

## Progress in Radionuclide Therapy and Immunoscintigraphy

# SCIENTIFIC HIGHLIGHTS OF THE EUROPEAN NUCLEAR MEDICINE CONGRESS 1985

*Prof. Dr. Udalrich Buell, head of the nuclear medicine department at the University of Aachen in Germany, presented the scientific highlights of the European Nuclear Medicine Congress before the meeting's closing ceremony. The Congress, which attracted almost 4,000 attendees, was held September 3-6, 1985, in London, England (see Newsline, Oct. 1985, pp. 1105-1106).*

**I**n reviewing the scientific presentations at the European Nuclear Medicine Congress, it is apparent that nuclear medicine investigators are making significant progress in developing therapeutic radionuclide procedures.

Josep G. Llaurodo, MD, et. al., at the Veterans Hospital in Loma Linda and at the Loma Linda School of Medicine in California, reported a procedure that may be useful to destroy inoperable cancer of the lung and other organs (A20).<sup>\*</sup> This group delivered microspheres labeled with 20 mCi of phosphorus-32 into a selected lobar branch of the pulmonary artery in dogs. Post mortem examination 12 months later showed contraction of the injected lobe with collagen replacing alveoli, and no obvious alterations discernible in adjacent lobes or structures.

Prof. Dr. Eberhard Henze et. al. of the University of Ulm, Germany, reported that echo-guided therapy of liver tumors with phosphorus-32-labeled microspheres, which can deliver a radiation dose of 20,000 rads with one injection of 140  $\mu$ Ci into a 2-cm metastasis, "seems feasible"

(C2.95).<sup>†</sup> The group evaluated the distribution and persistence of various radiolabeled carriers in the liver tissue of five anesthetized dogs.

G. Hooker et. al. of the Hammer-smith Hospital in London, England, presented findings of a study using radiolabeled antibodies to irradiate lesions in advanced ovarian cancer (A34). Using iodine-131-labeled HMFG2 and AUA1 antibodies, 12 patients were treated with doses ranging from 20 to 150 mCi. Mild toxicity was observed with doses above 100 mCi. Three out of four patients with stage IV disease (extra-abdominal) died three to six months after treatment but were benefited symptomatically. All six patients with stage III disease (intra-abdominal) were "alive and well" three to 18 months after treatment.

A.J. McEwan et. al., of the Southampton University Hospitals in England, studied eight therapeutic doses of iodine-131 meta-iodobenzylguanidine (MIBG) in patients with malignant pheochromocytoma (A75). (Iodine-131 MIBG has an established role in diagnosis and localization of malignant pheochromocytoma.) No adverse effects were recorded in the five patients studied; symptomatic relief was noted in four patients, and there was evidence of tumor regression in two patients.

In another study of iodine-131 MIBG, Prof. Dr. Ulrich Feine et. al., of the Universitat Tubingen in Germany, conducted 20 therapeutic procedures in six children with neuroblastoma (A77). Two of the children have died, and four are in partial

remission up to eight months after therapy with a four-treatment series. Prof. Dr. Feine, who also reported results of a multi-center neuroblastoma therapeutic trial of a combination of cytostatic agents and iodine-131 MIBG, said that this procedure is considered "the best form of therapy for primary neuroblastoma."

Prof. Dr. Joachin Kutzner et. al., at the University of Mainz in Germany, have treated more than 50 patients since 1980 with a yttrium-90 citrate complex for pain caused by multiple bone metastases (A97). Pain decreased in nearly all patients within a few days and lasted an average of seven weeks.

### Immunoscintigraphy

Jean F. Chatal, of the Centre Gauducheau in Nantes, France, presented research on the immunoscintigraphic localization of gastrointestinal carcinoma and its recurrences (A17). This prospective multicenter clinical study, which included work done by investigators at the University of Frankfurt, Germany, and the University of Barcelona, Spain, assessed the diagnostic efficiency of immunoscintigraphy in 100 patients after injection of a combination of anti-carcinoembryonic antigen and

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<sup>\*</sup>Abstracts catalogued with the letter "A" are published in the *European Journal of Nuclear Medicine*, Vol. 11 No. 2/3, 1985.

