Proceedings of the 33rd Annual Meeting of
THE SOCIETY OF NUCLEAR MEDICINE
June 22–25, 1986 • Washington, D.C.
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Alan D. Waxman, M.D.

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# The Society of Nuclear Medicine

**33rd ANNUAL MEETING**

Saturday, June 21 through Wednesday, June 25, 1986

WASHINGTON CONVENTION CENTER, WASHINGTON, DC

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**SEMINAR I: CARDIOVASCULAR NUCLEAR MEDICINE**

- Sponsored by the Cardiovascular Council of the SNM.
- To highlight controversies and new areas of development in cardiovascular nuclear medicine.
- Topics include:
  - New techniques in coronary artery disease
  - Exercise left ventricular function
  - Imaging agents
  - Nuclear medicine imaging
  - Revascularization
  - Thrombosis

**SEMINAR II: NUCLEAR MEDICINE: THE NEXT FIVE YEARS**

- Sponsored by the SNM Cardiology Board of Directors.
- To discuss future trends and advancements in nuclear medicine.

**SEMINAR III: THE CHEMISTRY OF RADIONUCLIDE METABOLITES IN HUMAN TISSUE**

- Sponsored by the SNM Radiochemistry Board.
- To cover the chemistry of radionuclide metabolites in human tissue.

**SEMINAR IV: CURRENT ISSUES IN NUCLEAR MEDICINE**

- Sponsored by the SNM Nuclear Drug and Systems Board.
- To address current issues and challenges in nuclear medicine.

**SYMPOSIUM FOR THE REFERRING PHYSICIAN**

- Sponsored by the SNM Referring Physician Section.
- To discuss the role of the referring physician in nuclear medicine.

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**JUNE 22, 1986: EXHIBIT HALL, POSTERS, AND SCIENTIFIC EXHIBITS OPEN 10:00-6:00 TODAY**

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**SUNDAY**

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**Note:** 10:30 to 12:00 FUNCTIONAL BRAIN IMAGING, New Radiopharmaceuticals ROOM 33
<table>
<thead>
<tr>
<th>Day</th>
<th>Time</th>
<th>Event</th>
<th>Location</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>MONDAY</td>
<td>8:30</td>
<td>Consideration of imaging modalities to evaluate myocardial ischemia during stress.</td>
<td>Classroom</td>
<td>The potential impact of exercise echocardiography.</td>
</tr>
<tr>
<td></td>
<td>10:00</td>
<td>Pediatric nuclear medicine update</td>
<td>Classroom</td>
<td>Cardiac and vascular function in children.</td>
</tr>
<tr>
<td></td>
<td>12:00</td>
<td>In Vivo Applications of Multi-Nuclear MRI for Spectroscopy Imaging.</td>
<td>Classroom</td>
<td>Various applications of MRI in medical imaging.</td>
</tr>
<tr>
<td></td>
<td>15:00</td>
<td>Gastroenterology and radiopharmaceuticals</td>
<td>Classroom</td>
<td>Imaging and therapeutic applications of nuclear medicine.</td>
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<td></td>
<td>16:00</td>
<td>Radiopharmaceutical chemistry - Multiple Imaging Systems</td>
<td>Classroom</td>
<td>Advanced imaging techniques in nuclear medicine.</td>
</tr>
<tr>
<td></td>
<td>18:00</td>
<td>Poster Session: Presentations on Current Research Topics</td>
<td>Classroom</td>
<td>Presentations from researchers on the latest developments in nuclear medicine.</td>
</tr>
<tr>
<td>TUESDAY</td>
<td>8:30</td>
<td>Strategies for a successful nuclear medicine practice: Viewpoint of clinical practice</td>
<td>Classroom</td>
<td>Planning and execution phases in nuclear medicine practice.</td>
</tr>
<tr>
<td></td>
<td>10:00</td>
<td>Cardiac and vascular imaging - Clinical Applications</td>
<td>Classroom</td>
<td>Clinical applications of imaging modalities.</td>
</tr>
<tr>
<td></td>
<td>12:00</td>
<td>Instrumentation and signal processing</td>
<td>Classroom</td>
<td>Enhancing the efficiency of nuclear medicine.</td>
</tr>
<tr>
<td></td>
<td>15:00</td>
<td>Nuclear medicine review course</td>
<td>Classroom</td>
<td>Comprehensive review of current issues in nuclear medicine.</td>
</tr>
<tr>
<td></td>
<td>16:00</td>
<td>Pellet Spectroscopy: What are the key data analysis techniques?</td>
<td>Classroom</td>
<td>Advanced techniques in pellet spectroscopy.</td>
</tr>
<tr>
<td></td>
<td>18:00</td>
<td>Strategies for a successful nuclear medicine practice: The customer's perspective</td>
<td>Classroom</td>
<td>Planning and execution phases in nuclear medicine with patient input.</td>
</tr>
<tr>
<td>WEDNESDAY</td>
<td>8:30</td>
<td>Radiographic and functional brain imaging</td>
<td>Classroom</td>
<td>Imaging modalities for brain studies.</td>
</tr>
<tr>
<td></td>
<td>10:00</td>
<td>Clinical applications of bone mineral estimation in different groups</td>
<td>Classroom</td>
<td>Applications of bone mineral estimation in diverse patient populations.</td>
</tr>
<tr>
<td></td>
<td>12:00</td>
<td>Nuclear medicine milestones: William D. Myers, Ph.D., M.D.</td>
<td>Classroom</td>
<td>Expert insights into current nuclear medicine milestones.</td>
</tr>
<tr>
<td></td>
<td>15:00</td>
<td>Scientific meeting highlights: Henry W. Wagner, Jr., M.D.</td>
<td>Classroom</td>
<td>Highlighting the latest research and developments in nuclear medicine.</td>
</tr>
<tr>
<td></td>
<td>18:00</td>
<td>Poster Session: Presentations on Current Research Topics</td>
<td>Classroom</td>
<td>Presentations from researchers on the latest developments in nuclear medicine.</td>
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</tbody>
</table>

*Note: All events are subject to change.*
GASTROINTESTINAL ULCERATION: DETECTION UTILIZING Tc-99m-HSA-SUCRALFATE AND POTASSIUM SUCROSE SULFATE (PSS). Tc-99m-HSA-Sucralfate and PSS (C_{12}H_{14}O_{35}S_{8}K_{8}) is a small, water soluble, molecular weight compound with 8 sulfate groups and a protein interaction similar to Sucralfate: sucrose sulfate. PSS is a 90-105 F balloon placed across the T.F.S. Each of these patients had objective and quantitative hold-up of passage of pertechnetate. Images of 5 seconds each were obtained for 20 frames of 64 x 64 pixels. Subsequent static images were obtained for 60 minutes. In contrast to other esophageal problems, patients with achalasia have as much difficulty with liquids as with solids. Each of these patients had objective and quantitative delay in esophageal emptying by scintigraphic evaluation. These patients showed marked flattening of the time activity curves. Following the scintigraphic evaluation, each patient was subjected to esophageal dilatation using a 90-105 F balloon placed across the LES. The success of the pneumatic dilatation was evaluated by comparing the pre- and post-dilatation scintigraphic studies. In all pre-op cases, the scintigraphic studies showed qualitative and quantitative hold-up of passage of liquid radionuclide at the LES. The postoperative studies
demonstrated marked improvement of transit of 70-99m across the LES. The scintigraphic studies did not reveal any perforations resulting from the procedure. Follow-up evaluations up to 1 year after the dilatation have shown sustained benefits from the procedure and none required redilatation or surgery. Radionuclide scintigraphy has been extremely useful in the assessment of the degree of obstruction in achalasia and the information correlated well with the clinical picture.

No. 4
A SCINTIGRAPHIC EVALUATION OF COLONIC TRANSIT IN NORMAL SUBJECTS: THE PROKINETIC EFFECTS OF CISAPRIDE. V. Caride, J. Petersen, E. Prokoff, R.W. McCallum, Depts. Medicine and Nuclear Medicine, and Hospital of St. Raphael, New Haven, CT, and Univ. Virginia, Charlottesville, VA.

Our purpose was to investigate the effect of Cisapride (C) on colonic transit in normal subjects utilizing a radionuclide method and a randomized double-blind study design. After a 12-hr fast and on 2 separate days normal subjects received C (10 mg orally or placebo, and 10 minutes later a 100cc isotonie solution of the non-absorbable agent lactulose labeled with 500 microcuries of 99mTc-DTPA. They had a standard breakfast and lay supine under a large field of view gamma camera. After 3 hrs they took another dose of C 10 mg or placebo, ate a standardized lunch and gamma counts were again continuously monitored. The total study time was up to 8 hrs. Regions of interest were selected over the cecum, transverse colon (TRANS), ascending (ASC), descending (DESC) and sigmoid (SIGM) colon and the rectum. Table 1 shows time of appearance in each segment.

Table 1. ORAL-COLONIC TRANSIT (min).

<table>
<thead>
<tr>
<th>Placebo</th>
<th>TRANS</th>
<th>ASC</th>
<th>DESC</th>
<th>SIGM</th>
<th>Rectum</th>
</tr>
</thead>
<tbody>
<tr>
<td>77.71</td>
<td>93.12</td>
<td>234.13</td>
<td>190.79</td>
<td>355</td>
<td></td>
</tr>
<tr>
<td>Cisapride</td>
<td>65.23</td>
<td>108.37</td>
<td>146.77</td>
<td>159.71</td>
<td>150.46</td>
</tr>
</tbody>
</table>

We conclude that C is a promising new gas- trokinetic agent and well controlled trials to es- tablish its clinical efficacy are warranted.

No. 6
RESPIRATORY EFFECT IN RADIONUCLIDE ESOPHAGEAL TRANSIT TEST. H.A. Kleim, T.O. Graham, and A. Wald. University of Pittsburgh School of Medicine, Pittsburgh, PA.

Tests with swallowing of aqueous Tc-99m sulfur col- loid supine, analyzed by previously described methods (J Nucl Med 27: 947-964, 1984), revealed that some pa- tients with severe esophageal motility disorders had a large esophageal residual component that underwent recurrent retrograde and antegrade motion at a frequency of about 10 cycles/min. This occurred in cases of achala- sia, diffuse esophageal spasm, and systemic sclerosis. We sought to determine whether it was a passive phenome- non or the result of spasmodic contractions.

Condensed dynamic images having a spatial and a tem- poral dimension served to demonstrate the pattern and al- so provided the basis for an experiment that was applied in a case of achalasia and two of systemic sclerosis. At the completion of the routine test, imaging was con- tinued as the patient swallowed ad lib and sequentially performed tidal breathing, breath-holding, and slow breathing. An investigator repeatedly introduced a radionuclide source at the top of the imaging field to mark inspiration. The resulting images revealed that the dis- tal and proximal excursions of the residual liquid were synchronized with inspiration and expiration, respectiv- ely.

We conclude that oscillations of this frequency gener- ally represent a passive response to respiration rather than spasm, and that the pattern occurs in severe dis- ease without specificity as to the type of motility disorder, but (based on our additional experience) that it is not the only pattern that may be observed.

1:30-3:00
Room 40

C.A. I: NEW RADIOPHARMACEUTICALS
Moderator: Edward A. Deutsch, PhD
Comoderator: B. Leonard Holman, MD

No. 5
CISAPRIDE ACCELERATES GASTRIC EMPTYING OF SOLID AND LIQUID MEAL COMPONENTS IN PATIENTS WITH GASTRIC STASIS. R.W. McCallum, J.M. Petersen, R. Lange, Depts. Med. and Nuclear Medicine, University of Virginia, Charlot- terville, VA and Yale University, New Haven, CT.

Cisapride (C), a benzamide derivative, is a new prokinetic agent whose mechanism of action is thought to be through facilitation of acetylcholine release from the myenteric plexus. Our purpose was to investigate the effect of acute IV C on gastric emptying (GE) in patients with subjective and objective evidence of non-obstructive gastric stasis. 22 patients, 14 females and 8 males, mean age 41 yrs (range 20-62), with symp- toms of gastric stasis attributed to diabetic neuropathy (N=8), idiopathic (N=7) and post-gastric surgery (N=7) underwent a GE study basally (B) and on a separate day 2 hrs after receiving 10mg IV C. The solid (S) component of the meal was chicken liver labeled in vivo with 99mTc-sulfur-colloid and mixed with beef stew. The liquid (L) was 4 oz water labeled with 111 In-DTPA. GE was monitored for 2 hrs while patients lay supine under a gamma camera and results are below (* indicates p<0.05 after C versus baseline GE).

Table 2. DISTRIBUTION OF COLONIC ACTIVITY AT 480 MIN.

<table>
<thead>
<tr>
<th>Cisapride</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRANS</td>
<td>ASC</td>
</tr>
<tr>
<td>77.74</td>
<td>91.56</td>
</tr>
<tr>
<td>65±23</td>
<td>108±37</td>
</tr>
</tbody>
</table>

The solid component was monitored for 2 hrs while patients lay supine under a large field of view gamma camera. After 3 hrs they took another dose of C 10 mg or placebo, ate a standardized lunch and gamma counts were again continuously monitored. The total study time was up to 8 hrs. Regions of interest were selected over the cecum, ascending (ASC), descending (DESC) and sigmoid (SIGM) colon and the rectum. Table 1 shows time of appearance in each segment.

Table 1. ORAL-COLONIC TRANSIT (min).

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<th>Placebo</th>
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<td>77.71</td>
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<td>150.46</td>
</tr>
</tbody>
</table>

We conclude that: 1) a noninvasive assessment of colonic transit can be achieved with a non-absorbable radiotracer, and 2) C significantly enhances colonic transit in normal subjects.

No. 7

Clinical studies by Holman et al. (1984) have shown that Tc-99m-hexa-9m-isonitrile (NEN-14) to be useful, although not ideal, for myocardial perfusion scintigraphy. Therefore, a number of structural analogs of isonitriles have been synthesized with the goal of retaining the myo-
cardiac specificity and rapid blood clearance of TBI but to circumvent its pharmacokinetic problems of early high lung and peak liver activity demonstrated clinically. The most promising structures which have been identified are the aliphatic C-4 to C-5 ethers, 6 of which have been evaluated pharmacologically. Tc-99m-hexakis-2-methoxy-2-propyl-1-isonitrile (NEN-30) and Tc-99m-hexakis-1-methoxypropyl-2-isonitrile (NEN-42) have the best overall characteristics. Both exhibit good heart extraction in pigs (1.9 and 1.6 ID, T1/2 4 and 2 hours, respectively) and rapid and complete blood clearance (T1/2 1–2 minutes), low lung activity (1.5–2.3% ID) and low peak liver activity (1% and 8% ID) with substantial hepatobiliary clearance (T1/2 approximately 70 and 20 minutes, respectively). In comparison, 30–40% of TBI is extracted into the lung. Initially, this activity clears with a T1/2 of about 15 minutes and is sequestered by the liver from which there is little clearance. Imaging studies in miniature swine, monkeys, dogs and rabbits corroborate these results. In a rabbit coronary artery ligation-release model, neither agent redistributes measurably compared to TBI which shows up to 50% redistribution. Human imaging studies with NEN-10 confirm the biological characteristics predicted from animals. The potential clinical superiority of NEN-42 due to its lower peak liver activity and faster clearance kinetics is suggested.

No. 8

COMPARISON OF 3 TC99m ISONITRILES FOR DETECTION ISCHEMIC HEART DISEASE IN HUMANS.K. McKusick, Massachusetts General Hospital, L. Holman, A. G. Jones, Harvard Medical School, A. Davidson, Massachusetts Institute Technology, Boston, MA, P. Rigo, Univ. Liege, B. V. Sporn, Hospital Pravado Luis Guemes, Buenos Aires, A. Vosberg, Univ. Dusseldorf, C. J. Moretti, Hosp. Henri Mondor, Creteil, P.

To select the Tc-isonitrile with best properties for myocardial imaging, results with Tc-t-butyl isonitrile (TBI; 40 patients) with Tc-carbomethoxy isopropylisonitrile (CPI; 13 patients) and Tc-methoxypropyl isonitrile (MNI; 6 patients) were compared. For feasibility to diagnose CAD, correlation studies were done in those who had exercise induced TI201 defects (ischemia); these were re-examined within 1 month to same exercise level. Images after injection of 4–10mCi Tc TBI(18P), CPI(6P), MNI(2), and again after injection at rest with same agent. Ant., 40° and 70° LAO digital data were acquired at preset timed frames. Each view was divided into 3 segments(S) and 7 segments(S) and 70° LAO images were obtained using an APEX computer interfaced to an Elscint LFOV gamma camera in zoom mode. One attribute of a Tc-99m labeled myocardial agent is ability to measure both ventricular function and myocardial perfusion. The most promising structures which have been identified are the aliphatic C-4 to C-5 ethers, 6 of which have been evaluated pharmacologically. Tc-99m-hexakis-2-methoxy-2-propyl-1-isonitrile (NEN-30) and Tc-99m-hexakis-1-methoxypropyl-2-isonitrile (NEN-42) have the best overall characteristics. Both exhibit good heart extraction in pigs (1.9 and 1.6 ID, T1/2 4 and 2 hours, respectively) and rapid and complete blood clearance (T1/2 1–2 minutes), low lung activity (1.5–2.3% ID) and low peak liver activity (1% and 8% ID) with substantial hepatobiliary clearance (T1/2 approximately 70 and 20 minutes, respectively). In comparison, 30–40% of TBI is extracted into the lung. Initially, this activity clears with a T1/2 of about 15 minutes and is sequestered by the liver from which there is little clearance. Imaging studies in miniature swine, monkeys, dogs and rabbits corroborate these results. In a rabbit coronary artery ligation-release model, neither agent redistributes measurably compared to TBI which shows up to 50% redistribution. Human imaging studies with NEN-10 confirm the biological characteristics predicted from animals. The potential clinical superiority of NEN-42 due to its lower peak liver activity and faster clearance kinetics is suggested.

No. 10


The hexakis(isonitrile)technetium(1) complex of the analog Tc(carbomethoxyisopropyl isonitrile) (CPI) has high myocardial uptake and rapid lung and liver clearance in most animal species, but poor myocardial uptake in the rat and mouse. To evaluate Tc-99m CPI as a myocardial imaging agent in the human, we administered this tracer in 2 normals and in 4 patients with coronary artery disease. In normals, Tc-99m CPI cleared quickly from the lungs and accumulated in the liver and heart. Planar images were of excellent technical quality with high myocardial to background ratios as early as 10 min after injection. The heart to lung activity ratio was 1.7:1, 2.21:1, and 2.0:1 at 10, 30 and 60 min after iv injection of 5mCi Tc-99m CPI. The liver activity peaked at 10–15 min and cleared the hepatobiliary system. Myocardial activity fell gradually with a T1/2 of about 60 minutes activity profile. In 4 patients with CAD, defects corresponding to those seen with TI-201 imaging were present on planar images obtained immediately and at 1 hour after exercise and injection. In 4 patients, radiation had occurred 4 hours. In all 4 patients normal perfusion patterns were observed one hour after reinjection of Tc-99m CPI at rest (4 hours after the initial injection). Tc-99m labeled CPI appears to have excellent physical and biological properties for use in association with myocardial imaging with exercise.

