imaging and other data to distributing the results to all parties involved in the patient's care.

The entire archival procedure is controlled centrally by a "postman" program residing in a server connected via Ethernet to the computers of all the departmental imaging devices of multiple manufacturers. All data from 12 scanners are extracted and inserted into a database that is available throughout the hospital. The system has been in operation for 2 years.

In the next few years, most nuclear medicine departments will be able to be connected in a worldwide nuclear medicine "community" network. The SNM will be involved in its creation.

The Future

The practice of medicine is still based primarily on the patient's history of his/her illness, the physical examination, tests of available body fluids, anatomically oriented images, and organ, tissue, and cellular pathology. Today, molecular homeostasis is being assessed by functional and molecular imaging, based on the use of perturbations, or stress tests. Molecular genetics has joined pathophysiology as the new foundation of medicine (Fig. 33). The presentations at the meeting provide strong evidence that the future of nuclear medicine has never been brighter. All that is needed is our continuing wholehearted commitment.