<sup>†</sup>Abstracts catalogued with the letter "C" are published in *Nuclear Medicine Communications*, Vol. 6 No. 9, 1985.

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19-9 antibodies. Out of 53 sites confirmed by surgery or other diagnostic methods, 23 were visualized by planar scintigraphy and 19 by single-photon emission computed tomography (SPECT). For nine patients, immunoscintigraphy was the only diagnostic test that detected recurrence.

Results of a clinical trial designed to determine the best method for immunoscintigraphy of malignant melanoma using radiolabeled 225.28S monoclonal antibodies were reported by Prof. Dr. Gianluigi Buraggi of the Istituto Nazionale Tumori in Milan, Italy (A16). Over a 33-month period, 43 patients with 74 localizations were examined using the whole antibody labeled with iodine-131, and F(ab')<sub>2</sub> fragments labeled with iodine-131, iodine-123, technetium-99m, or indium-111. The maximum value of the tumor/background ratio was usually reached within 24 hours of injection, and therefore the technetium-99m compound seems to be the reagent of choice, reported the research group which included investigators from New York Medical College and the Centro Ricerche Nucleari in Saluggia, Italy.

Maria Granowska et. al. of St. Bartholomew's Hospital in London, England, presented a kinetic analysis of immunoscintigraphy, using probability mapping, compared with multiple biopsy findings in ovarian cancer (A14). Using iodine-123-labeled HMFG2 monoclonal antibodies, the group studied six patients who had

completed chemotherapy to determine whether kinetic analysis with probability mapping could be used to predict biopsy results. They concluded that this method may reduce the need for follow-up laparotomy.

A group at the University of Nottingham in England reported that patients develop antibodies to a monoclonal antibody used for diagnostic scintigraphy, which “may be a serious limitation for repeated imaging” (C2.92). M.V. Pimm reported that 25 of 26 patients with colorectal or ovarian carcinoma or osteosarcoma, who were injected with iodine-131-labeled 791T/36 monoclonal antibodies, produced antibody to the injection. The antibody response was detected within seven to ten days and persisted for a minimum of ten months. A reduction in image quality was seen in patients receiving labeled 791T/36 for a second and third time.

H.J. Danpure et. al., of the Hammersmith Hospital in London, England, studied three mouse monoclonal antibodies for selective in vitro cell labeling of human leukocytes (A151). Using iodine-125, the group found that AB29 antibody (specific for granulocytes) and AB44 antibody (specific for granulocytes and monocytes) selectively radiolabeled human leukocytes in whole blood; AB24 antibody (specific for monocytes and tissue macrophages) did not.

Zvi H. Oster, of the State University of New York at Stony Brook, presented work on technetium-99m-labeled monoclonal antiplatelet frag-

ments for imaging experimental thrombi in dogs, done in collaboration with Brookhaven National Laboratory in Upton, NY, and Summa Medical Corp. in Albuquerque, NM (C1.57). This method may simplify the preimaging preparation required by the currently used procedure, indium-111-oxine-labeled platelets. Thrombi in peripheral and pulmonary veins and in arteries could be imaged within three hours of injection and, in some dogs, visualization of intimal damage without visible thrombi was also possible.

### New radiopharmaceuticals

Claude Brihaye of the Cyclotron Center in Liège, Belgium, reported the clinical potential of a new osmium-191/iridium-191m generator (A110). The investigators, also of the Free University of Brussels and Oak Ridge National Laboratory in Tennessee, performed preliminary gamma camera studies on volunteers, comparing iridium-191m (half-life = 4.9 sec) to technetium-99m in angiography for clinical applications such as the measurement of cardiac function, the evaluation of venous and arterial drainage, renal and cerebral perfusion, and the diagnosis of peripheral occlusions.

Prof. Dr. Gerhard L. Stoecklin, of the Institut für Chemie in Juelich, Germany, reported an evaluation of bromine-75-labeled butyrophenone neuroleptics for positron emission computed tomography (PET) mapping of dopaminergic receptor areas (A108). The group, including investigators from the Max Planck Institut in Cologne, Germany, found that bromine-75 bromspiperone is the agent of choice for these studies.