No. 11


Hospital L. Guemes, Buenos Aires, Argentina*, CNEA, Argentina*, Harvard Medical School, Boston, MA* and E.I. du Pont de Nemours, Biomedical Products, Billerica, MA*.

One attribute of a Tc-99m labeled myocardial agent is the feasibility to measure both ventricular function and myocardial perfusion with a single injection. To assess this, 5 normal volunteers and 14 symptomatic patients were injected with 8-10 mCi Tc-99m hexakis(isonitrile)technetium(1) complex at peak semi-recumbent bicycle exercise and again at rest. Thirty msc per frame first pass data, and 5 min. static anterior, 40° and 70° LAO images were obtained using an APEX computer interfaced to an Elscint LFOV gamma camera in zoom mode.
Standard TI-201 stress tests were also done within one month, and were at the same level of exercise.

The left ventricular ejection fraction (EF) increased with exercise (69-76%) in 4/5 normals; perfusion was normal in all five including the one with an abnormal EF response, who also had a normal arteriogram. The EF increased in 4/14 patients, decreased in 6/14 patients, and remained unchanged in 4/14 patients of whom 2 had ischemia and 2 had scar on perfusion imaging. The interpretation of patient Te-CPI perfusion studies generally correlated with the TI studies.

The results support the concept of dual ventricular function and perfusion studies using a single Te-99m labeled myocardial agent, and suggest that this could become the standard radionuclide stress test in the future.

**NEUROLOGY I: RECEPTOR IMAGING (Part 1)**

Moderator: Michael J. Welch, PhD

Comoderator: Dean F. Wong, MD

No. 12

3-(2'-[F-18]Fluorooethyl)spiperone (FESP), a new positron-emitting-labeled neuroleptic tracer, was synthesized in multimicrocurie amounts and used for dynamic characterization of dopamine receptor binding in living primates with positron emission tomography. When non-carrier added FESP (measured specific activity >500 Ci/mmol) was administered IV to nemestrina monkeys and serial PET scans obtained, radioactivity rapidly accumulated in the striatum. The striatum/ratio (low dopamine receptor concentration) ratio increased linearly over time at a rate of 0.02/min. By the end of 4 hrs, the radioactivity ratio striatum/cerebellum was about 5.0. In conjunction with the tomographic studies, arteriolar input function and temporal sequence of radiotracer metabolism were measured in monkey plasma. Chromatographic analyses of plasma extracts showed that FESP metabolites steadily increased with time, with only 5% measured in the FESP fraction 3 hr after IV injection. Temporal activity in striata analyzed by the Patlak plot shows that results are consistent with a two-compartmental model with small efflux of tracer from tissue. Rectilinear scans for a 3 hr period also permitted evaluation of the time course of radioactivity in various organs as well as the excetration mode of the drug. These tomographic studies were preceded by ex vivo experiments in rats followed for several F-18 half-lives. Similar striatum/cerebellum ratios were observed after a 4 hr period.

No. 13


Dept of Psychiatry and Psychology, Karolinska Institute, S-104 01 Stockholm, Sweden

SCH 23930 is a compound with high affinity and selectivity for binding to dopamine-D1 receptors. PET-scan experiments with C-11 labelled SCH 23930 were performed in healthy volunteers (1). The radioactivity in the dopamine rich caudate putamen was threefold higher than in the dopamine poor cerebellum 35 min after injection. There was also more radioactivity in necortical areas than in the cerebellum. The conspicuous accumulation of radioactivity in the caudate putamen was similar to the accumulation of C-11 raclopride, a ligand selective for dopamine-D2 receptors (2). Experiments were also performed in a schizophrenic patient treated with sulphiride, a neuroleptic with high affinity for D2 receptors. The regional uptake of C-11 raclopride in the striatum was reduced to about 15% whereas the uptake of C-11 SCH 23930 was about the same as in the healthy volunteers. These experiments demonstrate that C-11 SCH 23930 and C-11 raclopride are useful as selective ligands for clinical PET-scan studies on central dopamine-D1 and D2 receptors in patients with neuropsychiatric disorders and to examine how pharmacological agents interfere with these receptors.


No. 14


Department of Radiology, Washington University, St. Louis, MO and Department of Chemistry, University of Illinois, Urbana, IL

There is great interest in the application of positron labeled ligands to map the dopamine receptor in vivo. To prepare the commonly used ligands, spiroperidol (SP) and N-methyl-spiroperidol, requires either a multistep low yield synthesis with fluorine-18 or else uses carbon-11 whose 20 minute half-life limits the time of a study. We have prepared a series of fluorine-18 labeled N-alkyl and N-fluoroalkyl spiroperidol derivatives (F-18-methyl-SP; F-18-N-ethyl-SP; F-18-N-propyl-SP; F-18-N-3-fluoropropyl-SP; H-3-fluoropropyl-F-18-SP; H-2-fluoropropyl-F-18-SP; N-2-fluorobutyl-F-18-SP; N-2-fluorophenyl)-F-18-SP; and N-2-fluorohexyl-SP). The lipophilicity of these ligands (log octanol/water partition coefficient) varies from 2.7 to 5.5 and the initial brain uptake in rats; measured at 2 minutes, was greatest with the methyl, ethyl, and propyl derivatives.(1) The highest striatum/cerebellum values 1 hour after administration were obtained with the N-methyl, N-propyl, and N-3-fluoropropyl derivatives, while that N-2-fluorobutyl showed the greatest uptake of total activity in the brain at this time. The uptake of all these ligands in the striatum could be blocked by cold SP showing the striatal uptake to be by the dopamine receptors. This work suggests that other ligands more readily prepared than those currently in use may be substituted for in vivo studies.

No. 15

Imaging of MPTP-induced change in turnerover and damage to striatal dopamine. C.C. Chiuheh and G. Firmau.

Clinical Brain Imaging Section, Natl Inst of Mental Health, Bethesda, MD and Dept of Nuclear Medicine, McMaster Univ Medical Centre, Hamilton, Ontario, Canada.

1-Methyl-4-phenyl-1,2,3,6-tetrahydrodopridine (MPTP) is a specific dopamine neurotoxin to the nigrostriatal system. It produces a parkinsonian syndrome in man and monkey. MPTP acutely decreases the turnerover of striatal dopamine while two to three weeks later it causes an irreversible lesion of the dopaminergic system. In these studies, the MPTP-induced damage was determined either neurochemically or histologically at autopsy.

In the present study, we employed a PET brain dopamine imaging procedure (Garnett et al., 1983) by using 6-18F-
L-dopa (Firnau et al., 1984) and McMaster PET scanner (Nahmas, 1984) to visualize the effect of M3P in anesthetized rhesus monkeys.

The PET procedure was used to monitor repeatedly the changes in dopaminergic activities in an MPTP-treated monkey for 15 days. The determination of 18F-dopa increased sharply three days after MPTP and then declined sharply ten days later. Furthermore, we compared in tandem the 18F-PET activity in the basal ganglia measured in vivo with the striatal content of endogenous dopamine assayed postmortem in control, subclinical, clinical and severely affected parkinsonian monkeys. There was a linear relationship between the logarithm of the percent decrease in the content of endogenous dopamine and the decrease in specific 18F-dopamine PET activity in these parkinsonian monkeys. This preclinical trial has demonstrated that the degree of brain damage and/or turnover in living parkinsonian monkeys appears to be quantifiable by the PET imaging procedure.

No. 16
THE EFFECT OF LITHIUM ON DOPAMINE RECEPTOR BINDING OF C11-N-METHYLSPERIONE IN THE LIVING HUMAN BRAIN.

Lithium is widely used in the treatment of bipolar affective disorders. In the study of dopamine receptors in depressed patients, it may be undesirable to risk cessation of lithium therapy. Animal studies of the effect of lithium on dopamine receptors have been inconclusive, some suggesting a decrease in receptors and others no change. Therefore, we examined the effect of lithium administration on normal volunteers, who had C11-N-methylspiperone (NMSP) PET studies of D2 dopamine receptors before and following administration of therapeutically relevant doses of oral lithium. Each subject was maintained on a plasma level of least 0.7 mEq/1 of lithium for at least 1 month before the second study. In 6 subjects there was an increase in the index of the rate of binding of NMSP to the dopamine receptors in the caudate nucleus, i.e. the slope of the straight line relating the caudate/cerebellum ratio to time. The slope averaged 0.0114 ± 0.0072/min., which represents an increase of 7-30%. In the sixth subject the slope fell to 0.00016/min., a 0.24% decrease. The increase was statistically significant (p<0.05) on the basis of a paired t test. Reproducibility studies in normal subjects, have shown changes of less than 5-10%.

No. 17
SERIAL [18F]-N-METHYLSPIROPERIDOL (18F-NMS) PET STUDIES MEASURE CHANGES IN ANTIPSYCHOTIC DRUG D2 RECEPTOR OCCUPANCY IN SCHIZOPHRENICS.
M. Smith, Psychiatry Dept., SUNY at Stony Brook, Stony Brook, NY; A.P. Wolf, C.-Y. Shiue, J.S. Fowler, J.A.G. Russell, C. Ross, G. Pearlson, J.D. Brodie, Psychiatry Dept., NYU Medical Center, NY.

Using [18F]-N-methylspiroperidol, a potent butyrophenone neuroleptic, and PET, we have developed a method for probing the effects of antipsychotic drugs at their presumed locus of action. Six schizophrenic subjects taking haloperidol or chlorpromazine underwent two 18F-NMS PET studies, the first 2 hours after receiving their usual dosage of antipsychotic medication and the second after a 24 hour drug-free interval. Plasma samples were obtained for therapeutic drug levels. Cerebral radioactivity distribution and plasma 18F-NMS concentration were measured for up to 5 hours from time of injection. The relative rate of dopamine receptor binding was estimated by the slope of the basal ganglia/cerebellum activity ratio versus time. Therapeutic drug dose and plasma level were highly correlated with this measure. The 24 hour therapeutic drug withdrawal resulted in a significant increase of tracer uptake in the basal ganglia reflecting appreciable clearance of the antipsychotic drug from the D-2 receptor. This is the first report of a PET method which measures the effect of alterations in antipsychotic drug plasma level on central D-2 receptor blockade. A further evaluation of the clinical management of schizophrenia relative to therapeutic drug dosage and dosing interval is now feasible.
21M, 39-77y, 860.5y) suffering from colorectal cancer were examined without knowledge of the results of other investigations. Serum CEA ranged from 1.3 to 2000 ng/ml. 3 Mabs (35, 25, 19) were used either as Fab (1-2) (n=14) or Fab (n=20) fragments. 5 patients were excluded from evaluation because of lacking further work-up. 2/2 primary and 8/9 recurrent tumors were correctly diagnosed with 1 false positive (FP) and 1 false negative (FN). 18/21 liver involvements suspected by immunoscintigraphy were subsequently confirmed (0 FN, 3 FP). Correct diagnosis of peritoneal involvement was made in 1/2. There were two true positive (TP), 5 FP and 1 FN lung, 4 TP, 1 FP and 1 FN osteogenic metastases.

These preliminary prospective data show that immunoscintigraphy gives satisfying results in the detection of local recurrences and liver metastases of colon carcinoma. In the lungs several FP were observed and not enough data are yet available to assess its value for the diagnosis of peritoneal and node involvement.

No. 20

RIS should now be past the stage of anecdotal success yet there are few prospective studies or definitions of its clinical purpose. RIS in colorectal cancer is accurate but of little use in detecting primary tumours because endoscopy and radiology are reliable. Uptake in excised tumour specimens taken 24-48h after patient received 3.5 mCi In-111 anti-CEA (American International) as % administered dose per gram was Mean 7.0 x 10-3%/G (range 0.03-206 x 10-3%/G for tumour weights between 3.95 and 25.55G).

Tumour to normal uptake ratio was Mean 4.95 (range 2.04-9.54). Lymph node uptake was Mean 4.7 x 10-3%/G (range 0.7-13.3 x 10-3%/G) and node to normal ratio was Mean 6.92 (range 0.4-21.9). Tumour to node ratio was Mean 3.95 (range 0.26-7.75). These results, taken with pathological findings, may have implications for prognosis as well as in vivo staging. RIS was most clinical use in follow-up, identifying whether pelvic x-ray CT masses were due to tumour recurrence (positive uptake) or fibrosis (no uptake).

A prospective study in ovarian cancer showed RIS cannot distinguish whether or not a pelvic mass is due to ovarian cancer. A single blind, biopsy controlled study (54 sites) showed that RIS, with kinetic analysis and probability mapping, has a role in identifying peritoneal seedlings, clinically negative recurrences and in evaluating chemotherapy.

Efforts should now be directed in controlled trials at the clinically important or difficult problems and not in imaging the obvious.

No. 21

12 patients with oat cell carcinoma and 28 pat. with epidermoidal carcinoma of the lung, have been studied using the fragments Fab (1/2) of a monoclonal antibody raised against CEA (pFO23C5-SOBIN BIOMEDICA) labelled with 131I or 111In. We succeeded in imaging all primary tumours and, in the field of metastatic lesions, we were able to detect 4 out of 7 bone metastases and all the recurrences in brain, liver, lymphnodes and skin.

Furthermore, 30 unexpected "hot spots" of the chest and other areas of the body were investigated; of these, 23 have been confirmed as neoplastic lesions in the follow-up. In 5 patients already submitted to operation, we found neoplastic spreading when other radiological investigations were negative. 3 patients with chronic pulmonary disease were studied with immunoscintigraphy because of their doubtful X-ray findings and resulted true negative. In four patients with positive scans an equal amount of a non specific MoAb raised against melanoma has been injected as negative control: no positive scans have been obtained in any cases.

No. 22
THE POTENTIAL UTILITY OF 111In-LABELLED OC-125 ANTIBODY IN PATIENTS WITH GYNECOLOGICAL TUMORS. P.W. Doherty, T. Griffin, M. Rusckowski, M. Gionet, R. Hunter, D.J. Hnatowich. University of Massachusetts Medical Center, Worcester, MA.

Monitoring the response to therapy of these tumors, particularly ovarian cancer, is difficult; frequently requiring surgical re-staging. The finding of elevated levels of the antigen (CA-125) in the majority of these patients with recurrences lead us to evaluate the utility of using the antibody (OC-125) to this antigenic determinant for radiolabeled detection. We studied 11 patients (ovarian n=8) whose tumor status was documented by surgery (n=8) or biopsy (n=3) and correlated the results of imaging with their CA-125 levels and other studies (CT scans). Following the infusion of 1 mg of the Fab (1/2) fragments (1-2 mCi In-111) quantitative SPECT and planar imaging was obtained daily for 72 hours along with analysis of serum. Mean doses to the liver and kidneys of 2.6 and 2.1 V/Rads/mCi were lower than we observed with other antibodies and this was associated with a slower blood clearance (T 1/2 24 hours).

The images of sites of tumor recurrence were of surprisingly good quality and correlated well with surgical and CT scan findings. There were 6 true positives, 3 of whom had normal CA-125 levels, with one false positive and one false negative. Those with multiple small metastatic nodes showed a pattern of diffuse uptake which increased with time, whereas those with nodal or larger recurrences showed more focal uptake. The combination of favorable biodistribution and positive images, especially in patients with normal antigen levels, suggest a role for OC-125 imaging in their management.

No. 23

We have shown in previous studies that 1-131 labelled monoclonal antibody (MAB) 3F8 can image human neuroblastoma tumors. 3F8 is an IgG3 murine monoclonal antibody specific for the ganglioside GD2. The GD2 is known to be present on neuroblastoma, melanoma and osteogenic sarcoma, but does not appear on normal human tissue except neurons. We report here our experience with 20 patients (13 neuroblastoma, 7 melanoma and 2 osteogenic sarcoma). Three to 5 mCi of 1-131 labelled MAB was administered intravenously and the patients imaged daily for 3 to 5 days. Strong focal accumulations were seen in neuroblastoma tumors with tumor-to-normal tumor ratios ranging from 10:1 to 20:1. Osteogenic sarcoma tumors also...
showed strong uptake, but the uptake by melanoma was not as strong and in addition showed wide heterogeneity. No non-specific uptake in normal bone, liver, spleen, or brain was observed. Time-activity curve showed activity half-times of approximately 10-20 hours for blood, 30 hours for normal tissue, and 60 hours for tumors. Our results indicate that the 3F8 MAB is a good agent for imaging of neuroblastoma, osteogenic sarcoma and some melanomas, and has potential for therapy.

1:30-3:00

GASTROENTEROLOGY II: HEPATOBILIARY

(Part 1)

Moderator: Darlene M. Fink-Bennett, PhD
Comoderator: Aldo N. Serafini, MD

No. 24

The increased incidence of cholelithiasis in morbid obesity may not be entirely explained by abnormalities in bile composition as a functioning gallbladder (GB) could theoretically evacuate cholesterol crystals prior to stone formation. Fasting GB volumes (vol) were determined ultrasonographically (U/S) and 90-minute postprandial radionuclide GB emptying studies using Tc-99m DISIDA and In-113m DTPA in 10% cream, were performed in 18 morbidly obese subjects (9 M and 9 F) and in 18 age and sex-matched volunteers (+20% of ideal weight).

For emptying of cream was similar in the two groups t 1/2 5 20 (min) (SD) for the obese and 75 ± 20 for the normals (p > .05).

The integrals of the increase of cholecystokinin (CCK) were similar in the obese, 625 ± 197 (pmol/L) min) and in the normals, 617 ± 192 (p > .05). The obese had lower GB ejection fraction (EF) (EF) = 74 ± 14% (p < .02).

Fasting GB vol were greater in the obese, 71 ± 14 mL than in normals, 61 ± 14 mL (p < .005). Calculated postprandial GB vol (fasting vol X EF/100), were greater in the obese, 36 (+ 22) mL than in normals, 7 (+ 6) mL. U/S GB were acalculus.

Bile stasis may be a factor contributing to the increased risk of cholelithiasis in morbid obesity.

No. 25
GD-DISIDA - A POTENTIAL CONTRAST AGENT FOR MR IMAGING OF HEPATOBILIARY SYSTEM. G.B. Saha, B. Bateson, T. Meaney, R.T. Go, R.J. MacIntyre, J.K. O'Donnell, D.H. I Felgin, Cleveland Clinic Foundation, Cleveland, OH.

