# Scientific Highlights of the EANM Congress 1991

*The European Association of Nuclear Medicine Congress took place from September 1-5 in Vienna, Austria. The following report includes excerpts from a commentary by Prof. Dr. Gerhard F. Fueger, division of nuclear medicine, Central Radiology Institute, Graz, Austria, on the scientific highlights of the meeting and also draws from the abstracts published in volume 18, number 6 of the* European Journal of Nuclear Medicine. *(The letters and numbers in parentheses designate abstracts in that publication.)*


Photo: Lisa Bauso

*The Austria Center of Vienna, site of the European Association of Nuclear Medicine Congress 1991.*

OVER 3,000 NUCLEAR MEDicine physicians, technologists, and exhibitors from Europe, Asia, and the Americas gathered in Vienna for the European Association of Nuclear Medicine Congress. Of the nearly 700 papers and posters presented, highlights lecturer Prof. Dr. Gerhard F. Fueger singled out 24 that illustrate the advance of nuclear medicine on many fronts, from sweeping multicenter trials demonstrating the effectiveness of new radiopharmaceuticals and techniques to experiments uncovering mechanisms of illnesses such as epilepsy, diabetes, and heart disease. One research team reported the surprising use of a monoclonal antibody fragment to "vaccinate" patients for improved survival against cancer.

### Multicenter Studies Praised

Dr. Fueger made a point of encouraging investigators to conduct further long term, multicenter studies, which he called scientific and technical feats of special merit. "By their very nature, such studies are laborious and time consuming and require a high level of organization and competence," he said.

The first of two multicenter studies to draw Dr. Fueger's particular attention, entitled "Captopril Radionuclide Test in Renovascular Hypertension: Final Results of the European Multicentre Study," reported on 424 patients, 229 with renal artery stenosis and 195 without (FP-5D0-5). The study, by Fommei and colleagues from the CNR Institute of Clinical Physiology, Pisa, Italy was presented on behalf of the CRT European Multicentre Study Group.

The second report, "Exercise Tc99m-Teboroxime Cardiac SPECT: Results of a Canadian Multicentre Trial," by Burns and colleagues from The Toronto Hospital, Vancouver General Hospital, Victoria General Hospital, Ottawa Heart Institute, and Squibb Diagnostics Canada, compared the results obtained in 66 patients who underwent exercise SPECT imaging with technetium-99m ($^{99m}$Tc) teboroxime and with thallium-201 ($^{201}$Tl) in the space of two weeks (FP-3D1-5). The researchers concluded that the $^{99m}$Tc agent yields diagnostic information comparable to $^{201}$Tl.

### Techniques and Devices

At least 34 papers described new devices, clinical software, the physics and techniques of imaging, and quantitation of system performance. A notable example identified by Dr. Fueger was "Quality Assurance of Nuclear Medicine Software: The Purpose and Scope of Cost B2" by Britton and colleagues of St. Bartholomew's Hospital in London (FP-2H2-6). In this paper, Dr. Fueger proposed that nuclear medicine provides a microcosm for the study of quality control, quality assurance, and cost analysis confronted by medicine in general.

Another technically oriented paper Dr. Fueger noted was "Compton Scatter Correction by Spectral Iterative De-

Photo: Lisa Bauso

*Karlskirche, an example of Vienna's architecture.*

convolution [SID]" from Ben Younes and co-investigators from Besançon, France (FP-3H1-1A). "These are papers that need attention," said Dr. Fueger. "We have to sit down when we get back home and look at these closer because this is where the progress in our technique will come from—the quality of our work is supported by the quality of our measurements, the quality and the use of the instruments."

### Absolute Relief from Pain

Beyond progress in diagnostic measurement, Dr. Fueger was also able to report advances in easing the often intractable pain from bone metastases. "To alleviate pain," he said, "is certainly one of the foremost tasks and responsibilities of the physician." It is now possible to alleviate pain in patients with bone metastases by the administration of strontium ($^{89}$Sr) chloride, yttrium ($^{90}$Y) citrate, or rhenium ($^{186}$Re) HEDP.