L.R. Canning reported a new imaging agent, technetium-99m hexamethyl-propyleneamineoxine (HMPAO), developed by the University of Missouri and Amersham International, for SPECT imaging of re-

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**COMMENTARY**


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## UNITY IN EUROPEAN NUCLEAR MEDICINE

**F**or too many years, the European nuclear medicine community has been fragmented by the existence of two European societies with multiple national societies. By the end of the European Nuclear Medicine Congress 1985 in London, both scientist and commercial participants agreed that a single society, the European Association of Nuclear Medicine, was now a necessity rather than a hope. Once the legal formalities have been sorted out, the new association should be a



thriving focus for new ideas and innovations.

The Society of Nuclear Medicine—Europe (SNME) was founded in 1964 and until recently has been essentially a German-oriented organization. The meetings have been of excellent scientific quality, but in general were attended by German-speaking scientists oriented toward German-based research. The European Nuclear Medicine Society

(ENMS) was conceived in 1972 to encourage the cooperation between the Eastern- and Western-Bloc scientists. Although the ENMS operated on the truly democratic principle of representative delegates from each nation, in practice the original idea has not worked well because of the difficulty encountered by nondelegate scientists in visiting Western Europe.

Mr. Edward Heath, MP, who served as the British Prime Minister from 1970 to 1974, gave the opening address at the Congress in which he urged nuclear medicine scientists to unify as one European cooperative body. Mr. Heath's advice seemed quite appropriate since he played a leading part in the negotiations to include Britain in the European Economic Community. A truly international spirit prevailed during the Congress, which was exemplified at the traditional banquet and dance attended by over 500 registrants. The participation in this Congress exceeded all expectations, and bodes well for the future of a unified nuclear medicine society in Europe.

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gional cerebral blood flow (A1). Biodistribution studies show that the agent crosses the blood-brain barrier, and its retention of activity represents a "major improvement" over other lipophilic technetium-99m tracers, which exhibit rapid washout.

### Cerebrovascular disease

At the Middlesex Hospital in London, England, Dr. Peter J. Ell et. al. evaluated technetium-99m HMPAO in patients with established stroke and in normal subjects (A2). The group found that SPECT imaging with the new radiopharmaceutical demonstrates good quality images compared to iodine-123 IMP and x-ray computed tomography (CT).

Prof. Dr. Wolfram H. Knapp of the Institut für Nuklearmedizin in Heidelberg, Germany, presented a SPECT imaging study to determine the blood flow-to-volume ratio in patients with cerebrovascular disease (A112). The group, which included investigators from the Neurologische Universitätsklinik in Heidelberg and the Herzzentrum Nordrhein-Westfalen in Bad Oeynhausen, Germany, reported that their findings mirror the characteristics of cerebral blood flow autoregulation in patients with decreased arterial perfusion pressure.

Prof. Dr. Udalrich Buell reported work done at the University of Munich, Germany, on a comparison of SPECT and nuclear magnetic resonance imaging (NMRI) to quantify

cerebrovascular disease (A54). The group found that NMRI may be used to examine this disease, and was found to be most sensitive in detecting altered cerebral areas. SPECT with lipophilic tracers, however, was superior in demonstrating the size of the low-flow areas.

In another study from the University of Munich, Wolfgang Krappel et. al. studied 24 patients with cerebrovascular disease to determine an optimum time frame wherein cerebral IMP distribution reflects regional cerebral blood flow, using xenon-133 gas studies as a reference (A56). The group found that cerebral IMP uptake and distribution represent regional cerebral blood flow only during the

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first 30 minutes after injection.

Dr. Jean Luc Moretti of the Hôpital Henri Mondor in Creteil, France, presented work that compared SPECT imaging at one hour and four hours after injection with iodine-123 IMP, and x-ray CT for patients with stroke (A117). Early SPECT imaging showed reduced activities in all cases, even in patients with normal CT. Late SPECT imaging may be useful in giving information concerning remaining viability of ischemic brain tissue, reported the group, which included investigators from the Hôpital Frédéric Joliot in Orsay, France.