The objective of this study was to evaluate gadolinium-dlisisopropyl iminodiacetic acid (Gd-DISIDA) complex as a potential paramagnetic contrast agent for magnetic resonance imaging (MRI) of the hepatobiliary system. GD-DISIDA was prepared by mixing Gd and DISIDA solutions at appropriate chemical conditions and adjusting pH to 7.5. The yield was determined by thin layer chromatography (TLC) using Gd-153 as the radiotracer and found to be 97 ± 3%. The complex was found to be stable both in vivo for 24 hrs, determined by dialysis of the plasma sample, and in vitro over a period of 4 days determined by TLC. Approximately 0.05 mmol/kg of Gd-

DISIDA was injected intravenously into each of a group of 5 Swiss mice. Normal and injected mice were sacrificed 30-35 min after injection and different organs were removed and wiped. T1 and T2 values of all tissue samples were measured at 20 MHz on an IBM PC-20 spectrometer. T2 values did not change significantly with Gd-DISIDA. T1 values of the normal liver were reduced by almost 56%. No significant change in T1 was observed in kidneys, lungs, heart and spleen with this agent. The T1 values of blood decreased by almost 55%. MRI of the liver obtained in rabbits on a 1.5 Tesla machine prior to and 30-35 min after injection of 0.05 mmol/kg of Gd-DISIDA. Excellent contrast enhancement was observed. Nearly 50-60% decrease was obtained in T1 values calculated from the pre- and post-injection images. These results indicate that Gd-DISIDA may be a potential contrast agent for MRI of the liver.

No. 26
CHOLECYSTOKININ (CCK) CHOLESCINTIGRAPHY (C) IN ACALCULOUS BILIARY DISEASE (ABD). D. Fink-Bennett, P. DeRidder, W. Kolozs, R. Gordon, J. Rapp. William Beaumont Hospital, Royal Oak, MI and Northern Columbus County Hospital, Salem, OH.

We retrospectively analyzed the max. gallbladder (GB) ejection fraction response (EFR) to CCK in 374 symptomatog (neg. GB US) pts. and 27 "normal" (asymptomatoc) volunteers (NV).

Pts. received 5 MCI of Tc-99m Disofenin. Post-max. GB filling, 0.02 ug/kg CCK was infused. GBFRS were determined q.5 min X 4 by pre-CCK - post-CCK/pre-CCK GB cts.

Symptomatic Patients
CC EF < 35%
Surg. DX Med. DX
Surg. DX Med. DX
CC 108 69 7 9
Normal GB 7 13 4 110
Lost to FU 18 9
Predictive Value Surg. pts. 94%; All pts. 90% (CC - Chronic Cholecystitis; FU - Followup)

In 9/27 NVs max. GBFRS were > 35%: unexpectedly, 16/27 < 35%, 2 non-calculable. 2 NVs have stones, 5 delayed GB filling or biliary-to-bowel transit (B-B-T). I symptoms (Surg. scheduled), 1 NV no EF obtained has stones, 1 delayed B-B-T.

CCK C can reliably confirm the clinical impression of ABD. It detects GB disease whether symptomatic or asymptomatic.

No. 27
SENSITIVITY (SENS), SPECIFICITY (SPEC), AND ACCURACY (ACC) OF CCK CHOLESCINTIGRAPHY (C) IN ACALCULOUS BILIARY DISEASE (ABD).

L. Swayne, F. Palace, J. Rothenberg, D. Heitner, and J. Trivino. Morristown Memorial Hospital, Morristown, NJ.

87 patients (pts.) were prospectively studied with CCK-C to determine the SENS, SPEC, and ACC of this modality in the detection of ABD. All patients had symptomatology suggestive of gallbladder disease of at least six months duration, and each had an ultrasound study demonstrating no stones. After an overnight fast, each pt. was administered 5 MCI of technetium-99m Hepatolite. At maximal gallbladder filling (60-90 min.), 0.02 ug/kg CCK was infused IV over 5 min. followed by a 40 min. computer acquisition. A latent period, ejection period, ejection rate, and gallbladder ejection fraction (GBEF) were calculated from background subtracted images. A GBEF < 35% was considered indicative of ABD.
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EMERGENT TC-99m DISOFENIN HEPATOBILIARY SCINTIGRAPHY: CLINICAL EFFICACY AND COST-EFFECTIVENESS. F. Gagliardi, J. Sulzer, C. MacDonald and P. Hoffer, Yale University School of Medicine, New Haven, CT.

This study investigated whether hepatobiliary scintigraphy performed outside of regular hours influenced patient care during the time interval before a scheduled study would have been available and whether the cost savings generated offset costs of providing the service. Charts of all 38 patients having off-hours hepatobiliary during a 17 week period were reviewed. Of the 28 scans on outpatients 13 were normal; 5 of these patients were not hospitalized. Admitting these patients for scanning the next working day would have cost at least $3000, compared to a cost of $1360 providing the scans emergently. 23 patients were admitted; 9 with normal scans were admitted with diagnoses other than biliary disease. Of 14 outpatients with abnormal scans, 10 had confirmed cholecystitis (mean time since surgery 3-6 days), 2 elected for later surgery, and 2 had non-diagnostic scans due to fasting. 2 patients not admitted in spite of scans diagnostic of acute cholecystitis had gangrenous cholecystitis confirmed at 7 and 10 days. In the 10 inpatients studied no diagnosis of biliary disease was made (8 normal, 2 non-diagnostic scans). Emergent hepatobiliary scans expedite outpatient management: cost savings generated offset the cost of providing the service. Although surgery followed diagnostic scans by several days, non-diagnostic scans due to post-admission fasting were probably minimized. The most efficacious use of emergency scans was in determining whether to admit patients who did not require admission on clinical grounds alone.

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THE SENSITIVITY AND POSITIVE PREDICTIVE INDEX OF BILIARY NONVISUALIZATION IN TOTAL BILIARY OBSTRUCTION. M.L. Lecklitner* **, A.R. Austin*, A.R. Benedetto**, and G.W. Growcock**. University of South Alabama Medical Center, Mobile, AL and University of Texas Health Science Center, San Antonio, TX.

Hepatobiliary findings demonstrating concurrent nonvisualization of gallbladder, common bile duct, and intestinal activities have been considered to be indeterminate, indicating an uncertainty as to whether a medical or a surgical disease caused the nonvisualization. The sole purpose of our study was to determine the sensitivity and positive predictive index of hepatobiliary scintigraphy in diagnosing total biliary obstruction (TBO), using TC-99m DISIDA, 8 mCi, in 401 adult patients and continuing the acquisition to 4 hrs, given the nonvisualization of the aforementioned structures. Of 26 patients having had fasting for a period of 3-4 hrs prior to the study, and no patient was receiving parenteral nutrition at the time of imaging. We identified 26 patients who fulfilled the above criteria. One patient was removed from the study, because he departed the emergency service against medical advice following his study. Twenty three of the remaining 25 patients had surgically-documented evidence of TBO. Two false-positive studies were encountered.

No. 31

SCATTER MEASUREMENTS USING DUAL ENERGY WINDOWING IN PET. W.R. Hong. University of Texas Graduate School of Biomedical Sciences, Houston, TX.

The scatter events in PET quantitation has been the most difficult error to correct. One has to understand the scatter distribution for the object to be imaged in order to device method to correct the scatters. An obvious way to measure the scatter is to image with a high energy-acceptance-window to reject the scatters and then image with a lower or regular energy window. This paper states the accuracy and practicality of this method. This study found that to reject most of the scatters in a 20 cm phantom, the energy window will have to be set at about 500 KeV. Since the energy detection response of the detector for true 511 KeV gamma is constant and can be measured on the bench, the counts collected at the high window setting can be normalized to that of the low/normal window to estimate the true counts in the normal window run. The difference between the extrapolated true count and the total counts collected at
the normal energy window will be the scatters. Error analysis based on the detector photopeak efficiency for BGO scintillators, 20 cm phantom, and 5 millions events per image with the normal window, the scatter measurement error is about 20% for each 6x6mm pixel. The data collection period can be extended longer than normal to lower the error, but the distribution of activity should remain fixed in the extended period. This dual-energy technique can only be used for directly measuring scatters but cannot directly improve the accuracy of extracting the true events with the normal window in routine studies. This method can be used as a gold standard to judge the accuracy of other scatter correction methods which can be easier to use in routine clinical studies.

No. 32
EVALUATION OF SCATTER CORRECTION METHODS IN SPECT.
M.C. Cilardi, V. Bettinardi, C. Pantalone, A. Todd-Pokropski, P. Cerussini, and F. Fazio. CNR, University of Milan, Istituto S. Raffaele, Milan-Italy, and University College London, UK.

The detection of Compton scattered radiations results in qualitative degradation and quantitative inaccuracy of images in SPECT. Aim of this study was to evaluate and compare three scatter correction methods. The first, proposed by Axelsson et al., consists in a convolution and subtraction of scattered events from the measured projection data. The second, by Jaszcak et al., is based on the subtraction of a fraction of Compton events (92-125 keV) from the photopeak data (140 keV, 20% for Tc-99m) after reconstruction. The third, developed by Todd-Pokropski et al., is based on a weighted subtraction of the filtered Compton events from the photopeak data, before reconstruction. Line spread functions were measured at various distances (d) of the source from the center of rotation in air and scattering medium. A slight improvement in spatial resolution (2.6% reduction in FWTM) was found after scatter correction for all three methods. Ratio between corrected and measured counts (d=0) was 0.81, 0.80, 0.76 for the 1st, 2nd and 3rd method respectively; these results agreed with the theoretical expected scatter fraction of 0.78 evaluated by Monte Carlo technique. A 25% increase of contrast, calculated on cold lesions, was found for all three techniques. Recovery on hot lesions (6-4 cm), for each lesion to background activity concentration ratio, was measured to be within 100%, 5%, 4% from the expected value (100%) for the 1st, 2nd, 3rd method respectively. Clinical cerebral perfusion studies show improvement of image quality following scatter correction.

No. 33
The use of 1-D and 2-D scatter deconvolution techniques for contrast enhancement and quantification in SPECT.

Introduction: A major part of photon interactions with body-tissue in most nuclear medicine applications is due to Compton scattering. In SPECT, the loss of primary photons may be compensated for by some accurate attenuation correction algorithm but large fractions (20-40%) of falsely positioned events may still be present due to insufficient scatter rejection capability of the detectors presently used. In this paper, we present the use of 1-D and 2-D post-acquisition scatter correction techniques for SPECT.

Method: Both methods are based on deconvolution of projections with a scatter distribution function before image reconstruction. The 1-D scatter distribution function is obtained from measurements of a line-source in water (and the ordinary energy discriminator window). This function operates pixel by pixel along each 1-D projection of a section. Axial variations of radioactivity may taken into account by this method. This is done with the 2-D correction method which is based on measurements of a point-source in water. A 2-D convolution kernel is calculated recursively from these data into a 31x31 matrix for subsequent 2-D convolution of the projected views (64x64 pixels).

Results and conclusions: Phantom measurements and patient studies show how both techniques improve detector contrast and quantification in SPECT. The 2-D correction technique seems to produce slightly better results than the 1-D technique, but the latter may be preferable in routine applications due to shorter reconstruction time.

No. 34
AREA WEIGHTED APPROACH TO ATTENUATION CORRECTION IN SPECT USING ARBITRARILY SHAPED NON-UNIFORM ATTENUATION MAPS.
R.B. Schwingler, S.L. Cool, and M.A. King. University of Massachusetts Medical Center, Worcester, MA, and Analogic Corporation, Wakefield, MA.

A different approach has been considered in the development of an attenuation correction algorithm for use in SPECT. This new algorithm takes advantage of the fact that any one pixel in a transverse section image to be corrected is incrementally attenuated by at most, through its nearest neighbors at any projection angle. Therefore, an area weighted sum of these three neighboring pixels (attenuation coefficients) can be performed. Also assumed is that a pixel will attenuate one half its own activity. These properties are incorporated into an efficient row by row column by column correction algorithm which can be used as a gold standard in clinical applications due to shorter reconstruction time. This method can be used as a gold standard to judge the accuracy of other scatter correction methods which can be easier to use in routine clinical studies.

No. 35
IMPROVED SPECT USING SIMULTANEOUS TRANSMISSION AND EMISSION TOMOGRAPHY.
B.F. Hutton, D.L. Bailey, P.J. Walker, Royal Prince Alfred Hospital and NSW Institute of Technology, Sydney, N.S.W. 2050, Australia.

The accuracy of attenuation correction, essential for SPECT quantitation, can be improved by determination of a valid body outline and map of attenuation coefficients (a) for each tomographic slice. A method has been developed for simultaneous recording of transmission and emission tomography to provide this information in a practical time.

A dual radionuclide SPECT acquisition is performed with a transmission source attached to a rotating gamma camera, of lower energy than the emission radionuclide. A suitable source for Tc-99m studies is O2-153 (103 kov). The lower energy window includes scatter from the emission source which must be removed prior to reconstruction. The geometric map is formed for each conjugate pair of images in both energy windows. The scatter can be predicted by convolving each upper energy image pair with an experimentally determined biexponential scatter function and scaling by the appropriate factor (k=0.60). Both the scatter function and fraction must be determined for the particular pair of radionuclides and can be shown to be relatively independent of activity distribution. After scatter correction the transmission data are...
The proximal femur affords excellent discrimination of bone mineral density (BMD) for the neck and trochanter regions of the femur was 35% lower (Z-score = 1.6). Measurement of BMD for the radius and 25% lower (Z-score = 1.4) while the Ward's triangle of the lumbar spine was 8% below the age-matched controls (Z-score = 0.4). Furthermore, oestrogen prophylaxis of bone-loss was shown to be effective in all parts of the skeleton. Finally it is concluded that bone loss in the early menopause is a generalized phenomenon including all parts of the skeleton.

### BONE/Joint I: Bone Mineral Analysis

#### (Part 1)

**Moderator:** Heinz W. Wahner, MD, MS  
**Comoderator:** C. Robert Appledorn, MS

#### No. 36

**Bone Mineral Densitometric Analysis of Disuse Osteoporosis in Paraplegics.** E.B. Silberstein, University of Cincinnati Medical Center, Cincinnati, OH.

The paraplegic patient is at risk for lower extremity fracture not only because of loss of sensation but because of a reported high prevalence of disuse osteoporosis. We have attempted to provide early detection of tibial osteoporosis, quantify its progression and evaluate the effect of computerized electrical muscle stimulation on the disorder using dual photon bone mineral densitometry (BMD).

Appropriate patient positioning for high precision measurements of tibial trabecular bone density was first developed using conventional femoral head software on normal volunteers in various positions and then employing new prototype software (Lunar Corp., Madison, WI).

Normal values for the target population (15-40 yrs) were:

<table>
<thead>
<tr>
<th>Region</th>
<th>Male Mean BMD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tibia</td>
<td>0.97</td>
<td>0.72-1.11</td>
</tr>
<tr>
<td>Central</td>
<td>0.99</td>
<td>0.70-1.10</td>
</tr>
<tr>
<td>Female Tibia</td>
<td>0.80</td>
<td>0.72-0.85</td>
</tr>
<tr>
<td>Central</td>
<td>0.78</td>
<td>0.67-0.89</td>
</tr>
</tbody>
</table>

Studies on ten paraplegic osteoporotic patients have shown a bone mineral loss exceeding 3% in 6 months in the majority, with higher BMD levels in patients involved in the electrically stimulated exercise program.

We conclude that BMD can detect early disuse osteoporotic in the tibia of paraplegics and evaluate the effect of exercise on this process.

#### No. 37

**Bone Mineral Density in Osteoporosis.** R.B. Marezza, N. Ettinger, and E. Schulz. University of Wisconsin, Madison, WI. Osteoporosis Bone Diagnostic Laboratories, Stuart, FL and Lana Linda University, Lana Linda, CA.

Bone mineral density (BMD) was measured in 158 normal young women, 244 normal older females and 26 women with hip fractures. Density of the lumbar spine and proximal femur was measured using dual-photon absorption densitometry (Gd-153) and the radius shaft was measured using single-photon absorption densitometry (I-125). The BMD in the older women with no fractures was about 20% below young normal women (age 20-39) for the radius and spine, and 30% below for the femur. The BMD in hip fracture cases was 8% below the age-matched controls (Z-score = 0.4) for the radius and 10% for the spine (Z-score = 0.6). The BMD for the neck and trochanter regions of the femur was 25% lower (Z-score = 1.4) while the Ward's triangle region was 35% lower (Z-score = 1.6). Measurement of the proximal femur affords excellent discrimination of early fracture risk of the hip compared to either the radius or the spine.

<table>
<thead>
<tr>
<th>Location</th>
<th>Control Mean BMD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Femoral Neck</td>
<td>1020</td>
<td>746-1057</td>
</tr>
<tr>
<td>Ward's Triangle</td>
<td>946</td>
<td>599-1074</td>
</tr>
<tr>
<td>Trochanter</td>
<td>803</td>
<td>643-929</td>
</tr>
<tr>
<td>Spine L2-L4</td>
<td>1267</td>
<td>962-1629</td>
</tr>
<tr>
<td>Radius Shaft</td>
<td>700</td>
<td>566-1141</td>
</tr>
</tbody>
</table>

### No. 38

**Age-Specific, Longitudinal Bone Loss Rates at Multiple Cortical and Trabecular Skeletal Sites.** R.D. Wasnich, J.M. Vogel, P.D. Ross, and L.K. Neibrom. Kaukini Medical Center and John A. Burns School of Medicine, Honolulu, HI.

Serial bone mineral content (BMC) measurements were obtained at yearly intervals, over a 4.5 year followup, in 1098 women ranging in age from 43 to 81 years. Lumbar spine (LS) BMC was measured by dual photon absorptiometry, and os calcis (OC), distal radius (DR), and proximal radius (PR) BMC by single photon. For the entire cohort, the greatest yearly, mean loss rates were observed for the OC (-1.7%), followed by DR (-1.3%) and PR (-1.0%). These results were lower, but proportionate to, the rates predicted by cross-sectional data on the same cohort. However, LS BMC, instead of showing the expected loss, showed a consistent positive change of (+5-6%), probably related to technical factors.

By 5 year age groups, BMC loss rates were -2.3% (under age 54), -1.7% (age 55-59), -1.4% (age 60-65), -1.7% (age 65-69), and -2.4% (over age 70). This heterogeneity of loss rates was also mirrored at the other appendicular sites. These findings suggest that rapid bone loss may occur in the older (>70 yrs) female, equal to that seen in the immediate postmenopausal years. The results also confirm marked heterogeneity of loss rates not only between individuals, but also in the same individual on a year-to-year basis. Loss rates also appear to be proportionate to the trabecular bone content of the measurement site.