Lewington and her co-workers at Southampton General Hospital, England, have studied a large number of patients with prostate carcinoma. She treated 59 with $^{89}$Sr and 55 by external beam radiation therapy. Pain relief was accomplished in 54% of the patients treated with $^{89}$Sr compared to 33% of the patients who received external radiation therapy. In addition, 52 of the 59 patients given radiostrontium were alive at three months; of 55 treated by wide-field radiation therapy, only 35 survived. Dr. Lewington concluded that $^{89}$Sr chloride is an effective alternative to external wide field radiation therapy and that it may even prevent the development of pain and newly developing metastases. The researchers provided data on the effect of $^{89}$Sr therapy on platelet count as a measure of bone marrow function. The decrease in bone marrow activity was minimal and reversible, occurring approximately six weeks after therapy (FP-2G2-2).

Odavic and colleagues from the Institute of Nuclear Medicine in Beograd, Yugoslavia used $^{89}$Sr chloride to treat 50 patients with various forms of cancer; 20 with advanced prostatic carcinoma, 6 cancers of the breast, 14 of the lung, 7 colorectal carcinomas, and 3 renal carcinoma. He too found dramatic relief of pain in about half of the patients; only about 15% did not respond (FP-2G2-4).

In Berlin, Buchali and researchers at Humboldt University looked at the relationship between $^{89}$Sr chloride and $^{90}$Y citrate in 17 patients with prostatic metastases to bone. Pain relief succeeded in about half of the patients. At 21 months, survival was 3 out of 7 with $^{89}$Sr, and 7 out of 10 with $^{90}$Y (FP-2G2- 3). Although preliminary, and backed by only a small group of patients, the authors conclude that yttrium may be the better agent. Nevertheless, Dr. Fueger reminded the audience, "you can alleviate pain in 50% of the patients." The selection of one agent over another "is a minor controversy," he said, "which isn't really much of a controversy at all—just trying to find the best method."

Researchers from The Netherlands presented results using $^{186}$Re HEDP in patients with breast or prostate cancer. DeKlerk of University Hospital in Utrecht reported absolute pain relief with one injection in 43% of the patients, and satisfactory relief in another 43%. In only 2 out of 14, or about 15%, was there no response (FP-2G2-1). There was a "flare reaction," Dr. Fueger noted, but bone marrow suppression was transient, and occurred between the fourth and fifth week. The dose, up to 15 mCi (1850 MBq), was safe and effective. Dr. Fueger pointed out the similarity of the whole-body distribution of $^{186}$Re and $^{99m}$Tc HEDP. "It's very hard for us to differentiate the rhenium from technetium," he said. He concluded that "the message is quite clear: we do have a means to alleviate pain."

### Immunotherapy for Improved Survival

Dr. Fueger was astonished by the success reported by Oehr and colleagues, University of Bonn, Germany, who found improved survival in patients with advanced ovarian carcinoma after repeated immunoscintigraphy between 1985 and 1990. The 14 women with stage three or four ovarian carcinoma received multiple injections of F(ab)2 antibody fragments labeled with iodine-131 ($^{131}$I). The researchers detected an apparent rise in an in vitro tumor marker antigen in five patients, and found the rise to be

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due to anti-idiotypic antibodies induced by the prior monoclonal antibody injections for immunoscintigraphy. Most strikingly, all five patients survived significantly longer than those who received no antibody infusion but otherwise the same treatment (FP-2G2-6). Dr. Fueger reiterated: "To me this is the absolutely most astounding result that was presented during this meeting."

From our vantage in this age of monoclonal antibodies and positron emission tomography, Dr. Fueger looked back in time and reminisced about the relationship between data collecting, quantitation of observations, and the understanding of physiologic processes exemplified even in as simple a procedure as taking the pulse. Nuclear medicine, he said, will continue to provide measurements of physiology for medicine to continue to gain insights into health and disease.

### Cardiac PET Studies

Applying PET imaging to look at the mechanics of heart disease, Czernin and co-researchers from the University of California at Los Angeles School of Medicine, compared and quantified myocardial perfusion with nitrogen-13 ($^{13}$N) ammonia, and metabolism with fluorine-18-2-deoxyglucose ($^{18}$F-FDG) imaging in 22 patients within four days after the onset of clinical acute myocardial infarction (FP-201-3). The researchers also performed carbon-11 ($^{11}$C) acetate studies. They defined PET criteria for ischemia as decreased ammonia distribution accompanied by increased glucose metabolism. For infarction, they looked for decreases in both perfusion and glucose metabolism (Figure 1).