Dr. I. Podreka et. al. of the Neurologische Universitätsklinik in Vienna, Austria, reported a study of SPECT visualization of changes in brain activity caused by acoustic memory tasks (A114). Using iodine-123 IMP, this group compared regional cerebral blood flow in subjects undergoing various degrees of auditory stimulation. The group found that memorization of nonsense syllables led to a marked increase in the left anterior basal ganglia, particularly in the caudate nucleus, whereas the memorization of concrete nouns led to an increase in the right temporal lobe. The two auditory tests led to a marked activation of both anterior frontal lobes and the left temporal lobe.

### Cardiovascular research

Richard Underwood et. al. of the National Heart and Chest Hospitals in London, England, reported a clinical validation of left and right ventricular stroke volumes determined by NMRI (A79). In 20 subjects, the investigators found a 13 percent margin of error in the determination of left and right ventricular stroke volume, and concluded that NMRI provides "an accurate and reproducible measure of left and right ventricular stroke volumes, allowing noninvasive assessment of ventricular function."

Prof. Dr. Agrege R. Itti et. al. of the Hôpital Trousseau in Tours, France, studied gated blood pool SPECT imaging in 14 patients with arrhythmogenic right ventricular dysplasia and in 10 normal subjects (A31). Right ventricular regional kinetic abnormalities were observed in all 14 patients, whereas left ventricular dysfunction was found in seven cases. Although final diagnosis requires left and right angiographic data, a noninvasive screening method may be clinically useful.

Ruediter Standke et. al. of the University Hospital in Frankfurt, Germany, evaluated a method of quantifying exercise-induced ischemia using phase analysis of ergometrical equilibrium radionuclide ventriculograms by measuring the regional phase shift between rest and exercise (A222). The group found that exercise-induced asynchrony is normalized in parallel to the left ventricular global ejection fraction and the regional ejection fraction values after successful transluminal coronary angioplasty.

C.M. de Landsheere et. al. at the University of Liège, Belgium, presented findings on the assessment of myocardial viability after an acute infarction (A199). Using PET with fluorine-18 deoxyglucose and ammonia-13 or potassium-38, the group studied 32 patients and four control subjects. They concluded that the combined study of flow and glucose uptake with PET allows clinicians to identify patients with viable myocardium and to adequately select candidates for surgery.

N.N. Khalil of the Groby Road Hospital in Leicester, England, presented a study of technetium-99m tertiary butylisonitrile (BIN) for myocardial perfusion imaging in five patients with myocardial infarcts, 10 patients with angina due to angiographically proven coronary artery disease, and in five normal subjects (A106). The group, including investi-

gators from the Leicester Royal Infirmary and the University of Loughborough, found that areas of inferior and anterior infarction could be detected. Regions of diminished activity on exercise were found in patients with angina without infarction at 15 minutes, corresponding with reversible perfusion defects on thallium-201 scintigraphy.

Stanley J. Goldsmith, MD, et. al., at the Mount Sinai Medical Center in New York, reported that indium-111-tropolone-labeled platelets, combined with blood pool subtraction, appears to provide good sensitivity for detection of left ventricular thrombi despite age of thrombus and anticoagulant therapy (A148). (Indium-111 tropolone is more convenient than indium-111 oxine for platelet labeling because the procedure can be performed in plasma.) While the specificity of the method is unknown, indium-111-tropolone-labeled platelets are suitable for platelet kinetic studies and imaging of arterial and venous thrombi.

Mike A. Smith et. al. of the University of Edinburgh, Scotland, reported a commercial 0.08T resistive NMR system modified to produce gated proton density and T1 cardiac images (A81). The system uses an interleaved saturation recovery and inversion recovery pulse sequence to produce a calculated T1 image. The group found that the variation in T1 in the ventricular wall is 2.7 percent in gated T1 images, as opposed to 10.2 percent in ungated images.