#### No. 39

**Spontaneous and Oestrogen Caused Bone Changes in Early Postmenopausal Women: A Local or Generalized Phenomenon?** C. Christiansen, A. Gottfredsen, L. Nilas, B.J. Riis, K. Thomsen. Glostrup Hospital, Glostrup, Denmark.

Regional values of bone mineral content (BMC) and bone mineral density (BMD) from a total body dual photon absorptiometry (DPA) scan were calculated in fifty-two similar placebo treated women. The six regions were head, arms, chest, spine, pelvis, and legs. Moreover values of lumbar spine BMC and PR (-1.3%) followed by OC (-1.7%), and PR (-1.0%). These results were lower, but proportionate to, the rates predicted by cross-sectional data on the same cohort. However, LS BMC, instead of showing the expected loss, showed a consistent positive change of (+5-6%), probably related to technical factors.

By 5 year age groups, BMC loss rates were -2.3% (under age 54), -1.7% (age 55-59), -1.4% (age 60-65), -1.7% (age 65-69), and -2.4% (over age 70). This heterogeneity of loss rates was also mirrored at the other appendicular sites. These findings suggest that rapid bone loss may occur in the older (>70 yrs) female, equal to that seen in the immediate postmenopausal years. The results also confirm marked heterogeneity of loss rates not only between individuals, but also in the same individual on a year-to-year basis. Loss rates also appear to be proportionate to the trabecular bone content of the measurement site.

<table>
<thead>
<tr>
<th>Location</th>
<th>Young Mean BMD</th>
<th>Old Mean BMD</th>
<th>California Mean BMD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Femoral Neck</td>
<td>1020</td>
<td>746</td>
<td>597</td>
</tr>
<tr>
<td>Central</td>
<td>946</td>
<td>599</td>
<td>407</td>
</tr>
<tr>
<td>Trochanter</td>
<td>803</td>
<td>643</td>
<td>491</td>
</tr>
<tr>
<td>Spine L2-L4</td>
<td>1267</td>
<td>962</td>
<td>889</td>
</tr>
<tr>
<td>Radius Shaft</td>
<td>700</td>
<td>566</td>
<td>519</td>
</tr>
</tbody>
</table>

BONE MINERAL DENSITY (mg/cm²) AT SEVERAL LOCATIONS

<table>
<thead>
<tr>
<th>Location</th>
<th>Young Range</th>
<th>Old Range</th>
<th>California Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Femoral Neck</td>
<td>746-1057</td>
<td>599-1074</td>
<td>597-1074</td>
</tr>
<tr>
<td>Ward's Triangle</td>
<td>599-1074</td>
<td>407-1074</td>
<td>407-1074</td>
</tr>
<tr>
<td>Trochanter</td>
<td>643-929</td>
<td>491-929</td>
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</tr>
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<td>566-1141</td>
<td>519-1141</td>
<td>519-1141</td>
</tr>
</tbody>
</table>

The purpose of this study is to evaluate the differential effect of primary hyperparathyroidism (HP) on cortical (Cr) and trabecular bone (TB) with the use of single and dual photon absorptiometry (SPA and DPA) in 13 patients (pts) with HP confirmed by parahormoneRIA T1-201 scintigraphy, and surgical localization of parathyroid adenoma. Two males and 11 females, ages 36 to 76 years, mean 61, were examined with SPA and DPA utilizing standard methodology validated in our laboratory. Paired t test analysis was performed to determine significant differences from age matched normal group data.

The result reveals significant reduction in 11 of 13 patients (with the mean approx. 2 standard deviation (SD) below the age matched normal mean) in bone mineral (BM) content of the radius, as measured by SPA. The mean value was 0.511 G/cm (SD 0.127), range 0.346-0.720 G/cm, versus (VS) 0.611 G/cm (predicted normal mean (PBNM)) There was a significant decrease in BM density of the lumbar spine (+2 SD) as measured by DPA in 11 of 13 pts, mean 0.851 G/cm2 (SD 0.156), range 0.668-1.048 G/cm2 vs 1.048 G/cm2 (PBNM).

Whereas it has been reported that midradius BM content is insensitive to the effects of HP, our population demonstrated significant reduction of BM of both lumbar spine and midradius sites suggesting active resorption of both TB and CB.


Re-analysis of our spine mineral measurement by dual photon absorptiometry (DPA) data base was performed for the osteoporosis patients under the management of one bone endocrinologist (FOK). There are now 77 patients with serial measurements of L-2 through L-4 by DPA using uniform data reduction by the same analysis software and edge finder. Patients were categorized as 32 Normal Menopause (NM), 11 Premature Spontaneous Menopause (PM), 4 Surgical Menopause (SM), and 30 Idiopathic Osteoporosis (IO) that was not, hypogonadal and 0.2%/yr at 6.17-52 yrs. Of the 167 who had metastases detected, 160 (95%) had metastases detected outside the neck. Eight (5%) had metastases confined to the neck. Seventy-six % had metastases detected at the initial surgery or initial postsurgical scan. The yearly cumulative incidence curve of detection of metastases after the primary surgery and scan was 16%/yr, 0.2%/yr from 0.6-7.3 yrs, and 0.17%/yr for 7.3-23.5 yrs. If the follow-up % uptake and scan show no significant remnant at 1 year and 3 years, patients should be asked to return every 5 years as long as they live.


The dose of radioiodine (I-131) used to survey patients for metastatic thyroid cancer varies from 0.2 mCi to 30 mCi, and has not been based on experimental data. Higher doses occasionally reveal smaller lesions, but deliver more radiation to the patient. We asked which dose would be sufficient to detect metastatic deposits. Using a 13 liter water tank with small-source phantoms and two gamma cameras, we sought to determine: 1) the minimum imageable activity and volume of I-131, 2) effects of background and source depth on detectability, and 3) the practical I-131 tracer dose based on these findings. In volumes of 10 to 300 ul, the lowest activity detectable at the surface (without background) was 0.03 uCi, and at 10 cm depth, 0.10 uCi. Background activity at 0.01 uCi/ml resulted in a three to tenfold loss of detectability; computer subtraction of background did not improve results.

Assuming uptake of 0.05%/gram and % effective of 3 days, 200 mCi is sufficient to impart 5000 rad to a 30 ug tumor, the smallest that can be sufficiently treated by the beta particles of I-131. At an uptake of 0.05%/gram, the above results indicate that a 2 mCi tracer dose would detect a 30 ug lesion, but only at the surface and without background radioactivity. With patient motion and background activity, some potentially treatable lesions may not be detected even with 30 mCi. Our data show that no reasonable tracer dose can detect all potentially treatable disease. Acknowledging these limitations, we have chosen a routine dose of 2 mCi to minimize the cumulative radiation burden to the patient from repeated studies.
with increasing frequency in follow up. The relationship between Tg and I-131 uptake was studied after radioiodine therapy to test the reliability of Tg in assessing the mass of functioning thyroid tissue. 158 pts with nonmetastatic disease were included in this study. Uptake tests with 18-74 MBq were started 14 to 29 days (19±3; mean ± SD) after radioiodine therapy. Blood samples measuring Tg were taken immediately before. The indication for therapy with radioiodine is an uptake >2% of the administered dose in the neck. Tg was measured with a double antibody RIA (Sensitivity: 0.1 ng/ml). Sero with Tg in subludies were determined. In 130 pts, Tg was >6 ng/ml and I-131 uptake >2% (Tg: 29 ± 18 ng/ml; I-131: 23.1 ± 13.2%). In 11 pts Tg was undetectable (<6 ng/ml) and I-131 uptake <2%. In 34 pts, however, with undetectable Tg, I-131 uptake values varied between 2 and 46% (12.4 ± 10.5%). Only in 4 of these 34 pts TSH was not maximal (50 μIU/ml) because of a shorter (9,10,11,13 days) period from thyroidectomy. In conclusion, a minimum of remaining thyroid tissue highly sensitive to TSH is required for detectable Tg levels, but is unable to produce detectable Tg-values. Therefore, in contrast to I-131, measuring Tg is insufficient to document the success of thyroid ablation.

No. 45  

Thallium-201 imaging was evaluated in the diagnosis of differentiated thyroid carcinoma. We performed 41 studies in 38 patients, including 23 with papillary and 13 with medullary carcinoma. Each was given 3-4 mCi of Tl-201 chloride and neck and body images were obtained at 0.5 and 4 hours with an LFOV camera/LEAP and pinhole collimator. In 23 cases of papillary carcinoma, 3 of 3 (100%) of pre-op cases correlated with surgically proven disease and predicted presence or absence of cervical node involvement. Of 21 total post-op studies, 20 of 21 (95%) tumor sites detected. 5 negative T1 studies were also negative by all modalities. 2 T1 studies (8% of total) were negative but later positive on follow-up studies. 26 of 32 (81%) total tumor sites (88%) as detected by all modalities were successfully localized with T1. Of 13 medullary cancer patients (all post-op), 28 were abnormal in 5 total sites and this was later confirmed by other studies. 8 others were negative despite detectable calcitonin levels in 6 of these.

Thallium-201 imaging is a highly sensitive method of detection of residual, recurrent or metastatic differentiated thyroid carcinoma. One Hurthle cell tumor was also localized. One "false positive" occurred in a giant cell tumor of bone. It is of definite, though lesser utility in medullary carcinoma. The studies correlated highly with other imaging modalities and required no withdrawal from thyroid medication. TI-201 imaging can be of major clinical utility in the lifelong follow-up of thyroid cancer and in selecting patients for withdrawal from thyroid medication for specific I-131 imaging and treatment.

No. 46  
EFFICACY OF RADIONUCLIDE THYROID SCAN IN EVALUATION OF UPPER MEDIASTINAL MASS FOR INTRATHORACIC LOCALIZATION. H.M. Park, R.D. Johnson, A. Siddiqui, B.S. Schauwecker, Indiana University, Indianapolis, Indiana.

Some chest radiology textbooks state that "many retrosternal goiters are not hormonally active" or "self-sustained functioning without adequate supportive data." We reviewed 54 (32F, 22M) consecutive cases that had a suspected upper mediastinal mass on CXR or CT and had a radionuclide thyroid scan between 1972-1985.

The mass was found to be a substernal goiter (SSG) in 42 patients and non-thyroidal in 12. In 93% (39/42) the thyroid scan correctly identified the SSG (26 with I-131, 14 with I-123, 2 with Tc04). In 7% (3/42) the scan missed the SSG. Two of the three had posterior mediastinal goiters and one had a large intrathoracic thyroid cyst. Of the patients with SSG, 2 were hyperthyroid, 4 were hypothyroid and 36 euthyroid (mean T4 8.4μg). The average radioiodine uptake was 20% (n=10-35%). The average TSH level was 2.9 μU/ml (0-4.4μU/ml). In 21 patients the substernal portion was equal to or greater than the uptake in the normal thyroid and in 21 it was less. In two patients the SSG was completely separated from the remaining thyroid in the normal position. We observed parallax error in 40% (8/20) of the cases who had pinhole thyroid imaging studies. Many SSGs may be missed if this technical error is overlooked.

In summary, most of the SSGs are hormonally active and can be accurately diagnosed by radionuclide scan. SSGs can be better identified by centering the pinhole collimator at the suprasternal notch to avoid parallax or by using an "old fashioned" rectilinear scanner.

No. 47  

Eighteen thyroid patients (12F, 6M) ranging in age from 20-80 (X = 49) were studied with MR and scintigraphy to evaluate clinical utility. Disorders evaluated included multinodular goiter (toxic and nontoxic) (pre- and post-therapy), Hashimoto's thyroiditis and solitary cold nodules. Tg weighted (TR 600/TF 25 msec) and T2 weighted (TR 2500/TE 80 msec) spin echo pulse sequence MR images of the neck and upper mediastinum were performed with a 1.5 T superconducting magnet equipped with a surface coil. Pinhole images and RAIU values were obtained 24 hours after 200-300 μCi of 1-123. The MR signal intensity of normal thyroid tissue was slightly higher than surrounding neck muscle on both TI and T2 weighted images. Cold (nonfunctioning) nodules had a signal intensity of normal gland on T1 weighted images and markedly increased signal intensity on T2 weighted images. MR revealed excellent anatomic detail of tracheal deviation and/or compression and substanial thyroid extension. Colloid and hemorrhage had very high signal intensity with both T1 and T2 weighted images. Scintigraphy accurately detected palpable nodules, though MRI frequently detected additional smaller lesions of uncertain clinical significance. Surface colloid MR is more sensitive in detecting lesions not evident on scintigraphic images though specificity has yet to be ascertained. MR provided superior anatomic detail in multiple imaging planes without any radiation exposure.

3:30–5:00  Room 39

NEUROLOGY II: SPECT

Moderator: Richard A. Holmes, MD
Comoderator: Thomas C. Hill, Jr., MD, BS

No. 48  

This study was undertaken to prove the clinical reliability of Tc-99m-HMPAO SPECT. 120 patients with various neurological disorders (seizures n=25, stroke n=31, micrognathe n=10, Parkinson's syndrome n=7, Alzheimer's disease and dementia n=10, psychiatric disorders n=12, others...
n=25) and 5 normal volunteers were investigated. Additionally 20 stimulation studies (employment of imagery, VEP, SSEP) were performed. CT-scan of all patients was available and 44 was performed on a Dual-Row scan Station camera 15 min after i.v. injection of 12-20 mCi Tc-99m-HMPAO. During 30 min 60 projections have been acquired. Transversal sections were obtained after filtration of projections and correction for tissue absorption, by filtered back projection (128x128 matrices). SPECT studies revealed regional hypefusion in 90% of seizure patients. Ischemic areas were detected in all stroke patients, in case some perifocal edema was observed 5 days after onset of symptoms. Regional flow patterns allowed good differentiation of cases of Alzheimer's disease and other forms of dementia. All patients with Parkinson's disease showed low tracer uptake in the anterior basal ganglia and cortex. During an attack 4 migraine patients showed regional hypoperfusion. Stimulation studies showed relatively increased CBF compared to resting state in various brain regions corresponding to the stimulus. In our experience excellent image quality is obtained by brain SPECT with the new compound Tc-99m-HMPAO. This technique allows detection of CBF changes caused by different pathological and physiological mechanisms in the brain.

No. 49
BRAIN SPECT IMAGING WITH Tc-99m-HM-PAO IN THE EARLY DETECTION OF CEREBRAL INFARCTION: COMPARISON WITH TRANS-MISSION COMputed TOmography.


Tc-99m-HMPAO SPECT, 69 LFA were detected. Of these, 48 were found in the hemispheric periphery, 21 in the basal ganglia or the internal capsule. In 53% of the pts, HMPAO defects were more extended than LFA in TCT, in 38%, sizes were equal and in 9%, LFA were larger. A cerebellar diachisis occurred in 8 pts with a timely interval to the ictus of 9±5 days. We conclude that Tc-99m-HMPAO SPECT is a safe and reliable method to evaluate CBF in TCT without critical time schedules of imaging after iv injection. It provides a powerful means in assessing the true size of low flow areas adjacent to morphological changes.

No. 51

This study evaluated a new cerebral blood flow agent, Tc-99m-hexamethylpropylene amine oxide (HM-PAO), in early detecting acute cerebral infarction, in conjunction with the transmission computed tomographic (TCT) studies.

Brain SPECT imaging was performed within 24 hr after the initial CT scan in patients (pts) with acute stroke without CT evidence of hemorrhage after IV injection of 10 mCi of Tc-99m-HM-PAO. Diagnosis of cerebral infarction (CI) was confirmed by the initial and/or sequential late CT scans. Individuals without evidence of cerebral diseases served as controls.

In 8 controls, no perfusion defects were seen in the cortex and basal ganglia. Of 15 pts with acute stroke due to CI, 14 (93%) were detected within 48 hr of onset by HM-PAO scans in contrast to only 5 (33%) by CT. Discordance of HM-PAO perfusion defect with initial negative CT scans occurred in 60% (9/15) of pts. One pt had both negative HM-PAO and CT studies. In 3 of 5 pts with abnormal CT scans as well, the perfusion defect with HM-PAO was much larger than edema seen on CT. In the other two, both SPECT and CT were equal in the extent of abnormalities.

In summary, Tc-99m-HM-PAO is able to early detect acute cerebral infarction prior to CT with rather proper depiction of its extent in the majority of pts. This plus no logistical problems will make it a useful and practical agent for diagnosing and managing acute cerebral infarction.

No. 50

Tc-99m HMPAO has shown considerable promise for imaging cerebral blood flow. Thus, it was employed in patients (pts) with CVD to experience changes of relative regional cerebral uptake in diseased (di) and undiseased (un) areas with time after injection and to compare sizes of low flow areas (LFA) to low density areas (LDA) in TCT. 46 pts with completed stroke (CS, n=31) or reversible neurological deficit (RND, n=15) were examined 15, 60 and 300 min after iv injection of 400 MBq Tc-99m HMPAO using rotating gamma cameras and 360° rotation. Transversal slices of 20 mm thickness were reconstructed and regional interhemispherical ratios of di-to-un (DUR) were computed by ROI programs. All pts had TCT, angiography or Doppler sonography within the same week.

DUR in pts with visible LFA was .75±.15 (15min), .76±.12 (60min) and .84±.12 (300min) (mean±SD). Size of LFA did not decrease within this period. In pts with RND, DUR (15min) was .84±.10 (p<.025 vs CS). With HMPAO SPECT, 69 LFA were detected. Of these, 48 were found in the hemispheric periphery, 21 in the basal ganglia or the internal capsule. In 53% of the pts, HMPAO defects were more extended than LFA in TCT, in 38% sizes were equal and in 9%, LFA were larger. A cerebellar diachisis occurred in 8 pts with a timely interval to the ictus of 9±5 days.

We conclude that Tc-99m-HMPAO SPECT is a safe and reliable method to evaluate CBF in TCT without critical time schedules of imaging after iv injection. It provides a powerful means in assessing the true size of low flow areas adjacent to morphological changes.

No. 52

Chronic cerebral infarcts are known to present a larger IMP hypofixation area than the infarct zone defined by the X ray CT. High and dense contrast of the peripheral area is shown by the PET. The existence of a functionally depressed peri-infarct zone suggested by these results was studied in 17 chronic cerebral infarcts with IMP at 10th min and 5th hour with 133-Xe for rCBF, using a highly sensitive SPECT system, TOMOMATIC 64. Two types of an increased IMP uptake areas were differentiated.
METABOLIC AND HEMODYNAMIC STUDIES OF GLIOMAS
proven by biopsy to have gliomas; 3 were Grade II, one was Grade IV.

