Scientific Highlights of the European Association of Nuclear Medicine Congress—1989

Nuclear Medicine Continues Its Innovative Development

"From the standpoint of the purpose of the investigation... diagnostic studies remained the most frequent indication, but evaluation of [both] therapy and prognosis... accounted for [an equal number of] studies."

The dynamism of nuclear medicine was identified as the guarantee of its future by Dr. Rigo during his highlights presentation at the 1989 Congress of the European Association of Nuclear Medicine, during which 2,900 participants gathered in Strasbourg, France, and close to 750 abstracts from all over the world were presented.

Cardiovascular nuclear medicine presentations were most numerous, followed by oncology, said Dr. Rigo, adding that this reflects "the growing importance and development of radioimmunoimaging." Oncology was followed by basic sciences including instrumentation, radioassay, and radiopharmaceuticals, "a reflection of the fact that progress in nuclear medicine has mainly come about through the development of chemistry and radiopharmaceuticals," Dr. Rigo noted.

Stanley J. Goldsmith, MD, associate editor, Newsline, *has excerpted the following summary from the Highlights Session of the European Association of Nuclear Medicine (EANM) Congress — 1989, delivered by Pierre Rigo, MD, Liège, Belgium.*

Number of Abstracts Received by The EANM's Organizing Committee, by Continent

Europe	836
North America	87
Asia	46
South America	11
Africa	10
Australia	9

There were a relatively small number of papers in neurology. "PET [positron emission tomography] presentations in that field were particularly lacking....The primary focus of the 58 PET presentations and tracers was...clinical, with 33 papers [in that area]," said Dr. Rigo. Only three papers dealt with experimental aspects of nuclear medicine, while there were 11 papers presented in each of the areas of radiopharmaceutical developments and instrumentation. Fluorine-18 was the most widely used PET tracer, as it was earlier this year at The Society of Nuclear Medicine (SNM) Annual Meeting.

"From the standpoint of the purpose of the investigation," Dr. Rigo said, "diagnostic studies remained the most frequent indication, but evaluation of [both] therapy and prognosis...accounted for [an equal number of] studies."

In the area of cardiology, myocardial blood flow was the subject of 79 presentations, followed by ventricular function — 47, metabolism — 19, and receptors — 3. Categorized by disease entity, 20 studies were primarily concerned with defining viability or necrosis in jeopardized myocardium, 5 were concerned with rejection, and 7 with thrombosis. Dr. Rigo underscored the growing importance of tomography in nuclear cardiology, with 30 presentations on single photon emission computed tomography (SPECT) and 40 on PET techniques.

Myocardial Blood Flow Studies

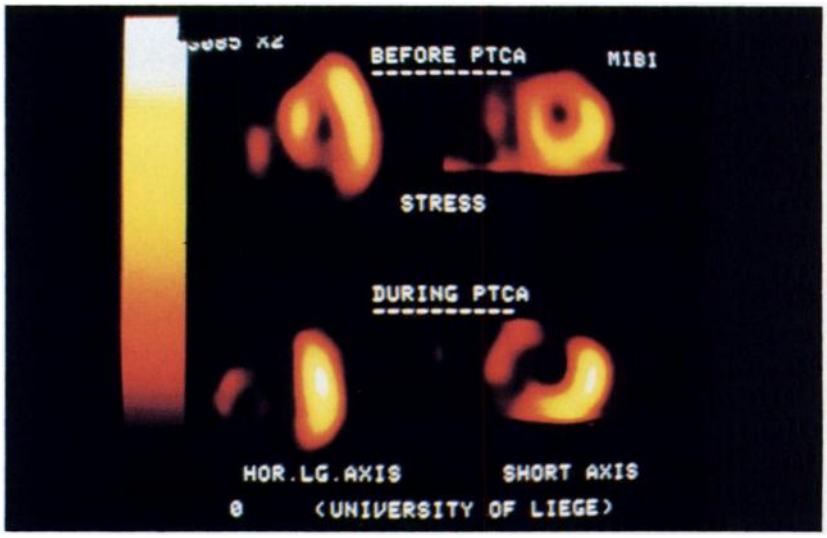
Dr. Rigo noted that many tracers have been used in myocardial blood flow studies. "Oxygen-15 water, which is freely diffusable across myocardial membranes, has many theoretical advantages," he said, "but

spillover of counts from the left ventricular cavity into the myocardium limits the applicability of the technique for intervention studies that usually [also] require carbon monoxide [labeled red blood cells for] blood pool subtraction."

Dr. Rigo described alternative techniques to perform blood flow studies presented by Oda et al. (Ab. No.165)* from Kyoto, Japan and Cuocolo et al. from the National Institutes of Health in Bethesda, Maryland (No.164). "Cuocolo includes the spillover collection in the convolution equation for myocardial blood flow. Their technique yields accurate myocardial blood flow measurements but does not produce myocardial blood flow images." By contrast, Oda "applies factorial analysis to extract the myocardial component images... which...clearly differentiates [myocardium] from both cardiac cavities ...and the lungs. Myocardial factor images also correlate very well with myocardial images obtained by subtraction technique."

Dr. Rigo reported a renewed interest in rubidium-82, a generator-produced positron emitter with a half-life of 75 seconds. In studies by Marwick from Cleveland, Ohio (No. 71) and Stewart from Ann Arbor, Michigan (No. 166), he noted, "rubidium appears more sensitive and...more specific than thallium for the detection of ischemia....thallium probably underestimates viability."

Mueller-Brand from Basel, Switzerland (No. 68) and Larock from Liège (No. 305) studied patients with single vessel disease and reversible perfusion defects before and after percutaneous transluminal coronary angioplasty (PTCA). "During PTCA," noted Dr. Rigo, "flow



^{99m}Tc MIBI during PTCA allows evaluation of myocardial perfusion. This example compares pre-intervention exercise-induced ischemia with more extensive area at risk defined during balloon dilatation **(Abstract No. 305).**

obstruction produced defects in the majority of patients. No dependence on the duration of balloon occlusion was observed except [in the case of] very short occlusion - less than 30 seconds. Ischemia was not observed in four of seven patients with collaterals. The size of the prePTCA defect...was smaller and not related to the size of the ischemic defect during the occlusion," as evaluated in nine patients before PTCA and during PTCA. According to Dr. Rigo, "these studies suggest that exercise ischemia cannot predict the area at risk."