In the normal myocardial segments, blood flow was 0.84 ± 0.20 ml/g/min; ischemic segments were 0.57 ± 0.20 ml/g/min; and infarcted segments were 0.32 ± 0.12 ml/g/min. These differences were statistically significant. Acetate utilization (k mono/min) was 0.063 ± 0.012 in normals, and was reduced in ischemia (0.055 ± 0.01) and infarcted segments (0.033 ± 0.01). Myocardial glucose utilization was unchanged between normal and ischemic myocardial segments. The value in infarcted segments was 65% of the normal value. The ratio of the percentage of myocardial glucose utilization to myocardial blood flow was increased in ischemia (1.70 ± 0.7) compared to the normal myocardial segments (1.2 ±0.30) and infarcted segments (1.1 ± 0.30).

The researchers classified 51 of 103 myocardial segments, or 33%, as hypoperfused and the remainder as normal. They found that 29, or 57%, of the hypoperfused segments were infarcted and 22, or 43%, were ischemic.

Dr. Czernin and colleagues observed an increase in the ratio of acetate utilization to myocardial blood flow in ischemic and infarcted segments compared to normal, suggesting "increased oxygen extraction in the low flow range," noted Dr. Fueger. The authors concluded that the PET perfusion and metabolism data demonstrate considerable viable tissue within zones of so-called clinical infarction.

### Investigating Seizures

Bartenstein reported on the use of PET and $^{11}$C-diprenorphine to study the type of seizures known as "absence seizures." Eight patients with a generalized epilepsy and eight normal controls underwent PET studies of cerebral blood flow measures with oxygen-15 ($^{15}$O) carbon

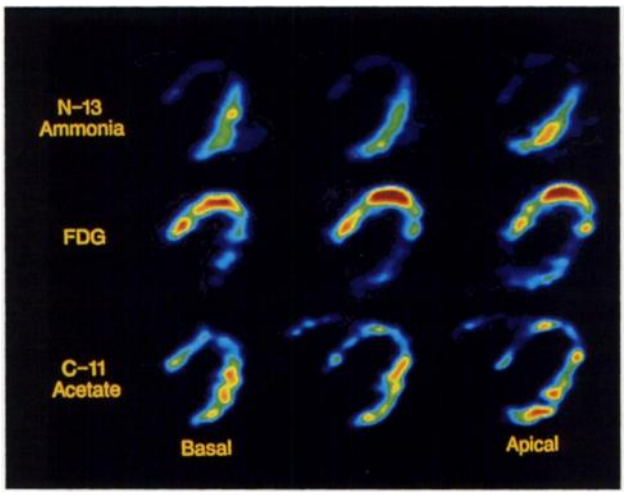


***Figure 1: Midventricular transaxial N-13 ammonia, F-18 deoxyglucose, and early C-11 acetate images in a patient with an acute anteroseptal Q-wave infarction. With $NH_3$, a large perfusion defect is identified in the anterior wall and septum. Prominent uptake of FDG in this region indicates metabolic viability. Early C-11 acetate images are similar to N-13 ammonia perfusion images.***

Courtesy J. Czernin, MD, UCLA

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dioxide and the opioid receptor ligand $^{11}$C-diprenorphine. The researchers dynamically recorded ligand distribution for 90 minutes. The subjects hyperventilated to initiate seizure activity 30-40 minutes after injection of the ligand. EEG readings confirmed that absences occurred in the seizure group with generalized spike-wave discharges during 10-51% of the activation period.

Regional cerebral blood flow did not change in either the normal or seizure group of subjects. Following seizures, washout of the labeled ligand from areas of the brain stem, and posterior cingulate and lateral parietal cortex increased significantly. Interpreting this increased washout to indicate the local release of endogenous opioids, the authors suggest that the release of opioids during serial absences may have a role in suppression of generalized absences (FP-4D1-1). The work involved investigators from Hammersmith Hospital and the Institute of Neurology in London, England, and the University of Munster, Germany.

### Insulin Kinetics

Signore and co-workers from the University of Rome, Italy, evaluated the kinetics of $^{123}$I-iodoinsulin by gamma camera recording of hepatic activity in eight normal subjects, eight with insulin dependent diabetes mellitus (type 1), and eight non-insulin dependant diabetic patients (type 2). The investigators generated time-activity curves over the liver and heart, corrected for confounding factors, and analyzed the curves with a two compartment model. They demonstrated normal insulin receptor binding kinetics but a delayed post-binding insulin metabolism in type 2 diabetic patients (FP-4G1-2).