3:30-5:00
Room 38
ONCOLOGY II: PET AND CENTRAL NERVOUS SYSTEM METABOLISM

Moderator: Frank H. DeLand, MD
Comoderator: Thomas P. Haynie, MD

No. 53

We studied the potential of I-123 N-isopropyl p-iodoamphetamine (IMP) SPECT in the diagnosis of Alzheimer’s disease (AD). All 27 AD patients (pts) underwent detailed neurological examination laboratory tests and CT scans and matched research criteria for AD (McKhann); 17 had severe dementia (dementia scale BBS25) and were institutionalized; 10 pts were mildly to moderately demented (BBS25). The pts were compared to normal controls (nl) who were all gainfully employed or living independently. None of the pts or nl had any history or neurological sign of stroke (Hachinski score4). SPECT imaging was performed 15 min after intravenous injection of 5 mCi IMP using a rotating gamma camera with a long bore collimator. The reconstructed resolution after prefiltering of the projection data with a 2D Butterworth filter (cutoff .4) was 4.5 ± 0.5 mm. The mean Ki for high grade astrocytomas was 0.098 ± 0.030 (n=4) in contrast to 0.078 ± 0.045 and 0.024 ± 0.007 ml g-1 min-1 respectively (ratio:3.25) for low grade astrocytomas and normal brain tissue were 0.027 ± 0.008 ml g-1 min-1 respectively (ratio:3.25) whereas the ratio of GM for tumor and normal brain tissue was 1.2 ± 0.5. The mean Ki for high grade astrocytomas was 0.098 ± 0.030 (n=4) in contrast to 0.027 ± 0.008 ml g-1 min-1 (n=2) for low grade astrocytoma. Active, high grade astrocytomas also showed marked CT contrast enhancement and regional glucose hypermetabolism. In one subject, both I-123-PUT uptake of 11C after I-123-PUT injection was unidirectional peaking at 15 minutes. Time-activity data for tumor and brain were measured to calculate blood-to-brain influx constants (ki) (Patel, et al. J. Cereb. Blood Flow Metab. 3:1, 1983). The mean Ki’s for I-123-PUT for tumor and normal brain tissue were 0.078 ± 0.045 and 0.024 ± 0.007 ml g-1 min-1 respectively (ratio:3.25). The comparison of Ki values between the two hemispheres was variable, but seemed to be higher in the higher grade tumors. This finding is supported by NIH and MRC grants.

No. 55
SERIAL PET STUDIES OF HUMAN CEREBRAL MALIGNANCY WITH [1-11C]-PUTRESCINE (11C-PUT) AND [1-11C]-DEDDOXY-D-GLU- COSE (11C-2DG). E. Hiesiger1, J. Logan2, A.P. Wolfe3, J.D. Bradle1, B. McMahan1, K.R. MacGregor1, J.S. Fowler2, D. Christmann1, and E. Flamm3. 1Radiology, 2Psychiatry, 3Neurosurgery Departments, NYU Medical Center, NY, NY. 9Neurology, 10Psychiatry, 11Neurosurgery Departments, NYU Medical Center, NY, NY.

PET imaging with 11C-PUT and 11C-2DG was performed in eight patients with a radiological or clinical diagnosis of primary or metastatic cerebral tumors. Serial PET studies were performed over a 4 month period. These results support the contention that PET studies with 11C-PET are useful for locating small hypometabolic tumors providing a far better signal/noise ratio than GMR measurements and also an index of degree of malignancy when used in longitudinal studies in a single subject. Research supported by DOE, OHER and NIH Grant NS-15638.

No. 56
METABOLIC AND STRUCTURAL FINDINGS RELATED TO WHITE MATTER DISORDERS AS SHOWN BY PET, MRI AND CT. J.B. Alavi, A. Alavi, J. Powe, D. Hackney, M. Revich. Hospital of the University of Pennsylvania, Philadelphia, PA. 19104

We and others have observed locally decreased cortical metabolism in areas adjacent and remote from brain tumors. We have analyzed 18F-FDG PET scans of 28 pts with cerebral astrocytomas, to look for possible correlations with other brain disorders. All 27 pts had CAT scans and most had MRI scans. A Laterality Index (L.I.) was calculated from the PET studies. The L.I. is the percent difference in metabolism between the two hemispheres at certain areas of interest. When quantitative PET data were not available, the PET visual images were examined for areas of cortex which showed suppression of metabolism.
In 19 cases, there was at least 1 area of depressed metabolism ipsilateral to the tumor, with L.I. of 20-84%. Most of these pts had "hot" tumors; all but 1 of these pts had CAT or MRI evidence of probable peritumoral edema or extensive tumor in the white matter. In 9 cases with no suppression or less than 20% L.I., the CAT and MRI showed no white matter disease or else white matter change which was more compatible with radiation leukoencephalopathy than edema. Only 1 of these 9 patients had a "hot" tumor, all others were low grade tumors or clinically indolent grade III astrocytomas, with low or normal metabolic activity.

We have observed that ipsilateral cerebral glucose metabolism is often suppressed in patients with brain tumors. We suggest that this may be a remote effect of the tumor. It appears that white matter damage from radiation therapy, when it does not induce edema, is not associated with the same degree of metabolic suppression.

No. 57

C11-methionine and FDG studies were performed in patients with known brain tumors who had had a recurrence of their neoplastic symptoms. Prior to the PET study, there was uncertainty about the persistence or recurrence of the tumor or the presence of radiation necrosis. Most patients had CT and MRI as well as PET. Before each PET scan, the neurosurgeons described their proposed course of treatment based on clinical, CT, and MRI evidence alone. Then recorded how the PET data affected their management plan. In 5/5 patients the surgeons concluded that the data from the PET scan modified their approach to the solution of the patient's problem. As reported by Lilja and others, the extent of the tumor was predicted better with C11-methionine than with FDG. With FDG, the size of the affected areas of brain was usually larger than the tumor itself, reflecting the secondary effects on regional brain metabolism. The decision to operate, the surgical approach, and the extent of surgery were influenced by the PET results.

Our preliminary data suggest that PET imaging: 1) influences the neurosurgeons' management of brain tumor patients; 2) helps differentiate tumor from radiation necrosis; 3) helps delineate the extent of tumor; and, 4) provide information about the metabolic effects of the tumor.

No. 58

MRI and CT give a high accuracy in the detection and differential diagnosis of brain tumors, but an exact delimitation and grading of malignant tumors are not always met. It is the purpose of this study to evaluate uptake of C-11-methyl-L-methionine in tumors to non-tumor ratios (T/N) for the clinical need for differential diagnosis.

Methionine uptake was measured in 32 pts (F-18-FDG: 12/36 pts) with brain tumors prior to surgery, and in 6 patients with strokes, using PET. The diagnosis was ascertained by CT, MRI, angio- gramy, histologically and in 8/36 pts by To-99m-scans.

A penetrable blood brain barrier (BBB) is not a prerequisite for methionine accumulation. Relevant details are given in the table.

<table>
<thead>
<tr>
<th>Pts</th>
<th>Diagnosis</th>
<th>C-11-L-Methionine T/N</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>astro/glio I</td>
<td>2.5 (1.8-3.1)</td>
</tr>
<tr>
<td>5</td>
<td>astro/glio II-III</td>
<td>1.8 (1.6-2.8)</td>
</tr>
<tr>
<td>9</td>
<td>astro/glio II</td>
<td>1.3 (0.9-1.6)</td>
</tr>
</tbody>
</table>

PET, MRI, and CT are complementary with regard to extent of tumor tissue, necrotic areas and edema. It is concluded that the uptake reflects metabolic activity in brain tumor tissue rather than a diffuse uptake due to BBB damage. PET with glucose has limitations with regard to delineation of low-grade astrocytomas, while PET with C-11-L-methionine usually reflects the extent of tumors better.

No. 59

A high-resolution positron camera has been used for positron emission tomography (PET) of the diseased human liver in-vivo. The patients included in this on-going study present with primary and metastatic liver malignancy, the clinical diagnosis confirmed by histological examination from a liver biopsy obtained prior to the PET study. Tomographic images are made 20 min. after i.v. administration of the positron emitting radionuclide Ga-68 (physical half-life: 68 min.) in the form of Ga-68 labelled colloids, with activities varying between 2 and 4 mCi to patients scheduled for intraarterial, loco-regional chemotherapy of their liver disease.

The preliminary results obtained from a small patient group show clearly the superiority of PET liver imaging for the detection and precise localisation of liver malignancies, when compared to planar scintigraphy and to SPECT imaging using To-99m labelled colloids. The PET results are also in good agreement with the results obtained from CT and Ultrasound liver imaging. Calculations of the total and regional functional liver volume from both the initial PET study and a follow-up study provide new insight into tumour tissue replacement, which reflects the effective focality of loco-regional chemotherapy.

It is hoped to display PET data of individual cases as a three-dimensional (liver) object using shaded graphics techniques, offering a global view of the diseased liver before and following chemotherapy. This approach has already proved successful for the display of tomographic images of the thyroid.

3:30-5:00
Room 40

CARDIOVASCULAR II: MYOCARDIAL METABOLISM & VIABILITY

Moderator: Heinrich R. Schelbert, MD, PhD
Commoderator: R. Edward Coleman, MD

FEATURE PRESENTATION

Radionuclide Radius of Myocardial Metabolism

Heinrich R. Schelbert, MD, PhD

No. 60
GLUCOSE METABOLISM IN POST-ISCHEMIC CANINE MYOCARDIUM. K. Schwaiger, R. Neese, W. Wijns, J. Wisneski, M. Grover-McKay, M.E. Phelps, H.R. Schelbert, and E. Geritz. UCLA School of Medicine, Los Angeles, CA and UCSF School of Medicine, San Francisco, CA.

F-18 deoxyglucose (FDG) uptake is frequently increased in ischemic and in reperfused myocardium and indicates tissue viability. Because FDG traces only the initial uptake and phosphorylation of glucose, the meta-
bolic fate of glucose was studied with [6-14C] glucose, infused intravenously in 8 dogs 24 hrs after a 3-hr balloon occlusion of the left anterior descending artery (LAD). Samples were withdrawn simultaneously from the left atrium (art.), LAD vein and coronary sinus (CS) and plasma concentrations of chemical and labeled glucose, CO2 and lactate determined. Compared to the entire heart (art−CS), glucose extraction by perfused myocardium (art−LAD vein) was 68% higher and averaged 0.37±0.15 % mol/mL. Of the extracted glucose, 72±15% was metabolized to C14 CO2 (43%) or C14 lactate (57%). The remaining 28% entered an undefined storage pool. The fate of infused glucose was inversely related to plasma free fatty acid levels (r=−0.86). Thus, increased FDG uptake in perfused myocardium reflects increased glucose extraction. Glucose is largely metabolized anaerobically as indicated by lactate release. Residual glucose oxidation occurs probably in cells responsive to normal regulatory mechanisms as shown by the relationship to plasma free fatty acid levels. Thus, reperfused myocardium contains myocytes in which anaerobic glycolysis persists for prolonged time periods after restoration of blood flow. The persistence of anaerobic glycolysis can be demonstrated noninvasively with PET and FDG.

No. 61
SEVERITY OF SEGMENTAL MYOCARDIAL BLOOD FLOW REDUCTION ASSOCIATED WITH PERSISTENCE OF METABOLIC ACTIVITY IN PATIENTS WITH CHRONIC ISCHEMIC HEART DISEASE. R. Brunken, M. Schwaiger, J. Tilisch, R. Marshall, M. Phelps, and H. Schelbert. UCLA School of Medicine, Los Angeles, CA

Persistence of glucose metabolism in hypoperfused myocardial segments on PET distinguishes viable from infarcted myocardium. We hypothesized a relationship between persistence of metabolic activity and the severity of the blood flow deficit. Thus, 13 patients with chronic ischemic heart disease were studied with PET using tracers of blood flow (N-13 ammonia, NH3) and glucose metabolism (18F deoxyglucose, FDG). Five ventricular segments were analyzed: septal, anterior, lateral, apical and inferior. Normalized tracer concentrations were calculated for each of 12, 30° sectors on circumferential activity profiles of each cross-sectional image. Relative concentrations were corrected for partial volume effect by use of ratios derived from the study of normals. Using previously reported criteria, 34 segments with depressed NH3 were identified. In 20 segments with depressed FDG activity (PET infarct), mean relative NH3 activity was 64.7±10.8%. In contrast, in the 14 segments with preserved FDG activity (PET ischemia), mean relative NH3 activity was 61±22±0.2% (p<0.01). In PET infarction, the decrease of FDG activity paralleled that of NH3 (44.0±9.1%, FDG/NH3=0.99), while in PET ischemia FDG activity was augmented relative to NH3 (83.8±10.7% FDG/NH3=1.37). Thus, residual metabolic activity can persist and glucose utilization is accelerated relative to blood flow when myocardial perfusion is moderately severely depressed. More severe flow reductions are associated with concordant decreases in glucose utilization, suggesting tissue necrosis.

No. 62

We have reported that in coronary artery disease (CAD) patients, 15-(Orono-I-123-phenyl pentadecanoic acid) (o-IPPA) was avidly incorporated by the normal myocardium and retained for several hours with long T1 (>200 min). The elimination of the activity from the blood was rapid (an initial component with T1 of 0.7±0.23 min, followed by another with T1 219±24 min). The activity in the aqueous phase (including iodides, hippoc and benzoates) was related to less than 10% of the initial organic activity, even at 30 minutes, suggesting either slow catabolism or minimal accumulation of the aqueous metabolites in the blood. These findings are in contrast to those with p-IPPA where at 20 minutes the water soluble catabolites in the plasma had reached 20% of the initial activity. Chromatography of the organic phase showed only one major peak (95%) of the original tracer (o-IPPA) and some minor activity in the triglyceride band. These findings suggest that o-IPPA is not or very slowly, converted to final labelled organic catabolites in the plasma.

No. 63
MYOCARDIAL IMAGING WITH IODINE-123 PHENYLPENTADECANOIC ACID IN ISCHEMIC HEART DISEASE. C. Hansen, PW. Kulkarni, JT. Willerson, V. Ugolini, M. Kennedy, DE. Jansen, LM. Karni, JR. Corbett. Univ. Texas Health Science Center at Dallas, TX.

In this study, we tested the hypothesis that 1-123 phenylnpentadecanoic acid (IPPA) with single photon emission tomography (SPECT) is useful in the identification of patients (pts) with ischemic heart disease (IHD). Nine normal volunteers (age 27.2±2.0 yrs) and 15 pts (age 53.3±9.3 yrs) with IHD were studied with exercise limited treadmill exercise. IPPA (4-8 mCi) was injected 1 minute (m) prior to termination of exercise, and SPECT imaging was performed at 5 m and repeated at 40 m following injection. Normals showed uniform segmental IPPA activity and washout. Pts showed a maximal variation (M%V) in IPPA activity on 9 m images of 35.5±14.3%, on 40 m images of 32±14%, and a M%V in washout rate of 21.6±7.1%. Four of 15 Pts had M%V in IPPA activity >2SD outside the normal range, and 14 of 15 had variations in IPPA washout >2SD outside the normal range. Thirteen of 15 Pts had at least 1 segment with IPPA washout >2SD below the normal range. All Pts had abnormalities (>2SD) in at least 2 of the variables measured. There was excellent agreement between coronary anatomy and IPPA. 19 of 25 vessels stenosed >70% showed corresponding areas of abnormality. Nine Pts with myocardial infarcts (MI) were studied at rest. All Pts demonstrated marked reductions in activity (46.4±11.9%) and washout (2.4±4.5%) in MI segments. We conclude that IPPA imaging with SPECT and exercise is a highly sensitive means to detect significant IHD noninvasively. *p<0.001.

No. 64

Myocardial uptake of N13 glutamate (G) is high and related to regional flow and to metabolic extraction. It has been suggested that the uptake of G could be increased in patients (pts) with ischemia.

In this study, we have analysed data in 17 pts. Three control subjects (CS) and 11 pts with CAD underwent rest and stress 6 positron emission tomograms (PET) at 3 levels of the myocardium. Three additional pts had tomograms before and after diprydamole infusion with isometric exercise. Comparative rest-stress tomograms were also obtained with N13 ammonia as a reference flow tracer. Pts were divided into 2 groups: 6 pts with myocardial infarction and 8pts with exercise-induced ischemia. Data were normalized to...
the region of maximum uptake. Normal regional myocardial uptake (RMU) was defined in CS and averaged 96.2±5% at exercise. G resulted in a high target to background ratio with little lung uptake. RMU in infarct regions was decreased to 41.1±6.6% at rest and 37.3±6.6% during exercise (NS). In pts with ischemic response RMU decreased from 84.3±3.1% at rest to 75.1±3.8% (p<.02) after exercise and from 76.4±6.5% at rest to 47.3±5.7% (p<.01) during dipyridamole infusion. N13 ammonia scans when performed showed similar directional changes in the ischemic and non-ischemic regions.

We conclude that N13 G gives excellent definition of the myocardium with high target to background ratios. G myocardial uptake appears to decrease in ischemic regions as compared to normal tissue illustrating the flow dependence of the uptake mechanism.

3:30–5:00
Room 27

RADIOASSAY

Moderator: Howard J. Dwarkin, MD
Comoderator: Avir Kagan, MD

No. 65
ASSOCIATION OF CYCLOSPORIN A WITH HUMAN SERUM PROTEINS. C.A. Pickering and D.E. Drum, Radioassay Laboratory, Department of Radiology, Harvard Medical School and Brigham and Women's Hospital, Boston, MA.

Cyclosporin A (CsA) is a neutral, highly lipophilic, cyclic endecapeptide proven to be a very effective immunosuppressant. Because its nephrotoxicity is a major side effect, post-dose trough levels in serum are measured by RIA. As in evaluating other therapeutic drugs, we examined the binding of CsA to serum proteins in an initial step toward identifying nephrotoxic moieties.

For all samples studied, several peaks of CsA eluted between totally excluded (Vo) and totally diffusable (Vt) solutes. The major CsA peaks when studied weekly for 12 week periods.

No. 66

We evaluated a CEA assay requiring no sample pretreatment (Diagnostic Products Corporation (DPC)) employing antisera raised against CEA in goats. This assay and the Abbott polyclonal (A-P) and monoclonal (A-M) RIAs yield essentially equivalent results (Clin Chem 31:981, 1985). DPC-CEA between assay CVs (8 assays) were 7.3–10%. We measured CEA in 88 normal subjects (19 smokers), 91 ill patients, and in 473 samples from 193 patients with colon or rectal CA (27 preoperatively, 111 followed 6-20 mo.). Metastatic or recurrent CA was present at the time of 120 samplings. CEA-DPC was <3.5 in 90% and <5.0 ng/ml in 100% of normal non-smokers. It was 5.0–8.5 in 21% of smokers and 5.9–9.5 ng/ml in 19% of ill patients. In bowel CA patients, sensitivity/specificity was:

For 3.5 ng/ml:
True + 67%, False - 23%
True - 83%, False + 17%

For 5.0 ng/ml:
True + 52%, False - 48%
True - 34%, False + 17%

CEA-DPC remained normal in 3 patients, was elevated before (2–8 mo) in 4, and coincident with clinical recurrence in 5; and paralleled disease course in 29 patients. Discrepant results occurred in 10 of 133 patients. CEA was elevated, no mets (A-M 5, DPC 1, A-P 1) or normal, mets (A-M 1, DPC 3, A-P 1). DPC provides a clinically effective measure of CEA.