The use of ^{18}F fluorodeoxyglucose (FDG) to detect residual myocardial blood flow to identify ischemic but viable myocardium, (as proposed by Schelbert) was the subject of seven presentations — by Oda from Kyoto (No. 189), Henrich from Jülich, Federal Republic of Germany (FRG) (No. 190), De Landsheere from Liège (No. 191), Buck from Zurich, Switzerland (No. 192), Buell from Aachen, FRG (No.167), Höflin from Bern, Switzerland (No. 193), and Ahonen from Turku, Finland (No. 194), including one study (from Bern) performed with a camera fitted with a seven pin hole collimator. These studies are based upon the recognition that ischemic myocardium preferentially utilizes glucose.

In the study from De Landsheere (No. 191), Dr. Rigo noted that "patients with chronic or acute myocardial infarction and complete occlusions had [FDG] and perfusion defects. In patients with recent myocardial infarctions, FDG uptake and flow were dependent on previous therapy and severity of residual stenosis. After thrombolysis, in patients without residual stenosis, flow was higher and [the] FDG to flow ratio low, demonstrating the absence of residual ischemia." By contrast, in patients with an open vessel but a persistent high grade stenosis, he noted that "flow was low (37% of normal), and FDG uptake high (68%), with a high [FDG] to flow ratio of 1.84, indicating persistence of flow deficit and ischemia."

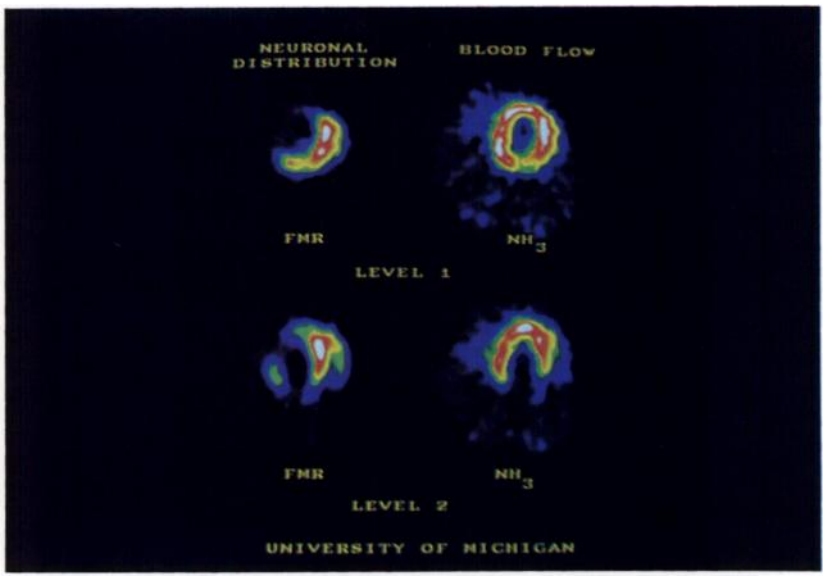
Several researchers used technetium-99m MIBI, injected before and after reperfusion therapy to identify myocardial salvage, reported Dr. Rigo. Faraggi et al. from Clichy,

*Subsequent numbers refer to abstract numbers in the Abstracts of the European Association of Nuclear Medicine Congress — 1989.

France (No. 2), Bisi from Florence, Italy (No. 4), and Varetto from Turin, Italy (No. 3), studied patients shortly after the onset of symptoms. "[^{99m}Tc] MIBI is injected before initiation of therapy. . . . imaging one hour later still showed the pretreatment uptake, even after thrombolysis." A repeat scan was performed three days later. These repeat studies, according to Dr. Rigo, demonstrated "a patient with a very large anteroseptal perfusion defect that's almost normalized after [thrombolytic] therapy." With MIBI, it is possible to inject the tracer and proceed with thrombolytic therapy and evaluate the pretreatment perfusion sometime later.

"Indium labeled antimyosin [studies are] frequently added to a perfusion [study] to [further] delineate the extent of necrosis and of myocardial salvage," reported Dr. Rigo. In a study from Göttingen, FRG, said Dr. Rigo, "Munz et al. (No. 195) demonstrated that the uptake of antimyosin antibody not only occurs in the area of necrosis but also in an area which is macrohistochemically reversibly damaged." Dr. Rigo presented slides of a myocardial slice in which the normally perfused myocardium is in one color, the necrotic myocardium in another, and the reversibly ischemic myocardium in a third, to demonstrate that the "infarct size may be overestimated by use of antimyosin antibodies alone."

The process of assessing viability is relevant to the evaluation of myocardial fatty acid metabolism, noted Dr. Rigo. ". . . fatty acids . . . sometimes demonstrate uptake in areas of thallium defect," he said, pointing out studies from Grossmann (No. 90) and Henrich (No. 190) from Jülich. In one example he presented, there was some uptake of 15-(ortho-^{123}I-phenyl)-pentadecanoic acid (OPPA) in the inferior segment of the myocardium while there was a thallium defect. "The authors postulate that this preserved metabolic activity may reflect viability and could be a good prognostic [sign]," said Dr. Rigo.



Blood flow and neuronal distribution demonstrated by PET with ^{13}NH and ^{18}F metaraminol. The regional myocardial denervation was obtained by phenol application in these dogs **(Abstract No. 103).**