Dr. Fueger highlighted another paper on carbohydrate metabolism—that of Burchert and co-authors from Medical School of Hannover, Germany, who studied glucose utilization of skeletal muscle in normal volunteers and six patients with cirrhosis (FP-5H0-2). Using $^{18}$F-FDG and PET, they demonstrated impaired glucose utilization in the cirrhotic group (4.4 $\mu$mol/100 g/min) compared to normal subjects (7.5 $\mu$mol/100 g/min).

In another PET study noted by Dr. Fueger, Inaba and his co-workers in Kyoto, Japan found that in carcinoma of the prostate blood flow was very much increased to 33.8 ± 18.6 ml/min/100 g. In benign prostatic hypertrophy, the value was lower (17.7 ± 5.2 ml/min/100 g), and normal patients had a still lower measured prostate blood flow (11.6 ± 5.0 ml/min/100 g). The researchers also found that normal prostatic blood flow decreases with age (FP-2H3-5). "I think this is an enormously important contribution," said Dr. Fueger, "because it allows us to standardize Doppler sonography of the prostate [possibly] to make early diagnosis of carcinoma."

Studying colorectal cancer, A. Dimitrakopoulou and others at the German Cancer Research Center in Heidelberg used PET and $^{18}$F-labeled 5-fluorouracil (5-FU) to relate the response of colorectal metastases after 5-FU therapy to the amount of 5-FU delivered to tumors. Uptake of the labeled compound by the tumors varied considerably and was indicative of the response to the subsequent therapy: the greater the uptake of tracer prior to therapy, the greater the reduction in tumor volume after therapy, which was determined by repeated computed tomography (CT) examinations over a three to nine month interval (FP-2G3-6).

In the realm of cardiology, H. Feistel and colleagues from Erlangen, Germany used 123I-MIBG and SPECT imaging to demonstrate defects in sympathetic innervation of the inferior and septal wall of the left ventricle in patients with long QT syndrome, characterized by dangerous heart arrhythmias, and the close relatives of these patients. Based on the demonstration by 123I-MIBG imaging of a specific defect in family members, the researchers concluded that long QT syndrome may follow an autosomal dominant mode of inheritance (FP-3D2-1).

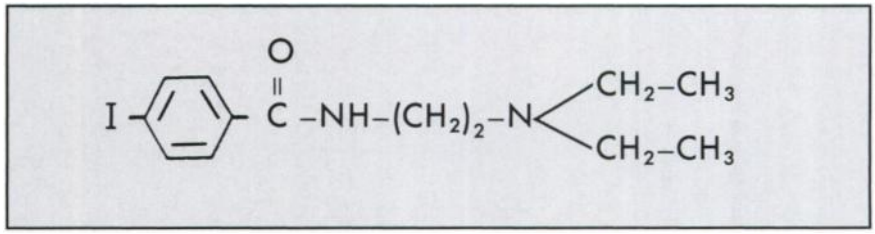


*Figure 2: An iodobenzamide compound.*

Krois and colleagues from Vienna used monoclonal antibodies to granulocytes to image pancreatitis. They obtained true positive images in 16 of 19 patients characterized as having severe pancreatitis. Surgical biopsy confirmed the findings (FP-3H3-4).

Aside from the diagnostic use of SPECT, some researchers demonstrated the prognostic capabilities of the mo-

dality. Guillet and co-workers from Centre Hospitalier, Agen, France studied the use of $^{123}$I-isopropyl amphetamine brain SPECT to predict brain disfunction in neonates as the 255 infants in the study cohort developed into school children (FP-4G3-5). Compared to EEG, evoked potentials, or clinical evaluation of neonates, "the predictive function of $^{123}$I-isopropyl amphetamine SPECT [findings] is very high, and is by far the superior measure," Dr. Fueger said. "The positive predictive value and the negative predictive values surpass by far any of the other techniques that are used to study impairment and the development of brain damage."

To study the development of Duchenne's muscular dystrophy, Scopinaro and others at the University of Rome, Italy determined the ratio of myocardial muscle to skeletal muscle uptake of $^{99m}$Tc-MIBI in 45 patients with the disease. The investigators compared the findings to results from five normal adult subjects, eight children (aged 1-12) with congenital heart disease, and ten patients with coronary artery disease. In the Duchenne's population, the heart-to-skeletal muscle ratio increased slightly with age (FP-3G3-6).