No. 67
CAN THE SCHILLING TEST BE REPLACED BY A RESORPTION TEST WITH COLD VITAMIN B12? E. Henze, S. Manner, W.E. Adam, University of Ulm, Germany.

It was the purpose of this study to evaluate the diagnostic usefulness of an oral resorption test using non-labeled B12 as suggested by a commercial distributor as an alternative for the more expensive Schilling test (ST). Plasma levels of cold B12 were measured with a commercial kit before and 4 hours after oral administration of 1 mg B12 in 36 normals, in 16 pts with normal ST (group 1) and in 11 pts with abnormal ST (group 2) for determination of sensitivity (SE) and specificity (SP) with the ST as golden standard. In normals, a mean±SD of 767.4±404.3 pg/ml before and 1095.8±775.8 pg/ml after oral B12 with a mean increase due to resorption of 331.4±562.8 pg/ml was measured, because of the obvious large variation and a non-Gaussian distribution of the mean increase, no meaningful value of normal resorption by using ±2SD of normal could be established. Assuming a minimum increase required in normal resorption of 100 pg/ml as suggested by the kit distributor, only a SE of 27% and a SP of 75% was calculated from the results in pts group 1 and 2, whereas an assumed minimum increase of 200 pg/ml resulted in a SE of 55% and a SP of 50%. There was also no correlation in the 27 pts between ST and the resorption test with r=0.0075. The lack of any diagnostic value of this approach might be caused due to the known passive resorption of approximately 1% of any B12 given orally even in complete absence of intrinsic factor and due to the relatively large amount of orally administered B12 (at least 1 mg) needed for a "cold" resorption test. In conclusion, not replace the Schilling test.

No. 68

Higher B12 levels have been reported in black (compared with white) adults living in the United States, and the use of separate reference ranges for these two populations has been suggested (J. Nucl. Med. 26:790, 1985). In order to gain further insight into this difference, we measured B12 levels and unsaturated B12 binding capacity (UBBC) in 26 black (42 males and 17 females) and 65 white (44 males and 21 females) blood donors, ranging in age from 17 to 66 years. A liquid-phase radioassay kit from Diagnostic Products Corp. (Los Angeles, California) was used for B12 measurements and 57Co-labeled vitamin B12.
obtained from the same company was used for UBBC measurements. The following mean values ± SDS were obtained:

<table>
<thead>
<tr>
<th>Race</th>
<th>B12(pg/ml) UBBC (pg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black</td>
<td>504 ± 205 *</td>
</tr>
<tr>
<td>White</td>
<td>395 ± 146</td>
</tr>
</tbody>
</table>
| * Significant race difference at p<0.001

Blacks had higher mean serum Vitamin B12 levels than whites. The reference ranges calculated from mean and standard deviation values were 94-914 and 93-677 pg/ml, respectively. Although elevated Vitamin B12 levels were accompanied by higher UBBC among blacks, there was no statistically significant correlation between these two values, suggesting that elevation of Vitamin B12 and UBBC among blacks was probably attributable to different causes.

No. 69
ADAPTATION OF AN AFP RADIOASSAY METHOD FOR OPTIMAL CLINICAL USE AT LOW LEVELS. K. Najpauer and D.E. Drum, Radioassay Laboratory, Department of Radiology, Harvard Medical School and Brigham and Women's Hospital, Boston, MA.

Recent reports suggesting an association of Down's syndrome with low values for maternal serum AFP (MSAFP) have led to application of methods designed originally for high value analytical and statistical evaluation. Low-end performance of these methods has not been well documented. In order to avoid low-end errors we investigated practical modifications to a well established FDA-approved vendor's materials and procedures for a standard double antibody radioimmunossay using 1-125 readout. By extending a recommended incubation time from 4 to 18 hours at 37°C and by changing the diluent for standards, we find a technically improved assay. The low-end sensitivity is less than 1 IU/mL (p<0.05). Dilution linearity is observed from 1 to 180 IU/mL, intersecting the origin. Intraassay precision, expressed as %CV, was 8% at 1 IU/mL (p<0.05). Dilution linearity is observed from 1 to 180 IU/mL, intersecting the origin. Intraassay precision, expressed as %CV, was 8% at 1 IU/mL (p<0.05). Over the range 5 to 98 IU/mL our relation to the CDC Biological Standard is linear, with [WHO value] = 1.00 [BWH value] + 0.47 IU/mL (p<0.01).

The development of a radioenzymatic assay for urinary salsolinol (SAL), a condensation product of dopamine and acetaldehyde, may play a role in alcoholics. This hypothesis, which has been controversial, has been difficult to test because of a lack of assays sufficiently specific or sensitive to detect the formation of this putative mammalian alkaloid. The present study reports the development of a single-isotope radioenzymatic assay for the simultaneous measurement of SAL and D in diluted urine. The technique involved the conversion of SAL and D in the presence of their respective radioactive O-methylated metabolites by the enzyme catechol-O-methyltransferase and [methyl-3-H]-O-adenosyl-methionine (5 uCi). A rapid thin-layer chromatographic separation of the formed tritiated metabolites contributed to the specificity of the differential assay of SAL and D. With the availability of this assay, we were able to study urinary SAL and D in hospitalized male alcoholics at admission (group A, n=20) and recovering male alcoholics (group B, n=7) with 2-5 years of abstinence. The results of this study demonstrated that alcoholics (group A, 6.11 ± 3.21 ng/ml; group B, 6.20 ± 5.5 ng/ml) excreted significantly (p<0.045) higher levels of SAL as compared to controls (1.0 ± 1.5 ng/ml). In contrast, high D output was noted only in active alcoholics. These preliminary findings demonstrate the prevalence of high endogenous output of SAL in alcoholics.

3:30-5:00 Room 31

RADIOPHARMACEUTICALS I: TC-99m CHEMISTRY

Moderator: Alan G. Jones, PhD
Comoderator: Gopal Subramanian, PhD, MD, MS

No. 71
BORONIC ACID ADDUCTS OF TECNETIUM OXIDE COMPLEXES (BTOX) A NEW CLASS OF NEUTRAL COMPLEXES WITH MYOCARDIAL IMAGING CAPABILITIES. A.D. Nunn, E.N. Treher, T. Feld, Squibb Institute for Medical Research, New Brunswick, NJ. A new technetium labelled myocardial imaging agent has been developed. The compound is Chloro(Methylboron(1-)-tris[1,2-cyclohexanedionedioxime(1-)]N,N',N",N"",N"""",N"""")Technetium (SQ 30217). SQ 30217 is a member of a totally new class of neutral, seven coordinate technetium complexes (the BTOX complexes) where the oximes, boron R groups or capping ligand can be varied together or independently. These complexes represent a major departure from proceeding radiopharmaceutical chemistry because the selectivity and chelating portions of the molecule are separated until the final complex is synthesized. This is done in quantitative yield at the no-carrier-added level via template synthesis around the technetium atom upon reconstitution and heating of a lyophilized kit. The complexes can also be made at the carrier level starting from pertechnetate plus reducing agent or TcOCl"- and TcCl"-

SQ 30217 has been fully characterized by X-ray crystallography, FAB- FD-, DCI- and LC-MS, conductivity, IR, UV, VIS, elemental analysis, photoelectron spectroscopy and chromatography. The coordination sphere of the technetium atom consists of three (N bonded) cyclohexane-dioxime molecules and one chlorine atom. The technetium has a mono capped distorted trigonal prismatic geometry. The dioxime molecules are held together at one end of the molecule via a proton bridge in which only two hydrogen atoms are shared by three oxygen atoms. The other end of the molecule is held together by a methylboron cap through the remaining three oxygen atoms of the oxime groups.

No. 72
IMAGING OF MYOCARDIAL PERFUSION WITH TC-99m SQ 30217: DOG AND HUMAN STUDIES. K.T. Coleman, M. Maturi, A.D. Nunn, W.C. Eckelman, P.N. Juri, F.R. Cobb, Duke University Medical Center, Durham, NC, and Squibb Institute for Medical Research, New Brunswick, NJ.

This study evaluates TC-99m labeled Chloro(methylboron(1-)-tris[1,2-cyclohexanedionedioxime(1-)]-N,N',N",N"",N"""",N"""")Technetium (SQ 30217), a new Tc-99m myocardial imaging agent. Planar images were obtained in 8 normal dogs and in 13 dogs with infarction (4 of these also had TI-201 injections and 3 had a second TC-99m SQ 30217 injection). In 9 volunteers and one patient with remote infarction, serial chest images were obtained following the administration of TC-99m SQ 30217. With TC-99m SQ 30217, non perfusion radiopharmaceutical images occur in the dog from 2-20 minutes. The radioactivity cleared rapidly from the lungs such that they were not visible...
after one minute. Hepatic activity peaks between 4.5 and 7.0 minutes. The infarcts were seen as areas of decreased or absent activity in all 13 dogs. TI-201 was used to confirm areas of decreased perfusion in 4 of the dogs given Tc-99m SQ 30217. The infarction could also be seen after a repeat injection of Tc-99m SQ 30217 given 30 minutes after the first.

In the 9 volunteers, the myocardium is visualized at 60 seconds and good visualization continuing through 20 minutes. One patient with remote myocardial infarction and abnormal TI-201 images had abnormal Tc-99m SQ 30217 images.

Tc-99m SQ 30217 is a new myocardial perfusion imaging agent which gives good images of the myocardium. The normal clearance from the myocardium permits a second injection within thirty minutes which would allow stress/rest studies.

No. 73


This study was initiated in order to test the hypothesis that a nonreducible 99m-Tc(III) cation would not suffer myocardial washout in humans. One of the reasons that the Tc(III) cation [99m-Tc(NMPE)2Cl2]+ fails as a myocardial perfusion imaging agent in humans is that it suffers in vivo reduction to the neutral Tc(II) form. This leads to washout of the Tc(III) complex from the myocardium and an unacceptably low heart/liver ratio. A new class of 99m-Tc(III) cations, containing a tetradentate-02N2 Schiff base ligand and two monodentate tert-butylnitrile ligands, has been developed. These complexes are not reducible in vivo, and correspondingly they do not suffer washout from the heart. Variations in the structures and properties of the Schiff base and phosphine ligands lead to a range of mixed ligand complexes which exhibit different biodistributions in test animals. The prototype for this new class of agents, [99m-Tc(acac)](P(01))3]2, where acac represents N,N'-ethylenebis(acetylene iminate), has been evaluated in human volunteers at both rest and exercise. The resulting myocardial images are superior to those obtained with [99m-Tc(NMPE)2Cl2] and no myocardial washout is observed. However, blood clearance is relatively slow and myocardial perfusion images are obtained only ca. one hour after injection. Chemical variations in the Schiff base ligand are likely to lead to other nonreducible Tc(III) agents that undergo more rapid blood clearance and yet do not suffer myocardial washout.

No. 74

ISONITRILE ESTER COMPLEXES OF TECHNETIUM. JF Kronauge, AG Jones, A Davison, J Lister-James, SJ Williams, SA Neussa, Harvard Medical School and Brigham and Women's Hospital, Boston, MA, Massachusetts Institute of Technology, Cambridge, MA and E DuPont de Nemours & Company Biomedical Products, N. Billerica, MA.

A new group of technetium complexes containing isonitrile ligands bearing ester functionalities are being tested as improvements over the cation hexakis(t-butylisonitrile)technetium(+1) (Tc-99m TBI) for cardiac perfusion imaging. Among these, the cation hexakis(carbomethoxyisopropylisonitrile)technetium(+1) (Tc-99m CPI) shows much promise. In the guinea pig, cardiac uptake peaks at 0.5 min (2.1±0.2 %ID/gorgan; mean ± SD) clearing with a T1/2 of 90 min. Tc-99m TBI peaks at 2 min (1.6±0.3) and a T1/2 of 9 h. Peak liver uptake is at 2 min (17.4±0.8) with a T1/2 of 35 min, but Tc-99m TBI levels continue rising to 2 h (24.9±0.1). Lung uptake of Tc-99m CPI is 2.3±0.4 at 0.5 min (Tc-99m TBI = 43.5±7.6). Scanning in swine and rabbits gave heart images immediately after injection. Experiments in rabbits using Tc-99m CPI, TI-201 and Nb-95 microspheres show a linear distribution with blood flow: for CPI, alone 0.92 intercept 6.9%; for TI-201, 0.9 and 5.9%. In a rabbit model of perfusion, the slope and intercept for Tc-99m CPI became 0.76 and 16%, indicating a slight filling upon release of the ligand. For TI-201 and Tc-99m TBI, the intercepts were 4x2 and 45%. The low initial lung uptake reflects the more hydrophilic nature of these ester complexes and the rapid liver clearance the hydrolysis of the ester groups to species more readily excreted, as intended. Tc-99m CPI is a promising agent for investigation in humans for myocardial stress studies.

No. 75


A series of bis-s-arene technetium(I) cations has been prepared by reaction of sodium pertechnetate, a phosphonium, aluminum chloride and suitable arenes. The cationic Tc(arene)4 complexes are purified by preparative TLC and characterized on the Tc-99 level by mass measurements using FABMS. Biodistribution studies show a number of complexes that have substantial myocardial uptake. For the methyl-substituted benzene derivatives, trends toward higher myocardial uptake, higher plasma binding and higher octanol-buffer extraction ratios with increasing number of methyl groups are observed, suggesting a relation between lipophilicity, myocardial uptake and plasma binding.

Gamma scintigraphy using trimethyl- and tetramethylbenzene complexes in dogs show that excellent myocardial images can be obtained after ten minutes, no doubt facilitated by rapid blood clearance and low plasma binding. In normal human volunteers, the same complexes show rapid clearance from the blood, relatively low plasma binding, and myocardial uptake.

No. 76


Tc-99m MAG, (R) has been described (JNM 1986, 27:111) as a useful alternative to I-131 Hippuran. To study the structural requirements for optimal renal tubular transport we have synthesized the D-, L- and DL-isomers of the 3 possible derivatives of MAG, in which glycol (A) is replaced by alanyl (ala): MAG-alaG (A), MAG-ala-G (B) and MAG-ala-G (C). The compounds were labeled with Tc-99m by the dithionite reduction method and biodistribution was studied in mice 10 min after injection. DL-, D- and L-Tc-99m-(A) did show a similar biological behaviour, nearly the same as that of (R). The diastereomers were also isolated but their renal excretion characteristics were not different. L-Tc-99m-(B) is accumulated and retained mainly in the kidneys (70%), whereas the D-isomer is efficiently transported to the urine (69%). The properties of the DL-compound are intermediate.

A similar difference is observed for the isomers of Tc-99m-(C): the D-isomer is rapidly excreted into the urine, the L-isomer is retained in the kidneys.

It appears that methylsubstitution in the terminal carbonylglycine of (R) does not impair the efficiency of tubular transport, as has also been reported for Hippuran. Introduction of a methyl substituent in one of the other glycyl moieties can drastically alter renal handling, depending on the orientation (D or L) of the substituent.
The purpose of this study is to demonstrate the potential for SPECT reconstruction by use of the circular harmonic transform (CHT) solution of the exponential Radon transform. The CHT algorithm is based on the 2-D Fourier transform of the projection sinogram and the 2-D cosine transform of the uniform attenuation. Accurate patient contours and correction for table attenuation are required for quantitative studies. Mathematical simulations, SPECT scans of an anthropomorphic phantom, the Jaszczak phantom and patients are used to compare the algorithm with the intrinsic algorithm based on ordinary backprojection and commercial software based on the precorrective method. The simulations and line source studies demonstrate improved resistance to streaking and a better signal-to-noise ratio for the CHT algorithm when compared to either of the other two methods. A volumetric study with the anthropomorphic phantom shows that the CHT algorithm provides better estimates of organ volume over a wide range from pancreas (145 ml) to liver (1950 ml). The correlation coefficient from a least-squares fit of the volumes was 0.9997 (CHT) and 0.9991 (commercial software). The CHT algorithm is much less prone to nonfocal geometric distortion when compared to the commercial software. The CHT algorithm is also computationally efficient, with processing times generally less than ordinary backprojection. For SPECT protocols in which the assumption of uniform attenuation is reasonable, the CHT algorithm is preferable to the algebraic-iterative methods which require long processing times.

No. 78
INVERSE MONTE CARLO IMAGE RECONSTRUCTION FOR SPECT WITH MAXIMUM LIKELIHOOD ESTIMATION. C.E. Floyd, R.J. Jaszczyk, S.H. Manglos, K.L. Greer, R.E. Coleman. Duke University Medical Center, Durham, NC.

The Inverse Monte Carlo (IMOC) algorithm has been applied to reconstruct SPECT images from projection data including quantitative compensation for scatter, attenuation, and depth dependent collimator effects. Monte Carlo simulation of photon transport through the SPECT acquisition apparatus (including scatter and attenuation interactions) forms a detection probability used in an EM maximum likelihood algorithm to estimate the source distribution. Scatter and attenuation compensation was achieved for studies with three isotopes: Tc-99m, TI-201, and I-123 for several phantom geometries as well as for clinical acquisitions. For line sources immersed in an interacting water bath containing background activity, ROI comparison showed agreement between the image of sources in air (without scatter and attenuation) and in water (with scatter and attenuation) to better than 1% for large ROI regions. Comparison between IMOC and filtered back projection revealed IMOC to simultaneously provide superior resolution and noise for this phantom. Reconstructions with compensation for scatter and attenuation were achieved for SPECT acquisitions which included only 180 degrees of projection data. Asymptotic behavior of the EM estimator was investigated out to 1000 iterations. For some projection sets, divergence in the chi-squared convergence criteria was noted at 500 iterations. These preliminary results indicate the IMOC can provide quantitative SPECT reconstruction including simultaneous compensation for scatter and attenuation.

No. 79
EVALUATION OF A FAST MAXIMUM LIKELIHOOD METHOD FOR ESTIMATION OF REGION-OF-INTEREST VALUES IN EMISSION TOMOGRAPHY. R.E. Carson, G.W. Berg, M.V. Green, S.M. Larson, National Institutes of Health, Bethesda, MD.