### Inflammatory diseases

Investigators at the Institut für Nuklearmedizin and the German Cancer Research Center in Heidelberg performed indium-111-acetylacetone leukocyte scans in 352 patients suspected of bone infections and compared results to final clinical diagnoses (A57). Hans-Peter Kaps reported that the procedure is helpful

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in detecting acute bone, joint, and soft tissue infections, except for infectious processes of the spine. Chronic infections show a negative scan. Because of a high false positive rate, the test is of minor value in differentiating rheumatic diseases, tumors, and non-infected loosening of endoprostheses from an acute infectious process.

David Feiglin et. al. of the Cleveland Clinic Foundation in Ohio presented his group's reappraisal of NMRI, radiography, x-ray CT, planar radionuclide scans, and SPECT imaging in 30 patients with suspected spinal infection (A98). The group found that NMRI is more sensitive and specific than plain x-ray films, and as sensitive as radionuclide studies while providing greater anatomic specificity. Gallium imaging may show changes prior to NMRI or planar radionuclide bone scans, but is influenced by antibiotic therapy.

A.N. Kahn et. al., of the North Manchester General Hospital in England, investigated the use of technetium-99m sucralfate scans to detect active inflammatory bowel disease in children (A171). The group, which included investigators at the Booth Hall Children's Hospital in Manchester, found the procedure more sensitive than conventional radiology, and concluded that it may prove useful as a screening test, as a noninvasive technique to exclude significant pathology, and as a method of serial assessment of disease activity.

### **Endocrinology**

A group at the University of Michigan and the Veterans Administration Medical Centers in Ann Arbor, MI, investigated the scintigraphic localization of androgen-secreting neoplasms using iodine-131 iodomethyl-19-norcholesterol (A135). Shawn D. Ripley, MD, reported that the scintigraphic findings correlated with the post-operative diagnosis in all of 12 patients with hyperandrogenism. In

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addition, this scintigraphic procedure distinguishes between adrenal and ovarian hyperandrogenism, “which may not be possible by other means.”

In another study from the University of Michigan, investigators studied the diagnostic efficacy of iodine-131 and iodine-123 MIBG in patients with suspected pheochromocytomas (A139). Results of iodine-131 MIBG scintigraphy in 550 patients referred for suspected pheochromocytomas were examined and compared with iodine-123 MIBG in 18 cases. Brahm Shapiro, PhD, reported that iodine-131 MIBG is safe, sensitive, and efficacious, but iodine-123 MIBG was found to detect smaller lesions.

Dr. T.M.D. Gimlette, of the Royal Liverpool Hospital in England, presented his work on quantifying the limitations of parathyroid imaging with thallium-201 (A47). The sensitivity of this test is limited by the difficulty in correctly localizing small parathyroid lesions, particularly those of less than 0.5 grams. Dr. Gimlette found that a parathyroid uptake of 0.01 percent of the imaging dose approximately defines the lower limit for correct localization by current methods using thallium-201.

Investigators at Guy's Hospital Medical School in London, England, and the University of Liege in Belgium, performed dynamic studies of iodine-123-labeled insulin distribution and its plasma pharmacokinetics in insulin-dependent diabetic and normal subjects (A91). S. Ng Tang

Fui reported that preliminary results of studies in six diabetics and six normal subjects indicate a wide variation in insulin handling and hepatic uptake in diabetics, which could possibly explain varying clinical characteristics.

### **Instrumentation**

The Technicare Corp. in Solon, OH, reported preliminary performance results of its triangular scintillation gamma camera SPECT system for total organ volume imaging (A213). Chun B. Lim, PhD, said that the new system is designed to overcome two major drawbacks of current SPECT systems—poor utilization of emitted photons, and inadequate system design for SPECT.

A. Jeavons of CERN in Geneva reported the development of a new high density avalanche chamber positron camera, which has been operational at the Geneva Cantonal Hospital in Switzerland since early 1985 (A215). The group developed an improved detector system which provided a six-fold increase in sensitivity over previous cameras. Further upgrades are planned.

### **Value of physiologic imaging**

Nuclear medicine shows great promise because of its unparalleled capabilities in physiologic imaging. Although structure has for some time been used as a guide to function, we must stress that macrostructure is a consequence of function.

*Udalrich Buell*