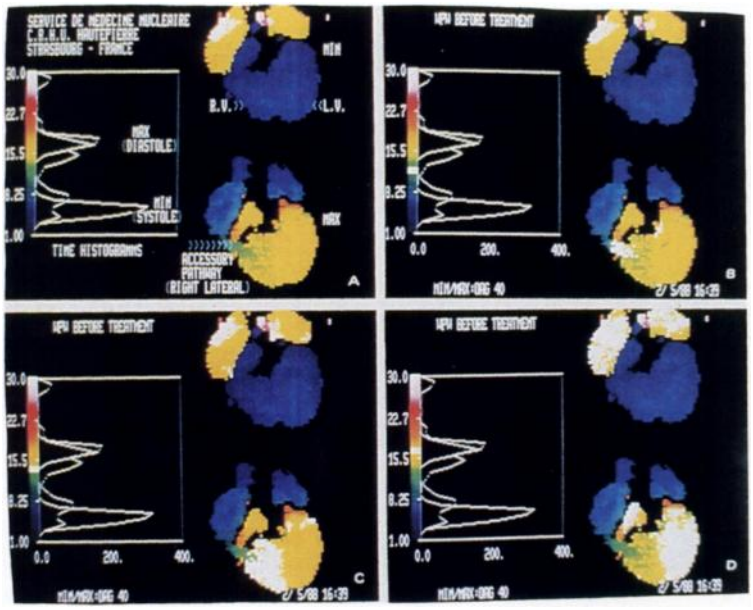
Myocardial Autonomic Control

Dr. Rigo highlighted "important progress . . . made in the area of . . . autonomic control [of the myocardium]." He reported a study from Schwaiger et al. from Ann Arbor (No. 103) demonstrating the value of new PET tracers such as ^{18}F fluorometaraminol [FMR] to assess sympathetic innervation of the heart and to trace norepinephrine uptake and storage in the myocardium. "Serial imaging and quantification using a three compartment tracer kinetic model can reveal marked reduction of tracer uptake after phenol application, [where] perfusion remains normal," he noted. Following an ischemic insult, there is a reduction in FMR uptake beyond the area of infarction demonstrating the greater sensitivity of the adrenergic nerve terminals to ischemia and the greater sensitivity of these tracers to demonstrate ischemia.

Dr. Rigo also noted a study by Bourguignon from Orsay, France (No. 105) assessing adrenergic innervation in patients with congestive and hypertrophic cardiomyopathy, with and without incident of heart failure. "MIBG [metaiodobenzylguanidine] uptake is markedly decreased in congestive cardiomyopathy [and] to a lesser extent in hypertrophic myocardiopathy, especially in patients with heart failure." The group from Grenoble, France (No. 104) reported the pharmacologic interference with MIBI uptake of labetalol and cardiac glycosides.

Ventricular Function Studies

There were 47 presentations on ventricular function studies, most on systolic function but also many on diastolic function. Buell et al. from Aachen (No. 167) studied wall thickening using magnetic resonance imaging (MRI) and correlated it with perfusion and glucose metabolism. "Diastolic function abnormalities are common in patients with hypertension," Dr. Rigo reported, "even in the absence of decreased systolic performance." He highlighted a study by Cuocolo et al. from the NIH (No.



Functional images of ventricular filling and emptying demonstrating alteration of the contraction sequence in a patient with WPW syndrome **(Abstract No. 231).**

229) that aimed to determine whether impaired diastolic function can precede the development of left ventricular hypertrophy. Cuocolo et al. studied 35 hypertensive patients with normal echocardiographic left ventricular mass. Peak filling rate at rest, normalized to end diastolic volume or stroke volume, or expressed as the ratio of peak filling rate to peak ejection rate, was reduced and time to peak filling rate was increased in hypertensive patients as compared to control subjects. "They conclude that diastolic dysfunction in hypertension may precede myocardial hypertrophy and represent the initial clinically detectable manifestation of the effects of hypertension on the left ventricle," reported Dr. Rigo.

Systolic abnormalities may also affect diastolic function, according to Dr. Rigo. "In the case of Wolff-Parkinson-White syndrome, alteration in the contraction sequence leads to alteration in the ventricular relaxation sequence." In a study by Facello et al. from Strasbourg (No. 231), functional images of ventricular filling demonstrated the accessory activation pathway.

"Magnetic resonance imaging also contributes greatly to functional evaluation of the heart, as demonstrated mainly by the group from Cologne," FRG (Sechtem, No. 168, and Theissen, No. 169), said Dr. Rigo.

Dr. Rigo noted that the role of antimyosin antibodies in evaluating transplant rejection was now established.

"The diagnosis of intravascular clot in the arterial, venous, and pulmonary vessels remains a. . .challenge," said Dr. Rigo, noting, however, that several monoclonal antibodies have been reported for these indications. Peltier from Nantes, France, used indium-111 antifibrin monoclonal antibody, in pulmonary embolism (No. 140) and deep vein thrombosis (No. 141). Antifibrin enables detection of thrombolic disease localized in the lower limb. In a 22-hour delayed image, a small thrombosis was seen clearly, while the earlier images identified only increased vascularity.

Broadhurst et al. from Harrow, United Kingdom (No. 142) also reported initial success using ^{99m}Tc antifibrin on patients with deep vein thrombosis.

Peters and Stuttle from London, United Kingdom (Nos. 151, 179) described the use of monovalent FAB fragment specific antibody P 256 to diagnose pulmonary arterial thrombus and venous thrombus, said Dr. Rigo. The results indicate that "monovalent FAB fragments do not produce platelet aggregation, but they produce excellent images of deep vein thrombosis, [and] the pulmonary artery clot, which was associated with pulmonary embolism, in the same patient."

Lavie et al. from Yavne, Israel (No. 117) reported on imaging of the fibrin clot with tissue plasminogen activator during the EANM Congress.

Monoclonal Antibodies

At the EANM Congress, there were 77 presentations involving monoclonal antibodies, 41 in cancer studies, and 36 in other areas. Two of these presentations involved PET imaging.

"Labeled lymphocytes have been used predominantly to detect rejection and monitor x-therapy, but the technique is difficult because of [persistent] high circulating activity," said Dr. Rigo. He described a new approach in which Loufti et al. from London (No. 61) studied the role of ^{111}In antilymphocyte antibodies against T-cell or activated T-cell and of antimajor histocompatibility complex (MHC) Class I or Class II monoclonal antibodies in a rat model. "Anticlass I MHC antibodies in this model recognize only determinants on the donor kidney," noted Dr. Rigo. He displayed images that showed tracer accumulation in the rejected kidney, which had been transplanted four days earlier and injected with anticlass I monoclonal antibody 24 hours before imaging. "In the nonrejecting rat, however," said Dr. Rigo, "[there is no] kidney expression of this antigen and uptake is much

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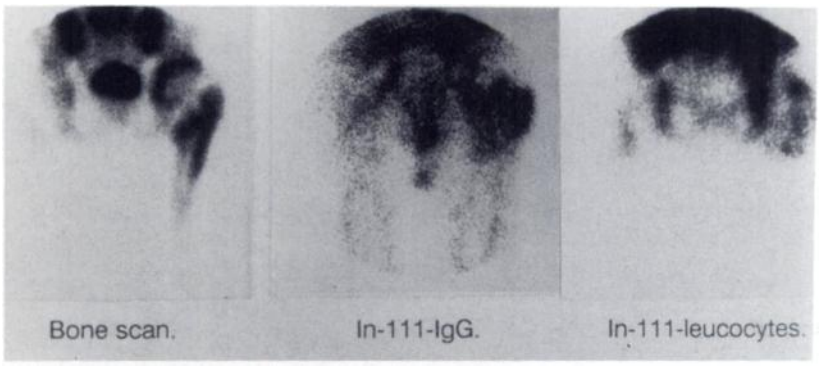
lower."