A maximum likelihood (ML) method for the unbiased estimation of region-of-interest (ROI) values and their variances for emission tomography has previously been developed. This study presents a significantly faster version of the algorithm and evaluates its performance against filtered backprojection (FBP) with a realistic brain simulation. Processing time has been reduced 8-10 times with the Fisher scoring algorithm instead of the EM algorithm, with convergence in 4-6 iterations. 100 ROI values can be estimated in 20 minutes on a PDP-11. The ML method requires ROIs defined over all radioactive portions of the field of view in each region. To evaluate the algorithm's sensitivity to violations of its assumptions, a simulated brain slice was constructed. FBP reconstructions were performed and ROIs were drawn covering the gray matter, with white matter filled automatically. 30 simulations of 3 million and 300 thousand count scans with resolutions of 10 and 6 mm FWHM were performed to calculate the bias and variability of ML and FBP estimators.

The ML estimates did not show the partial volume bias of FBP (0.8% for the smallest versus 12.4% for the largest resolution). ML showed a greater range of bias due to its sensitivity to placement and size of the ROIs. The variability of the ML estimates was accurately predicted by the algorithm and was slightly greater than FBP (3.7% for the smallest). ML variability and FBP bias increase with smaller ROI size or increasing FWHM. These studies demonstrate that ML can remove the partial volume bias without significant noise increase in reasonable computation time.
OBLIQUE MAGNETIC RESONANCE IMAGING FOR MYOCARDIAL INFARCT EVALUATION. R.F. Johnson, Jr., M. Ahmad, E.G. Amparo, D.J. Dornfest, W.J. Prevost. University of Texas Medical Branch, Galveston, TX 77550.

NMR imaging of the heart has been described in the literature illustrating the combination of patient positioning and oblique slice selection gradients to present images of the heart in an orientation that provides short and long axis views. These images are similar to the anatomic presentations seen in Tl-201 and 2-D echocardiography techniques. This paper describes an electronic technique that results in the same oblique views without patient rotation or other complicated positioning. The NMR imager has the capability of pulsing the gradient coils in a manner that will produce complex gradient angles that correspond to the precise orientation of the heart. The clinical result is an uncomplicated but tailored presentation of the heart in short and long axis views. Advantages include a clear view of wall thickness for a detailed analysis of all segments of the myocardium. Clinical comparisons of the short axis NMR images were made in 11 patients in which Tl-201 and 2-D echocardiography imaging had been performed. There was close correlation of the anatomic orientation and pathologic findings of the heart. In 2 patients with recent myocardial infarction, wall motion evaluation by echocardiography and perfusion deficits by Tl-201 corresponded with observed wall thinning of the left ventricle in the NMR images. Nine patients without recent myocardial infarction demonstrated similar cardiac anatomy by NMR imaging to that seen by Tl-201 and 2-D echocardiography. Thus, oblique NMR imaging has been determined to provide the best method of presenting the myocardium for infarct evaluation.

No. 448


To evaluate current methods of quantitating infarct size and the "volume at risk", we studied nine canines with surgically induced myocardial infarct (ligation of LAD beyond second diagonal) 24 hours after surgery with MRI and SPECT. Radiolabeled microspheres were administered into the left atrium immediately prior to and post ligation for flow determination.

MRI imaging was performed pre and post administration of Gd-DTPA (0.25 mM/Kg) using ECG gated short spin-echo techniques (TE=30mSec, TR=350mSec). SPECT scans were performed 2 hours post-administration of 25mCi of Tc-99m PYP. On completion of the in-vivo SPECT scan, a third set of microspheres were injected into the left atrium and the dog sacrificed by the left atrial injection of monastral blue dye ("volume at risk" determination).

The SPECT and MRI scans were repeated on the heart ex-vivo, the heart sectioned and stained with TTC to that seen by Tl-201 and 2-D echocardiography. The selection and application of the EC6 leads was performed. There was close correlation of the anatomic orientation and pathologic findings of the heart. In 2 patients with recent myocardial infarction, wall motion evaluation by echocardiography and perfusion deficits by Tl-201 corresponded with observed wall thinning of the left ventricle in the NMR images. Nine patients without recent myocardial infarction demonstrated similar cardiac anatomy by NMR imaging to that seen by Tl-201 and 2-D echocardiography. Thus, oblique NMR imaging has been determined to provide the best method of presenting the myocardium for infarct evaluation.

No. 447

OBLIQUE MAGNETIC RESONANCE IMAGING FOR MYOCARDIAL INFARCT EVALUATION. R.F. Johnson, Jr., M. Ahmad, E.G. Amparo, D.J. Dornfest, W.J. Prevost. University of Texas Medical Branch, Galveston, TX 77550.

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The SPECT and MRI scans were repeated on the heart ex-vivo, the heart sectioned and stained with TTC (infarct size determination) after the "volume at risk" had been determined. Each section was divided into four regions, ischemic and perfused endo and epicardium and counted in a well counter for Tc-PYP uptake and microsphere distribution. Analysis of these data indicate that Gd-DTPA and Tc-PYP localize in areas that exhibit less than 20% of the normal blood flow. Both techniques consistently overestimated the "volume at risk" and the infarcted volume when compared to pathological specimens.
tration in osteoblastic lesions giving high target to non-target ratios. To date, 23 dogs with primary bone tumors have been treated and progressively evaluated with radiographs, scintigraphy, bone marrow aspirates, hematology and serum chemistries. Most dogs received a single intravenous dose of 1.0 mCi of the complex/kg body weight producing a calculated dose to the lesion between 25 to 50 Gy. Most dogs demonstrated an early regression in pain as judged by improved locomotor function. None of the dogs demonstrated significant clinical problems from the treatment. Hematological abnormalities were limited to dose related reduction in platelets and white blood cells two to three weeks post-injection which returned to normal by six weeks. Of the 23 dogs treated to date, eleven are still alive with apparent clinical and radiographic arrest of the disease. One dog died of unrelated disease 1 year post treatment and had no evidence of active neoplastic disease at necropsy. Sm-153-EDTMP appears to be an effective therapeutic agent for treatment of neoplastic bone disease.

No. 450

Dual photon absorptionmetry (DPA) with the rectilinear scanning has been widely used to measure the bone mineral content (BMC) in axial skeleton. In this study, we have developed a new instrument system of DPA using a gamma camera. The system consisted of 50 mCi 153Gd (44 and 100 keV) as an emitting source, NaI crystal for a detector, 19 photomultiplier tubes and a computer. Fundamental studies were made, and the results were evaluated. The ininsic spatial resolution (FWHM) was 9.2 mm at 44 keV and 5.5 mm at 100 keV. The intrinsic flood field uniformity was 8.1% at 44 keV and 3.7% at 100 keV. The count rate performance was 2.3 μsec. The precision error for triplicate determinations on pig femoral bone in vivo was 1.6% for 9 min. and 1.2% for 15 min. of acquisition time. BMC, derived from this DPA system, on phantom immersed in KHP0, solution (bone equivalent material) correlated highly to actual density (r=0.99, p<0.001). Furthermore, correlation between BMC determinations obtained from DPA and those from SPA was observed (r=0.98, p<0.05). Irradiation dose of 50 mCi 153Gd was 16.3±4.5 mR at skin surface.

Thus, it was shown that DPA system using a gamma camera was reliable in evaluation of bone mass, and that the amount of 153Gd used in a gamma camera system was less than one tenth of that required for the scanning system. DPA system using a gamma camera promise as an investigative tool in quantifying bone mass.

No. 451
INTRA-ARTICULAR YTTRIUM-90 THERAPY OF CHRONIC HEMOPHILIC SYNOVITIS. M. Sackler School of Medicine, Tel Aviv, Israel.

Recurrent hemarthrosis in patients with hemophilia often results in severe joint deformity, limitation of movement, and bony ankylosis. Surgical synovectomy is associated with marked morbidity, is costly, and the results are disappointing. Synoviolysis represents an improved radiographic, bone marrow aspirates, and hematologic features. Y-90 as a single injection into the joint is performed under radiologic guidance. The gamma camera was done within 1 hour and repeated approximately 24 hours later by detection of bremsstrahlung radiation. Patients with high titers of antibodies to Factor VIII received a single dose of Autoplex 100 μg/kg prior to treatment and were immobilized in a cast for 3 days. Factor VIII levels were controlled at 30% for 48 hours.

No. 452
DIFFUSE INTRATHORACIC ACCUMULATION OF TECHNETIUM-99m MDP: EXPERIENCE IN 44 CASES. S. Kosuda, T. Hashimoto, A. Kudo, I. Nishiguchi, K. Kunieda, S. Hashimoto. Okura National and Keio University Hospital, Tokyo, Japan.

Diffuse intrathoracic uptake of technetium-99m bone seeking agents is uncommon, and the incidence and details of the causative diseases have not been reported. We reviewed the records of 8021 patients who were referred to us for bone scanning during the past four years. There were 3120 males and 4901 females, age range 1 to 91 yr, mean 55. Forty out of 8021 patients (0.50%) had bone scintigrams revealing diffuse intrathoracic uptake of technetium-99m methylene diphosphonate(MDP). 37 out of 40 cases (93%) showed unilateral diffuse intrathoracic uptake. All those cases with diffuse intrathoracic uptake were classified as strongly positive (2 cases, 5%), moderately positive (7 cases, 18%), and weakly positive (3 cases, 7%).

The causative diseases were malignant pleural effusion, diffuse pulmonary metastases, primary pulmonary carcinoma, pulmonary tuberculosis, radiation pneumonitis, fibrothorax. Diffuse intrathoracic uptake due to unknown origin was seen in 8 cases (20%). Only two cases (tuberculosis, fibrothorax) showed calcification on the chest roentgenograms.

Nineteen out of 40 cases underwent sequential gallium-67 citrate scan. Of those, 14 cases (35%) revealed diffuse intrathoracic uptake of Ga-67 in the same side. In conclusion, these observations stress the need for careful correlation in the interpretation of technetium bone scan, whereas the exact mechanism of localization of Tc-99m MDP remains undefined.

No. 453

Twenty five children aged from 7 to 18 years with histologically proved OS were treated in our institution according to the T10 protocol (Rosen et al, Cancer, 1982;49:1221-30). Bone scans were carried out before preoperative chemotherapy 3 hours after injection of 10MBq/kg of Tc-99mHMDP. The tumour to contralateral uptake ratio (R) was determined by the ROI method. A second scan was done at half course (6 weeks) of the chemotherapy and the ROI were drawn with reference to the previous scan. The procedure was repeated at the end of the chemotherapy. After surgical resection of the tumour, the pathologist classified the specimen into 3 categories: good response (GR: less than 10% of viable cells) and poor response (PR).

Eleven values of R were determined at the level of femoral and tibial metaphyses of 9 control patients whose bone scans were definitely classified as normal. The normal R was 1.01 ± 0.06. Values of R in OS patients are
No. 454


46 patients (22M, 23F) ranging in age from 19 to 79 with a clinical history of a non-union fracture, surgery, diabetes, or a soft tissue infection were studied with In-111-oxine WBCs to detect osteomyelitis. There were 27 TP, 9 TN, 2 FP, and 1 FN. The TP and the FN occurred in patients with soft tissue infections overlying the area of interest. All diagnoses were confirmed by intraoperative bone biopsy and cultures. Seven patients were excluded because of nonconcurrent indium scans and bone biopsies. Bone biopsy and scan were performed within 2 days of each other in the remaining 39 patients.

The overall sensitivity was 97% (27/28), specificity 88% (9/10), and the diagnostic accuracy 92% (36/39). The remaining 7 patients had negative indium scans several months after positive bone biopsies and definitive antibiotic treatment. This suggests that In-WBC scans become negative after appropriate therapy is undertaken.

Interobserver data was obtained from 4 nuclear physicians of varying experience blinded to clinical information. A high degree of agreement was found in over 90% of the cases. This study demonstrates the utility of In-WBC scans in the diagnosis and follow-up of complicated osteomyelitis and a high level of interobserver agreement in scan interpretation.

No. 455


We measured bone mineral content (BMC) of the proximal femur and lumbar spine (L2 to L4) by dual photon absorptiometry in 79 normal Canadian volunteer white women aged from 20 to 67 years. Were included in this study women with normal lumbar spine x-ray, without back pain, fracture of the spine or femur, or endocrinological, gastroenterological or hepatic disease, and no intake of thyroid hormones, steroids or diuretics. Results were expressed in grams of hydroxy apatite per cm^2 (lg ash bone equals 1.26 gHA/cm^2). The regression of BMC on age was linear and equal to:

\[ y = 1.15 - 0.006 \times \text{age} \]

This regression was found to be more accurate in older women. The correlation coefficient was 0.90. The age-related loss of bone mineral content was slower than the normal white American published data, but the annual rate of loss is slower. This discrepancy could be due to multiple factors such as geography (sun exposure), diet, (calcium, protein intake, etc), social and occupational status. Further studies are warranted to determine the relative importance. Meanwhile, normal local BMC values should be obtained before using dual photon absorptiometry clinically.


No. 456

WEIGHTED ACQUISITION: A METHOD FOR IMPROVING BONE AND GALLIUM IMAGES. M.E. Siegel, K.H. Lee, R.P. DeVito, O. Chen, D.C.P. Chen, USC School of Medicine, Los Angeles, CA and Siemens Gammanetics, Des Plaines, IL.

The pulse height analyzer is unable to reject scattered photons of similar energy as primary photons. We compensated for scatter contribution by weighting the importance of each photon according to its energy.

One image with conventional window and one using an energy weighted protocol were simultaneously collected using special acquisition hardware in the processor of the camera. Each event was modified by a weighting factor (WF) before adding to matrix. This WF’s were determined according to energy, contrast, and signal/noise ratios desired and were stored in ROM.

51 procedures, 9 of bone, and 12 gallium scans were performed as described. Images were evaluated by comparing the weighted (WI) to non-weighted images. Quantitative analysis of image contrast over the ribs (bone) or lesion (gallium) were computed by the ratio of counts in ROI to adjacent background. The contrast from weighting protocols was correlated with visual assessment. Ribs were better defined in 64%, vertebra in 65%, and pedicles in 50% of bone scans using the WI. In every gallium scan, the anatomy was better defined using WI. The mean contrast ratio for ribs increased from 1.5 to 2.2. For gallium the lesion contrast increased by 302. The best images were found using WF maximizing signal/noise ratio and altering slightly the contrast ratio.

For the same number of counts and scanning time, the weighted acquisition method appears to yield better quality images by suppressing the expression of the scatter contribution in the final image.

No. 457

DOES THE "THREE PHASE" BONE SCAN ADD DIAGNOSTIC INFORMATION IN BONE SCINTIGRAPHY? E.B. Silbersteln, A. Elgazzar. The University of Cincinnati Medical Center, Cincinnati, OH 45267.

The use of a nuclear scintiangiogram or flow study as a routine part of bone imaging is said to add additional diagnostic information. A priori the blood pool image obtained shortly after injection also provides information on the vascularity of a lesion however, without the requirements of additional camera time or special injection technique. We examined the additional information provided by the flow study in 19 consecutive patients referred for bone imaging to rule out osteomyelitis where a flow study was technically feasible.

Each patient received a flow study employing 20-25 mCi of 99mTc-MDP injected as a bolus with four second frames over the area of interest acquired for forty seconds. A blood pool study was then obtained with delayed skeletal imaging 3 hours later. Each study was read at least twice by two different nuclear physicians.

Osteomyelitis was confirmed by culture on 17 of 19 patients. In each case the blood pool and delayed skeletal scintigraph of the focus showed the abnormality. However there were three falsely negative flow studies (18Z).

One patient with arthritis and one with phlebitis had normal flow and blood pool studies. The latter also had a normal delayed bone scan.

We conclude that the flow study contributes no additional information to a bone scan which includes a blood pool image obtained shortly after injection and yielded almost 20Z false negative results.

No. 458

The value of skull scintigraphy in acute mastoid and ear infections. Twenty-one consecutive patients, age range 0.5-11 years, mean 2.5 years, suspected of acute mastoiditis, were referred by their pediatricians for bone scintigraphy within 2 weeks from the onset of symptoms. Patients' scintigraphies were carefully compared with normal skull anatomy and scintigraphies of children without ear infections. Thus, patient scan abnormalities were defined and correlated with their final clinical diagnoses independently made by an otolaryngology specialist. Consequently, several distinctive patterns of image abnormalities corresponding to acute otitis media (in 11 cases) or acute external otitis (in 2 cases), acute mastoiditis (in 6 cases) and occipital periostitis (in 1 case) were observed and found to be highly correlated with the final diagnoses.

We conclude that skull scintigraphy is highly efficient in assessing mastoidal involvement and periauricular tissue reaction in recurrent acute ear infections in children.

Monday, 3:30-6:00
Exhibit Hall
CVD: Blood Pool Imaging and Ventricular Function

No. 462
Preservation of Rest (R) and Exercise (E) Systolic and Diastolic Ventricular Function in Chronic Alcoholics (CA). M. Cerqueira, G. Harp, J. Ritchie, R. Dale Walker, VA Medical Center, Seattle, WA.

Autopsy studies have suggested that prolonged excessive alcohol consumption causes myocardial damage

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even in the absence of clinical cardiac symptoms. Echocardiography and phonocardiography have provided evidence for the existence of a preclinical alcoholic cardiomyopathy. These studies measure resting systolic function and maybe insensitive to early signs of myocardial damage. We used list mode acquired gated blood pool scans at R and E to study systolic and diastolic function in 18 CA (drinking 3 days/week, >5 yrs) and 12 age matched normals (N1). Following arrhythmia rejection (+10% mean RR interval), filtering, and 20msec interval forward and backward reformatting, time activity curves were generated using a variable region of interest. The 4th harmonic derivative was used to calculate EF, peak ejection time (PET, msec) peak ejection rate (PER, EDV/sec), peak filling time (FFT, msec) and peak filling rate (PFR, EDV/sec). There were no significant differences between groups, see below. (Mean ± S.D.)

<table>
<thead>
<tr>
<th>No.</th>
<th>R-NI</th>
<th>R-CA</th>
<th>E-NI</th>
<th>E-CA</th>
</tr>
</thead>
<tbody>
<tr>
<td>PET</td>
<td>183±28</td>
<td>179±21</td>
<td>85±39</td>
<td>81±19</td>
</tr>
<tr>
<td>PER</td>
<td>3.6±5</td>
<td>3.8±5</td>
<td>6.9±1.3</td>
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<td>FFT</td>
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<td>PFR</td>
<td>3.3±6</td>
<td>3.4±5</td>
<td>8.7±2.1</td>
<td>9.5±2.1</td>
</tr>
</tbody>
</table>

Thus, evaluation of systolic and diastolic function at R and E by sensitive radionuclide techniques fail to show evidence for the existence of a preclinical alcoholic cardiomyopathy in CA.