Kotzerke and investigators of Zentralinstitut fur Kernforschung, Rossendorf, Germany presented a new serum albumen derived microsphere to study mucociliar function. They showed that the peripheral and the central clearance of their particle are roughly equal, "which is very effective for studying mucociliar clearance." Dr. Fueger remarked. The researchers showed that in normal function, global clearance was 53% (38-65) in the first 45 minutes. In decreased ciliar function, initial clearance was 17% (7-25). After 24 hours, the particle is completely cleared from the lungs in normal cases. But when mucociliar transport is impaired there is about 25-84% retention at 24 hours, on average more than half of the initial inhaled dose (FP-4G3-4). Dr. Fueger said, "This is a method to physiologically follow children with chronic airway disease."

Of the many presentations of new or

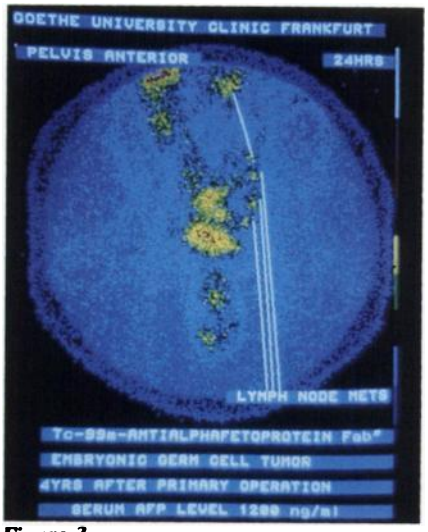


***Figure 3***
Courtesy of D.M. Goldenberg, MD, CMMI, Newark, NJ

improved radiopharmaceuticals, Dr. Fueger chose one representative of this vital area of research. Moreau and Michelot from INSERM, Nice, France and colleagues evaluated the use of iodobenzamide compounds in the diagnosis and treatment of malignant melanoma (Figure 2). They showed the usefulness of an $^{123}$I-labeled benzamide derivative for diagnostic imaging. Another benzamide derivative had pharmacokinetics and tissue distribution characteristics suitable for labeling with $^{131}$I to use as therapeutic agent (FP-213-6 and FP-3G2-5).

At the University of Vienna, Austria, Schatten and co-investigators used $^{123}$I-labeled monoclonal antibodies to epidermal growth factor to perform lymphoscintigraphy in patients with cervical cancer. Following injections into the web space of each foot, the researches obtained images of the pelvis and legs in 14 high-risk patients. In 8 of 11 positive scans, biopsy or other imaging technique confirmed the findings (FP-2G3-3). The results, though promising, require longer follow-up of clinical outcome.

### Imaging Tumors

Researchers at the meeting reported the first clinical results with a $^{99m}$Tc anti-AFP monoclonal antibody in patients with germ cell and liver tumors (FP-2G3-5). Dr. Fueger highlighted this work by Baum and colleagues at Goethe University Medical Center, Frankfurt/Main, Germany, and CMMI in Newark, New Jersey. The antibody imaging technique enabled the researchers to clearly visualize mesenteric lymph node metastases ten months prior to CAT scan diagnosis and surgical confirmation (Figure 3).

In view of the results using monoclonal antibodies, Dr. Fueger reflected on the necessity of obtaining data to make diagnoses and to understand disease. The data, he said, "must be correct methodologically" and the observation "appropriate." In an aside, he recalled how optimistic the nuclear medicine community had been about lymphoscintigraphy, and indeed, how enthusiastic radiologists have been about CT and magnetic resonance imaging (MRI) of tumor involved lymph nodes. A recent multicenter study of patients with various tumors compared CT, MRI, and contrast lymphography and found that the latter had the highest sensitivity (70%) and specificity (73%). Of course, lymphoscintigraphy with labeled monoclonal antibodies adds another dimension to this issue.

Before closing, Dr. Fueger noted that about a dozen European countries are trying to change their structures to pay for medical services. "Our goal," he said, "must be to come up with a decisive statement [confirming that] our results can guide therapy. Nuclear medicine should be the technique that tells the clinician [that] a pathophysiological disorder is still manifest [or]...that it is safe now to discontinue whatever therapeutic regimen we were using." With confidence and armed with the fundamental power of the tracer principle, he predicted, the nuclear medicine community will face the further challenges of diagnosis and treatment of human illness. "I think that the tracers are really what give us our strength," he said, "and we should trust them."

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