According to Dr. Rigo, "nonspecific host-reacting antigen is exposed on the cellular membrane of granulocytes in peripheral blood and of mature myelocytes in bone marrow." He noted a study in which Becker et al. from Erlangen, FRG (No. 226) compared in vitro ^{111}In oxine-labeled and in vitro anti-NCA-labeled granulocytes in 15 patients and found a similar disappearance curve, while after in vivo injection, the anti-NCA monoclonal antibody clearance was faster because this antibody bound to bone marrow and spleen cells as well as circulating granulocytes.

Using anti-NCA monoclonal antibodies in vivo, Bischof-Delaloye from Lausanne, Switzerland (No. 222) and Reske from Aachen (No. 227) studied the detection of subacute and chronic infectious foci in bone and soft tissue, noted Dr. Rigo. "They report high specificity and good sensitivity (around 80%) in the group of patients in whom a final diagnosis is [available]. Most images. . .demonstrate a hot spot by four to six hours," said Dr. Rigo. In osteomyelitis, however, he added, "infection was invariably characterized by reduced NCA antibody uptake compared to that of bone marrow."

Dr. Rigo noted that Claessens et al. (No. 224) from Nijmegen, The Netherlands confirmed the work from Fishman et al. (*1*) on the value of non-specific ^{111}In-or ^{99m}Tc-labeled polyclonal human IgG (HIG) for scintigraphic detection of inflammatory sites. In one example, Dr. Rigo described an 81-year-old man who developed a chronic infection after major abdominal surgery, pointing out that the HIG image revealed an abscess, which could also be visualized with ^{111}In leukocyte imaging. In a patient with acquired immunodeficiency syndrome (AIDS) and multiple infections, HIG identified sites of infection as well as gallium.



Scintigraphic detection of inflammation site with ^{111}In labelled polyclonal human gammaglobulin (IgG): Increased activity around both parts of a prothesis, three hours after administration of ^{99m}Tc-MDP (left); normal bone marrow uptake and increased uptake in soft tissue adjacent to lateral side of the prosthesis, 24 hours after administration of ^{111}In leukocytes (right); increased soft tissue uptake, 24 hours after administration of ^{111}In IgG (middle) **(Abstract No. 224).**

"Antibodies to the angiotensin converting enzyme (ACE) localize in the lung on the surface of endothelial cells," noted Dr. Rigo. He reported on a study by Danilov et al. from Moscow, Union of Soviet Socialist Republics (No. 170), which demonstrates "that injury to the lung microvascular endothelium after administration of endotoxin. . .drastically decreased the ACE antibody uptake in the lung compared to uninjured endothelium. Thus, specific accumulation of anti-ACE antibody might serve as a marker for a lung endothelial status."

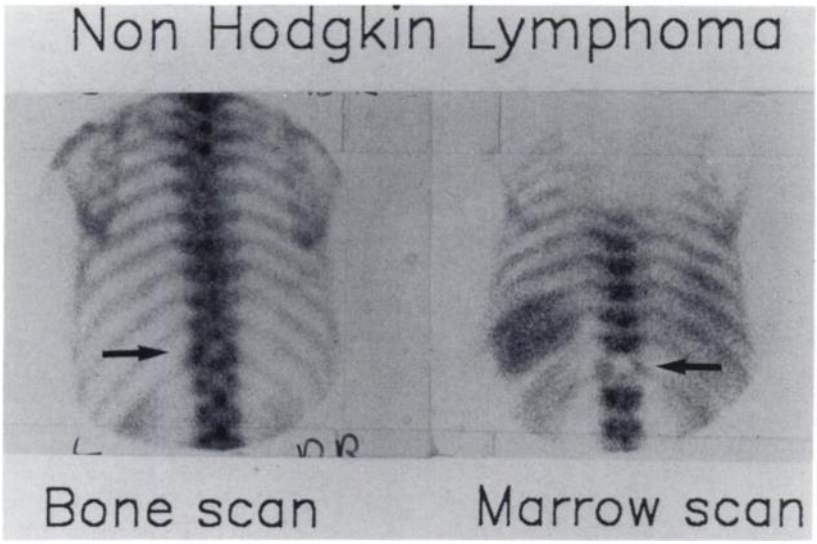
There were 89 presentations in oncology: 41 involved the use of local antibodies, 26 dealt primarily with the use of other tracers, 10 concerned the use of PET in oncology. Monoclonal antibodies were mainly used for colorectal, ovarian, and breast carcinoma and melanoma.

Chetanneau reported the results of European Multicenter Study (No. 159) of 34 retrospective and 48 prospective immunoscintigraphies using indium-labeled anti-CEA or 19-9 in colorectal recurrences. The final diagnosis was established by second surgery, clinical follow-up, or other examinations. Dr. Rigo said that "the sensitivity and specificity of the prospective study to define the number of anatomical sites in the pelvis and extrahepatic abdomen [were] 79% and . . .96% [respectively]. The difficulty of CT [computed tomography] and ultrasound to distinguish pelvic recurrencies from postoperative fibrosis led to the lower sensitivity of these two techniques. The results for immunoscintigraphy were especially good in the pelvis."

Lind et al. from Graz, Austria (No. 160) and Kroiss et al. from Vienna, Austria (No. 163) reported the use of ^{99m}Tc-labeled CEA antibody in the detection of primary and recurrent colorectal carcinoma even in the absence of elevated CEA levels in patients with a normal serum CEA level. Dr. Rigo showed one example from Lind in which a patient with recurrent pelvic tumor had a normal CEA level.

Goldenberg from Warren, New Jersey (No. 110) and Granowska from London (No . 162) presented promising results comparing ^{99m}Tc anti-CEA and anticolumnar cell surface antigen (CCSA) antibodies. "They report that [anti-CCSA] antibodies [had] a three times higher uptake than the anti-CEA antibody," said Dr. Rigo. Goldenberg reported detection of a tumor 0.3 cm in diameter via SPECT imaging.

"Ovarian cancer has been studied using a new indium-labeled mono-



Tc-labeled NCA antibodies used to image bone marrow in a patient with non-Hodgkins lymphoma: The bone marrow abnormality is more clearly seen than the bone scan abnormality **(Abstract No. 202).**

clonal antibody OV-TL 3," said Dr. Rigo. "Claessens from Nijmegen (No. 199) reports that 91% of patients with metastatic lesions identified at surgery were detected by preoperative SPECT imaging. . . .Only 58% of tumor positive sites more than 1 cm were correctly diagnosed."

Diot et al. from Tours, France (No. 171) used D25, a glycopeptide immunomodulator isolated from membrane proteoglycans of a nonpathogenic strain of Klebsiella pneumonia, "to demonstrate the recruitment of macrophages at the early stages of . . . inflammatory lesions," noted Dr. Rigo. D25 must be used as an aerosol labeled with ^{99m}Tc; intravenous injection results in micellar formations, which are rapidly removed by the RES system.

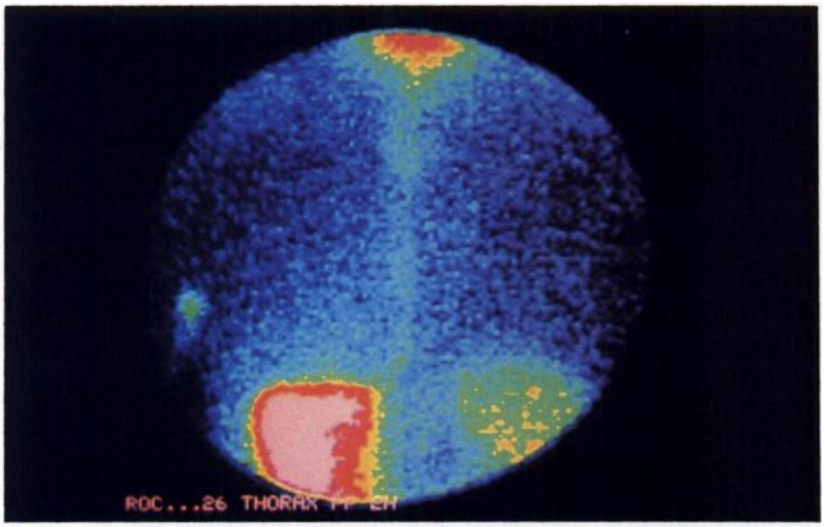
A companion abstract demonstrated use of this technique in lung carcinoma (No. 203).

"In breast carcinoma, as in malignant lymphoma, bone marrow metastases are frequent," noted Dr. Rigo. Reske from Aachen (No. 202) used ^{99m}Tc-labeled NCA antibodies to visualize bone marrow metastases in 15 patients with breast carcinoma and skeletal metastasis and in 10 patients with lymphoma. "NCA antibodies demonstrate homogenous bone marrow activity in the axial and proximal appendicular skeleton of controls," he said. "All patients with breast carcinoma and half the patients with lymphoma had uni- or multi- focal bone marrow defects on the technetium NCA antibody scan" despite some normal bone scans.

The uptake of epithelial growth factor (EGF), a peptide which stimulates tumor cell growth by malignant tissue is related to the degree of malignancy, according to Dr. Rigo. Senekowitsch from Munich, FRG (No. 95) has shown that "iodine-labeled EGF [is a] promising trac er to assess receptor sites in vivo and might become useful to help therapy in breast cancer," noted Dr. Rigo.

"In contrast to EGF, the presence of estrogen receptors and progestin receptors is correlated with the probability of responding to endocrine therapy," said Dr. Rigo. "Verhagen from Groningen, The Netherlands (No. 23) labeled norprogesterone with ^{18}F and used this tracer in mammary tumor models with both estrogen and progestin receptors — positive or negative. The images show high uptake of radioactivity in the responsive tumor, while no uptake is observed in the non-responsive variety or in the responsive variety after administration of cold progestin," noted Dr. Rigo.

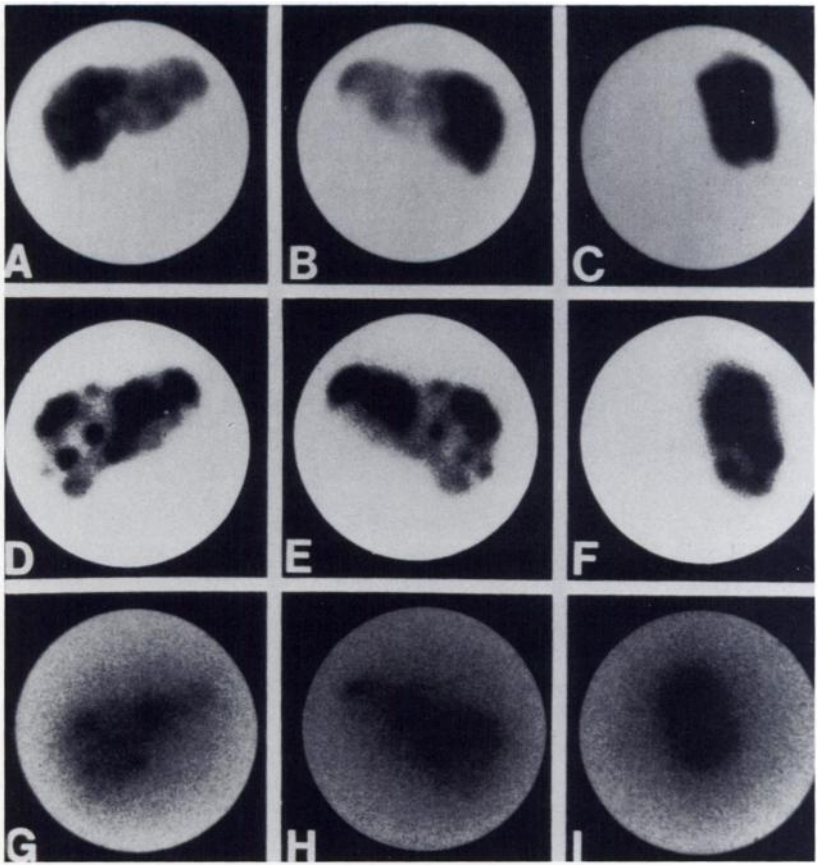
The role of PET in oncology is related to the progress of radiopharmaceutical development, indicated Dr. Rigo. "Although most of the work concerns metabolic studies, two



A metastasis in an axillary lymph node from an anaplastic lung carcinoma; Posterior view of the thorax two hours after inhalation of ^{99m}Tc labeled D25 **(Abstract No. 203).**

papers describe. . . PET. . . antibody studies. Goethals from Gent, [Belgium] (No. 152) prepared carrier-free gallium-66, a positron emitter with a half-life of 9.4 hours produced from copper-63. Gallium-66 is used to label the antibody. They used antimyosin antibodies as a model. Goodwin [from Palo Alto, California] (No. 148) described an improvement of the recently published technique of pretargeted murine immunoscintigraphy," reported Dr. Rigo.

"In a series of presentations, the group from Heidelberg, [FRG] presented the use of PET for the diagnosis and follow-up of tumor patients" (Strauss, Nos. 91, 92, Knopp, Nos. 93, 112, and Dimitrakopoulou, No. 94), Dr. Rigo noted. "They [reported] that FDG uptake appears to be a more sensitive parameter of [therapeutic] response than volume changes. . . . In addition to FDG, they used fluorouracil to evaluate the uptake of the cytostatic lesions in the lesions. Only 24% of the cases of all metastases have high tracer concentration and a negative growth rate. This frequency corresponds to the other response rate of colorectal metastases to fluorouracil chemotherapy, suggesting a potential role of PET to select these patients for therapy."



First row: multiple cold defects due to gastrinoma metastases; second row: distribution of ^{99m}Tc MAA co-injected with yttrium-90 glass spheres (with hot foci corresponding to the hypervascular metastases); third row: distribution of ^{90}Y as demonstrated by a Bremsstrahlung scan (Abstract No. 10).

Therapeutic Applications

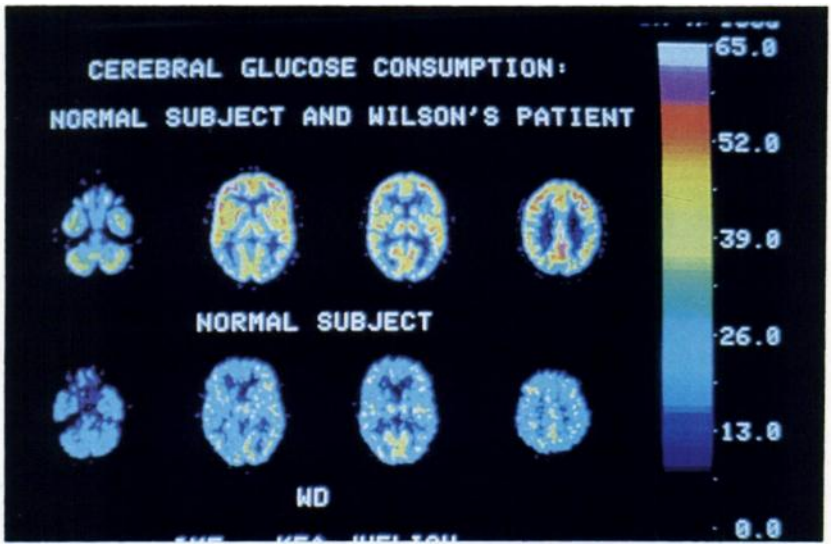
Dr. Rigo detailed novel approaches in the therapy of skeletal metastases that were described by Volkert from Freeport, Texas (No. 7) and Turner from Western Australia (No. 8). "These authors used samarium-153-EDTMP, a medium energy beta emitter with a 46.3 hour half-life and a 103 keV gamma ray to treat painful skeletal metastases unresponsive to conventional therapy." Dr. Rigo showed an example that compared the scintigraphic appearance of skeletal metastases with ^{99m}Tc MDP and ^{153}Sm. "Dosimetry was based on urinary elimination of a tracer dose. Pain was relieved within two weeks in 83% of the patients. Myelosuppression, particularly thrombocytopenia, was the limiting toxicity."

Perdrisot et al. from Angers, France (No. 9) and Shapiro from Ann Arbor (No. 10) "used microcapsules of either isobutyl-cyanoacrylate or glass to inject beta emitting isotopes into the feeding artery of a tumor," said Dr. Rigo. "In a mouse melanoma model, Perdrisot, using radium-186, observed curtailed evolution of the tumor volume and metabolic activity after injection of 30 μCi with an absorbed dose of 75 Gray. In patients with hepatic metastases, Shapiro described administration of [yttrium-90 to provide] doses up to 12,500 rads, [resulting] in partial responses in 10 of 18 treated patients."

In metastatic neuroblastoma, MIBG therapy has not provided uniformly satisfactory results, according to Dr. Rigo. Baum et al. from Frankfurt, FRG (No. 32) "studied the potential use of ^{99m}Tc-or iodine-labeled BW 575/9 monoclonal antibody to stage or treat neuroblastoma" demonstrating that "high tumor uptake can be obtained."

Neurologic Applications

"The growing importance of brain studies for the future of nuclear medicine, and the significant contribution that PET and now SPECT can make to brain research by [facilitating analysis] of the chemistry of the mind [was cited] by Henry Wagner" at the



Regional cerebral glucose consumption in patients with Wilson's Disease: Note decreased metabolic rate in the anterior cortical region, the striatum, and the cerebral cortex compared to control subjects **(Abstract No. 73).**

August 1989, p. 1283], said Dr. Rigo. Although not well represented at the 1989 EANM Congress, future meetings will need to address this.

Maziere (No. 19) and Loc'h (No. 20) from Orsay reported the characterization of lisuride, a D2 receptor ligand, using either a bromine-76 derivative for PET study or an ^{123}I derivative for SPECT study, noted Dr. Rigo. "These ligands accumulate in the [baboon] striatum, reaching a maximum 30 minutes after injection, and are specifically displaced by a haldoperidol." In man, the striatum to cerebellar ratio for the basal ganglia and the cerebellar level is 3.84 for PET; with SPECT, the ratio is 2.1, recorded two hours after injection. "Iodolisuride appears suitable for SPECT clinical studies of dopaminergic D2 [disorders]," said Dr. Rigo.

Dr. Rigo underscored the importance of serotonin S2 receptors in mood disorders and in migraine, noting, however, that the potential role of serotonin S2 antagonists, is not well understood. Mertens et al. from Brussels, Belgium (Nos. 21, 22) labeled the ketanserin analog with ^{123}I to perform S2 receptor mapping of the baboon and human brain and to study the potential role of these antagonists. Dr. Rigo showed images demonstrating the iodoketanserin distribution.

Brain Metabolism

Dr. Rigo reported on a study by Kuwert et al. from Jülich and Düsseldorf (No. 73) that examined regional cerebral glucose consumption in patients with Wilson's disease. The group measured the glucose metabolic rate in 28 regions of interest and compared the results to the clinical severity of symptoms. "Patients with Wilson's disease have a decreased metabolic rate in the anterior cortical region, the striatum, and the cerebellar cortex. Correlations were observed between metabolic rate and the severity of speech disorders in the striatum — and with the severity of occular motor disturbances," said Dr. Rigo.

"The importance of anaerobic glucose metabolism, which has been well studied in muscles in the heart, had not been previously demonstrated in the brain," noted Dr. Rigo. Ackermann from Los Angeles, California and Lear from Denver, Colorado (No. 74) together have "devised a technique to separate the oxidative and glycolytic anaerobic component of glucose metabolism by simultaneously measuring labeled FDG and glucose retention in the brain," said Dr. Rigo. "Accumulation of deoxy-

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"Patients with Wilson's disease have a decreased metabolic rate in the anterior cortical region, the striatum, and the cerebellar cortex. Correlations were observed between metabolic rate and the severity of speech disorders in the striatum — and with the severity of occular motor disturbances"

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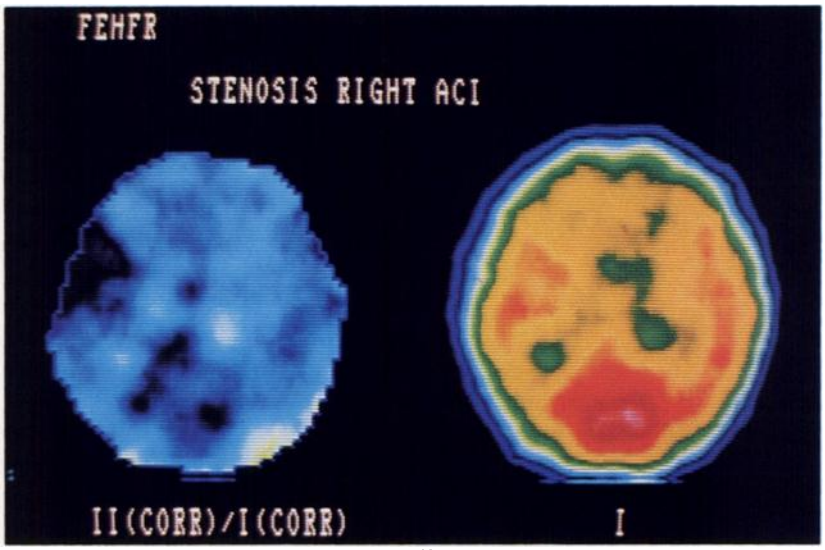
glucose in the brain is in proportion to the rate of the glucose phosphorylation, which occurs prior to diversions of oxidative and glycolytic metabolism, and thus reflects total glucose metabolism. On the other hand, after [carbon-14-] labeled glucose administration, only the oxidative glucose metabolites are retained for some time in the brain, while the lactate, which is the product of glycolysis, washes out of the brain rapidly. Using this principle. . . the authors [found] no anaerobic metabolism in the normal unstimulated brain. Stimulation however, such as unilateral optical stimulation in rats, induced anaerobic metabolism in specific regions of the brain. . . . Seizure, induced by tannic acid, induced striking metabolic changes in aerobic glucose utilization in the hippocampal region of the brain." Dr. Rigo said this study demonstrates why FDG can be a more useful tracer than oxygen to evaluate brain stimulation.

Amino acid transport and brain metabolites are important not only in brain research but also for oncology, indicated Dr. Rigo. Shulkin et. al. from Ann Arbor (No. 24) used aminocyclohexane carboxylic acid (ACHC), a non-metabolized amino acid analog, to assess transport of amino acids into the brain. They studied 14 normal volunteers before and after a drink sweetened with aspartame and one patient with phenylketonuria, before and after institution of a phenylalanine restricted diet.

"The patient with phenylketonuria showed a 2.5-fold increase in ACHC uptake after the diet," reported Dr. Rigo. "Volunteers in the aspartame group showed an average global decline of 13% of amino acid transport after aspartame, while plasma phenylalanine transiently doubled. Thus, ACHC uptake reflects plasma amino acid levels and appears as a useful probe for tomographic studies of amino acid transport in the human brain."

Paans et al. from Groningen (No. 219) and Langen et al. from Jülich (No. 41) did noteworthy work in this area using ^{11}C tyrosine and iodomethyl tyrosine, respectively.



***Regional cerebral perfusion images using ^{99m}Tc HMPAO: Response of cerebral perfusion to increased CO_2 level, (left); control, (right). The patient has stenosis of the right middle cerebral artery and decreased perfusion in the territory supplied by that vessel* (Abstract No. 236).**

"rubidium appears more sensitive and. . . more specific than thallium for the detection of ischemia. . . . thallium probably underestimates viability."

Cerebral Blood Flow Measurements

"The study of regional cerebral blood flow measurement has attracted a number of interesting contributions, mainly using single photon tracers," noted Dr. Rigo. He pointed out studies from Knapp from Bad Oeynhausen, FRG (No. 236), Leinsinger from Munich (No. 237), and Dingler from Darmstadt, FRG (No. 240), which investigated the cerebral vascular capacity using carbon dioxide stimulation or Diamox. After stimulation, there is decreased perfusion reserve in the territory of the

stenosed cerebral artery. "Leinsinger indicates that in the follow-up of patients after carotid endarterectomy, only patients who have preoperative moderate or severe cerebral vascular reserve capacity reduction show an increased reserve capacity postoperatively," reported Dr. Rigo.

Alzheimer's Disease

Several papers were presented on the diagnosis and follow-up of Alzheimer's disease. Herholz et al. from Koln, FRG (No. 136) and Steinling from Lille, France (No. 134) "studied the specificity of PET and SPECT and report a specificity of around 80% using ratios of affected to unaffected lesions," said Dr. Rigo.

Costa from London (No. 135) compared HMPAO SPECT quantitative follow-up of patients with Alzheimer's dementia with clinical assessment. "HMPAO demonstrates deterioration of the brain perfusion pattern in the frontal and parietal cortex that correlates with clinical assessment," reported Dr. Rigo.

Cerebellar Disease

"Patients with disease of the cerebellum may have altered neuropsychological performances," according to Dr. Rigo. Léveillé from Montréal, Canada (No. 137) demonstrated that "primary cerebrellar involvement appears in some cases to influence the HMPAO contralateral cortical concentration, suggesting cerebellar-frontal and cerebellar-parietal loops playing a role in cognitive thought. The patients displayed a unilateral right cerebellar infarct demonstrated by CT but no cortical lesion. HMPAO SPECT demonstrates the old cerebellar infarction and reduced HMPAO concentration both in the basal ganglia, magnitude of 20%, and in the left parietal cortex, 45%, supporting the hypothesis of reverse cerebellar cerebral diaschisis."

HMPAO SPECT has been used to study the brain in AIDS patients, Dr. Rigo reported. "SPECT demonstrates larger and more lesions than CT or MRI, though its value for early detection, follow-up, and prognosis has to be further established," he noted.

"...diastolic dysfunction in hypertension may precede myocardial hypertrophy and represent the initial clinically detectable manifestation of the effects of hypertension on the left ventricle."

"Iodine-labeled EGF [is a] promising tracer to assess receptor sites in vivo and might become useful to help therapy in breast cancer."

Neonatology

"In neonates, current techniques, for instance cranial echography, sometimes fail to detect cerebral injuries in patients who later develop neurological sequelae from severe perinatal asphyxia," said Dr. Rigo. "Tondeur from Brussels (No. 34) studied 36 babies at high risk for all neurological lesions. SPECT did not detect all abnormalities realized by echo but detected hyperperfused areas in 8 of 16 patients with normal ultrasound."

In complementary studies, Tondeur (No. 34) and Raynaud from Orsay (No. 35) "demonstrated basal or acti-

(continued on page 1931)

(continued from page 1930)
vation abnormalities in the cerebral areas implied in language control of patients with congenital dysphasia," reported Dr. Rigo.

Gastroenterology

Dr. Rigo presented one slide by Urbain from Leuven, Belgium (No. 123), which showed the effect of erythromicin on gastic emptying. "This antibiotic mimics the action of motilin and dramatically accelerates emptying of solids and liquids," he noted.

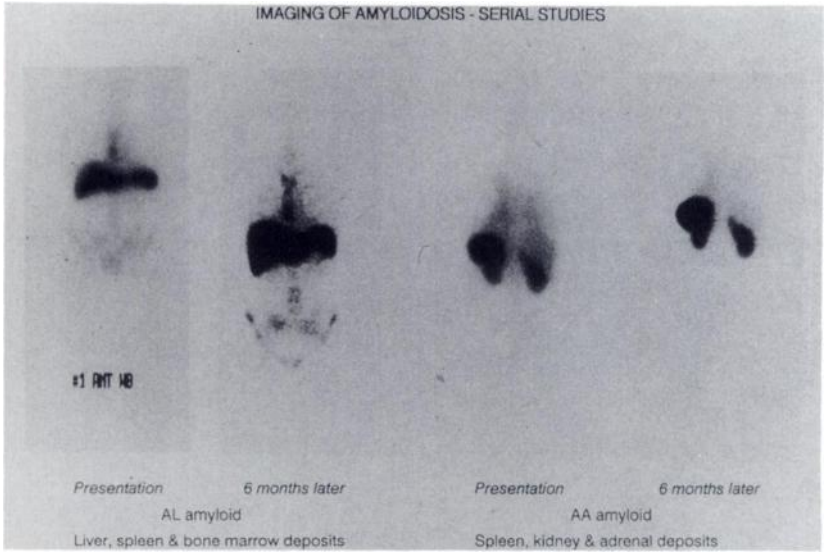
Pulmonary Disease

"In pulmonary disease, the value of nuclear medicine procedures for diagnosis and monitoring of opportunistic lung infection in AIDS patients has been discussed" and the role of gallium was confirmed, reported Dr. Rigo.

He also described work by Köhn et. al. from Vienna (No. 173), who described enhanced DTPA clearance in patients with acute pneumocystis carinii infections. "Clearance halftime is 14 minutes and returned to normal after three weeks of specific therapy." Technegas® provides an improved technique to evaluate ventilation, as reported by Peltier from Nantes (No. 176), Lemb from Bremerhaven, FRG (No. 174), and De Geeter from Brussels (No. 175), according to Dr. Rigo.

Dr. Rigo concluded his highlights presentation with a discussion of work in development by Hawkins et. al. from London (Nos. 149, 150) in the labeling of human serum amyloid P components with ^{123}I for the study of amyloid deposits. "In normal subjects," he reported, "radioactivity was confined to the blood pool in which serum amyloid P has a half-life of 25 hours. By contrast, in patients with amyloidosis, selective uptake of up to 90% of the tracer into the amyloid deposit persisted for the 48 hours observation period. . . ."

Hawkins identified uptake in the spleen, in the spleen and kidneys, in the liver and the spleen, and in some cases, in the adrenals and the other sites of amyloids, said Dr. Rigo. "This important new technique, based on the specific molecular affinity of a normal plasma protein, enhances knowledge of amyloidosis and permits objective assessment of response to therapy. . . . It provides a remarkable demonstration of the continuous [dynamism] of nuclear medicine."



^{123}I-labeled serum amyloid P components in two patients with amyloidosis, demonstrating evolution of the disease **(Abstract No. 149, 150).**

Ackerman and Lear have "devised a technique to separate the oxidative and glycolytic anaerobic component of glucose metabolism by simultaneously measuring labeled FDG and glucose retention in the brain" demonstrating why FDG can be a more useful tracer than oxygen to evaluate brain stimulation

References

1. Fishman et al. Detection of Acute Inflammation With ^{111}In-Labeled Nonspecific Polyclonal IgG. *Sem in Nucl Med* 1988;18:335–344.