No. 463

Endomyocardial fibrosis (EMF) is characterized by collagen deposition in the apical endocardium of either ventricle with extension to the inflow tract and progressive impairment of ventricular diastolic and systolic function. To determine scintigraphic patterns and their meaning in this disease we retrospectively correlated catheterization data with first pass (FP) and gated blood pool (GBP) studies of 14 patients (pts) with biopsy-proven EMF (12 female; 25-60 years).

Two scintigraphic patterns were recognized: I) Obliterative (n=9) with prolonged pulmonary transit time (PPT), marked RA dilatation, markedly reduced RV volume with hypo- or akinesis. normal or dilated PA usually tilted to the left, normal, dilated or thickened LV, usually normokinetic, equalization of mean pressures with RA, RV and PA hypertension, marked anatomic ventricular changes, with disappearance of the apex. II) Restrictive (n=5) with prolonged PTT, slight to moderate dilatation of RA, RV, PA and LV and normal mean pressure gradients in the right chambers.

FP and GBP imaging distinguished two scintigraphic patterns in EMF, which correlated well with catheterization data. These techniques seem promising as new tools for a non-invasive classification of these pts.

No. 464

To clarify the mechanism of inspiratory reduction of left ventricular (LV) stroke volume (SV) during spontaneous respiration (SR), we measured both ventricular volume changes from expiration (exp) to inspiration (insp) using radionuclide ventriculography with respiratory gating technique. In this method, scintigraphic data were acquired in a list mode with ECG R waves and respiratory volume curve derived from respiratory flowmeter. Cardiac cycles occurring during the second halves of inspiratory and expiratory phases were separately selected and used to produce multi-gated images. Twelve patients with normal LVEF (>50%) and RVEF (>40%) and without pulmonary diseases were studied. In this study, both ventricular volume changes during SR were determined as percent changes from exp to insp. LV end-diastolic volume (EDV) decreased in all subjects and the percent decrease was 11+5% (mean±SD). LV end-systolic volume (ESV) showed a significant decrease during SR. LVEF decreased in all subjects and the percent decrease was 17+7%. LVEF decreased from 64±6% during exp to 60±4% during insp (p<0.001). Right ventricular (RV) EDV and SV increased by 3±11% and 23±18%, respectively. RVEF also increased from 48±6% during exp to 52±5% during insp (p<0.001).

These results indicate that inspiratory reduction of LVEF during SR is due to a decrease in LVEDV (preload) and that this reduction of LV preload may be partly due to an increase in RV volume during insp through the mechanism of ventricular interdependence.

No. 465
A NEW METHOD FOR LABELLING PLASMA PROTEINS WITH A TECHNETIUM-99M LABELLED AGENT FOR RADIONUCLIDE VENTRICULOGRAPHY IN MAN. A. Lahiri. G.D. Zanelli, N.M. Patel, J.C.W. Crawley, T. Smith and E.B. Nattery. Department of Cardiology and Radiolosotope Division, Northwick Park Hospital and Clinical Research Centre, Harrow, Middlesex.

Radionuclide ventriculography with in-vivo Tc-99m labelled red blood cells (RBC) is limited because: 2 injections; the label is unstable; the count rate obtained from the ventricles are low due to poor labelling efficiency. We have developed phosphine ligands which can be labelled to Tc-99m: [TcDTCS2+]; D = bis diethyli phosphino ethane and X = -tort-butyli isocyanide. Five volunteers were studied (age range 37-58 years) with both the phosphine and the standard in-vivo RBC method. A gated MV study was performed with both methods. The counts over the LV were 3 times higher with the phosphine. The LV ejection fraction (%) were closely correlated (r=0.98) and the background counts were lower. The blood pool half-life was 4 hours. The label was bonded to plasma proteins and excreted via the gall bladder. [TcDTCS2+] has advantages over the red cell labelling method: a higher blood pool concentration is achieved, there is less background activity and a single injection is required. This technique has advantages over the RBC labelling method and a simple 'kit' may be prepared for hospital usage.

No. 466

Analysis of cardiac diastolic function by radionuclide ventriculography is reportedly useful in detecting coronary artery disease (CAD) in patients with normal left-ventricular ejection fractions (LVEF). Since the effect of age has not previously been considered, we determined the left-ventricular peak filling rate (PFR) in 30 normal subjects (age 48 ± 18) and in 25 patients with catheterization-proven CAD and normal LVEF (>50%) with ages between 40 and 65 yr. Regional wall motion changes from expiration (exp) to inspiration (insp) using radionuclide ventriculography with respiratory gating...
set of 10 young normal volunteers (N1), the other a group of 12 age-matched normals (age 60-63) (N2). Sensitivity (SENS) for detection of CAD was determined using the 95% confidence limit for the normal controls. Specificity was 100% in all cases.

<table>
<thead>
<tr>
<th></th>
<th>PFR</th>
<th>N1</th>
<th>N2</th>
<th>CADN</th>
<th>CADA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3.64±0.63</td>
<td>2.12±0.53</td>
<td>2.00±0.59*</td>
<td>2.01±0.66*</td>
<td></td>
</tr>
<tr>
<td>SENS(N1)</td>
<td>-</td>
<td>-</td>
<td>58%</td>
<td>57%</td>
<td></td>
</tr>
<tr>
<td>SENS(N2)</td>
<td>-</td>
<td>-</td>
<td>57%</td>
<td>57%</td>
<td></td>
</tr>
<tr>
<td>AGE</td>
<td>29±4</td>
<td>59±6</td>
<td>57±5</td>
<td>53±6</td>
<td></td>
</tr>
</tbody>
</table>
*p<0.001 vs N1, n=NS vs N2

Thus, using an inappropriate, but commonly employed, young group of normal controls, PFR appears to detect CAD in patients with normal LVEF. In fact, PFR cannot identify this group when the proper age-matched controls are used because of the strong age dependence of PFR.

No. 467
THE CORRELATION OF RIGHT VENTRICULAR AND LEFT VENTRICULAR EJECTION FRACTION AND VOLUME MEASUREMENTS.
H.L. Musynowitz, A.R. Benedetto, S.R. Starling, and R.A. Walsh, UTMB, Galveston and UTHSC, San Antonio, TX.

Right and left ventricular EF, SV, EDV, and ESV were determined by first pass radionuclide in 13 patients with acute myocardial infarction (MI) and 6 normal controls using a sequential technique. EF was 0.76±0.09 for R+ and 0.68±0.09 for R- patients, respectively (p<.001). EF during submaximal exercise (Ex) just before hospital discharge (12.3±4 days) was 0.71±0.08 for R+ and 0.60±0.08 for R- patients. EF during submaximal exercise (Ex) was significantly lower than during rest (R) in patients with normal LVEF. In fact, PFR cannot identify this group when the proper age-matched controls are used because of the strong age dependence of PFR.

No. 468
ASSESSMENT OF VENTRICULAR PERFORMANCE AND ITS FOLLOW UP AFTER AN ACUTE MYOCARDIAL INFARCTION BY RADIONUCLIDE ANGIOGRAPHY.
Osman RAUB, Alberto RIGHETTI, Vivianne STUCKI, Alex F. MULLER. Cardiology Center and Internal Medicine Dept., University Hospital, Geneva, SWITZERLAND.

A radionuclide angiogram (RNA) was performed in 98 patients (pts) within 24 hours after an acute myocardial infarction (MI). None of the pts had a previous MI. Early death occurred in 10 pts and 8 pts underwent a bypass surgery or coronary angioplasty during the first 10 days after MI. The remaining 80 pts had a RNA at rest (R) and 10 days after MI. The remaining 80 pts had a RNA at rest (R) and 10 days after MI. The following parameters were recorded: EF, SV, EDV, and ESV. EF was measured using the area-length method. EF increased from 0.46±0.06 at R to 0.51±0.08 (p<.01) during Ex RNA is a more sensitive means than Ex ECG for the detection of Mvx pts with residual ischemia.

No. 469
SUPERIORITY OF FACTOR ANALYSIS OF RADIONUCLIDE EQUILIBRIUM GATED STUDIES FOR EVALUATION OF REGIONAL WALL MOTION ABNORMALITIES (RwMA).
D.G. Pavel, E. Olea, J. Sychna, K. Zolnierzcyk, C. Kahn, J. Shanes, University of Illinois Hospital, Chicago, IL.

Factor analysis (FA) has been suggested as a superior method for detection of RwMA because of its ability to separate anatomically and functionally superimposed areas. We applied and compared a factor analysis based on 8 segments (SEG) in L.AO performed by comparing 14 normals to 54 patients (Pt) who underwent biplane contrast angiography (CA) and also phase analysis. The standard algorithm was optimized for ventricular WWMA. Comparison was based on number of abnormal SEG detected by CA, FA and phase image (Phi). In addition, based on CA findings, the results obtained by FA and Phi were compared to each other in each patient, for number of SEG and for type of abnormality detected. Four categories were used: better (B), much better (BB), equal (E), worse (W).

Results: the 14 normals generated a consistent pattern of reference. For the 432 SEG (54 Pts), CA detected 261 as being abnormal versus 222 for FA and 114 for Phi. Thus, FA detects 85% of abnormal SEG versus only 44% for Phi. On a Pt by Pt basis, FA versus Phi is 80% for SEG detection and only 43% for type of abnormality detected. The only 2 cases (4%) in which FA was W than Phi, had LVH and filling rate abnormality; FA indicated abnormality not seen on either Phi or CA.

Conclusion: FA improves significantly the detection and characterization of RwMA, by noninvasive means.

No. 470
EVALUATION OF LEFT VENTRICULAR REGURGITATION BY FACTOR ANALYSIS AND DECONVOLUTION OF FIRST-PASS RADIONUCLIDE ANGIOGRAPHY. COMPARISON WITH INVASIVE TECHNIQUES.
L. Philippe, I. Mena, J. Darcourt, W.J. French, Div. of Nuclear Medicine and Cardiology, Harbor-UCLA Medical Center, Torrance, Calif.

New deconvolution techniques of curves gathered by factor analysis have permitted Tc-99m DTPA First-Pass Radionuclide Angiography (FPNA) to produce a reliable evaluation of Regurgitant Fraction (RF) in aortic and mitral insufficiency. RF was computed in 26 patients: 13 Valvular (V), 8 mitral- 3 aortic- 2 mitro-aortic* and 13 Controls (C). FPNA was performed within 1 hour prior to the Contrast Ventriculography (CV). In 19 patients, CV was performed by determination of the cardiac output by green-dye dilution (n=16) or thermodilution (n=3) in order to calculate the catheterization RF (CATH RF). FPNA RF was assessed by a lagged normal deconvolution of LV and pulmonary curves gathered by factor analysis. The appearance of a long transit time component in the left heart transfer function was observed in V patients, and then quantified. The presence of regurgitation was determined from CV. FPNA RF was determined in 19 V and 14 C patients. The only 2 cases (4%) in which FA was W than Phi, had LVH and filling rate abnormality; FA indicated abnormality not seen on either Phi or CA.

Conclusion: FA improves significantly the detection and characterization of RwMA, by noninvasive means.

No. 471
DETECTION OF REGIONAL WALL MOTION ABNORMALITIES BY FACOR ANALYSIS AND DECONVOLUTION OF FIRST-PASS RADIONUCLIDE ANGIOGRAPHY. COMPARISON WITH INVASIVE TECHNIQUES. L. Philippe, I. Mena, J. Darcourt, W.J. French, Div. of Nuclear Medicine and Cardiology, Harbor-UCLA Medical Center, Torrance, Calif.

New deconvolution techniques of curves gathered by factor analysis have permitted Tc-99m DTPA First-Pass Radionuclide Angiography (FPNA) to produce a reliable evaluation of Regurgitant Fraction (RF) in aortic and mitral insufficiency. RF was computed in 26 patients: 13 Valvular (V), 8 mitral- 3 aortic- 2 mitro-aortic* and 13 Controls (C). FPNA was performed within 1 hour prior to the Contrast Ventriculography (CV). In 19 patients, CV was performed by determination of the cardiac output by green-dye dilution (n=16) or thermodilution (n=3) in order to calculate the catheterization RF (CATH RF). FPNA RF was assessed by a lagged normal deconvolution of LV and pulmonary curves gathered by factor analysis. The appearance of a long transit time component in the left heart transfer function was observed in V patients, and then quantified. The presence of regurgitation was determined from CV. FPNA RF was determined in 19 V and 14 C patients. The only 2 cases (4%) in which FA was W than Phi, had LVH and filling rate abnormality; FA indicated abnormality not seen on either Phi or CA.

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No. 472
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Conclusion: FA improves significantly the detection and characterization of RwMA, by noninvasive means.

No. 473
DETECTION OF REGIONAL WALL MOTION ABNORMALITIES BY FACOR ANALYSIS AND DECONVOLUTION OF FIRST-PASS RADIONUCLIDE ANGIOGRAPHY. COMPARISON WITH INVASIVE TECHNIQUES. L. Philippe, I. Mena, J. Darcourt, W.J. French, Div. of Nuclear Medicine and Cardiology, Harbor-UCLA Medical Center, Torrance, Calif.

New deconvolution techniques of curves gathered by factor analysis have permitted Tc-99m DTPA First-Pass Radionuclide Angiography (FPNA) to produce a reliable evaluation of Regurgitant Fraction (RF) in aortic and mitral insufficiency. RF was computed in 26 patients: 13 Valvular (V), 8 mitral- 3 aortic- 2 mitro-aortic* and 13 Controls (C). FPNA was performed within 1 hour prior to the Contrast Ventriculography (CV). In 19 patients, CV was performed by determination of the cardiac output by green-dye dilution (n=16) or thermodilution (n=3) in order to calculate the catheterization RF (CATH RF). FPNA RF was assessed by a lagged normal deconvolution of LV and pulmonary curves gathered by factor analysis. The appearance of a long transit time component in the left heart transfer function was observed in V patients, and then quantified. The presence of regurgitation was determined from CV. FPNA RF was determined in 19 V and 14 C patients. The only 2 cases (4%) in which FA was W than Phi, had LVH and filling rate abnormality; FA indicated abnormality not seen on either Phi or CA.

Conclusion: FA improves significantly the detection and characterization of RwMA, by noninvasive means.
Left ventricular stroke work (LVSW) as calculated from left ventricular pressure-volume (P-V) loops accurately defines cardiac function but is difficult to obtain in most clinical settings. Using the Scinticor, a portable multicrystal gamma camera, and high fidelity micromanometer catheters placed in the left ventricle during coronary artery bypass grafting, we acquired simultaneous dynamic intraventricular volume and pressure data during and immediately after surgery. Radionuclide left ventricular volumes and pressures were beat-matched to generate P-V loops for calculation of LVSW. A potentially less accurate, but more simple, method for calculating stroke work multiplies LVSW. A non-linear regression analysis was used to find the parameters of the regression curve that were best fit to the data. The two methods did not differ significantly by analysis of variance (N = 12, mean differences = 0.072 erg-10^-m, SD = 0.35 erg-10^-m). We conclude that accurate measurement of LVSW is possible from radionuclide calculated stroke work volume and mean arterial pressure. However, a more complete assessment of ventricular performance throughout the cardiac cycle is obtained only when left ventricular pressure is recorded and P-V loops constructed. Clinical application of this method of assessing cardiac function both during and after coronary artery bypass surgery appears promising for assessing the adequacy of revascularization and for use as a guide in postoperative patient management.

No. 473

Doppler echocardiography (DE) has recently become the non-invasive standard for detection of tricuspid regurgitation (TR). Using Tc-99m DTPA and a multicrystal camera we examined the ability of first pass radionuclide angiography (RNA) to detect TR in an unselected population of 44 patients (pts) who underwent pulse DE during routine echocardiography. During inflow of the bolus we examined the right atrial (RA) time-activity curve (TAC), using a region of interest drawn just above the tricuspid valve plane. In normal pts, once the tracer has passed the vena cava, the RA TAC falls during right ventricular (RV) diastole, and remains static during RV systole. With mild to moderate TR, the regurgitant stream of tracer increases the RA TAC during RV systole. With more significant TR, the the RA and RV TAC's oscillate out of phase with one another, and prolonged RA and RV transit times occur. When this RNA algorithm was applied to the pts in this study, significant TR was found in 13 of the 44 pts. DE and RNA agreed upon the absence of TR in 29 pts. 3 pts were graded mild to moderate for TR by RNA in whom no significant TR was found by DE, however, each of these pts had normal RA and RV by both RNA and echocardiography. Only 2 pts had TR by DE that was undetected by RNA. We conclude that RA TAC analysis during RNA detects TR with results similar to pulsed DE. Since TR can prolong RA and RV transit times and degrade left ventricular imaging, we suggest that the RA TAC be examined prior to RNA ejection fraction determination.

No. 474
REGIONAL PHASE MAPPING USING GATED NUCLEAR ANGIOGRAPHY OR TOMOGRAPHY DURING VENTRICULAR TACHYCARDIA. D. Casset, R. Itti, L. Philippe, P. Cosnay and J.P. Fauchier. Trousseau University Hospital, Tours, France.

In a second time all the patients were explored in sinus rhythm with the same technique. 360 degrees of ischemic origin and 4 VT of undefined (idiopathic) origin, have been studied during a prolonged episode of VT. During recording, VT was spontaneous in 2 cases and provoked in the others. Acquisition time could be long enough to record one projection (LAO = 5 min) in 9 patients; for 7 patients two projections could be registered and for 2 patients gated tomography (32 projections over 360 degrees = 32 min) could be performed. In a second time all the patients were explored in sinus rhythm with the same technique.

Data processing was mainly the mapping of bi-ventricular contraction using the Fourier method, and the site of earliest activation was defined both in VT and sinus rhythm. A good correlation was found regarding the sites of ectopic focus when compared with invasive procedures and, in 5 patients, with epicardial mapping during surgery. Advantage of tomography over single LAO projection imaging was a better approach of VT localization, allowing a distinction between anterior and posterior regions.
SKELETAL MUSCLE BLOOD FLOW DURING MAXIMUM AND SUBMAXIMUM EXERCISE IN PATIENTS WITH HEART FAILURE. L. Davis, J. Wexler, D. Mancini, B. Chadwick, J. Lejemtel. Albert Einstein College of Medicine and Montefiore Medical Center, Bronx, N.Y.

In normals, skeletal muscle blood flow (SMBF) increases linearly with workload during graded exercise (Ex). Changes in SMBF during Ex were studied in 7 patients (Pts) with symptomatic heart failure (HF) despite therapy to determine if SMBF increased during graded Ex in these Pts. The Pts underwent treadmill Ex at submaximum workloads (Submax Ex) of 50-70% of a predetermined Max VO2 uptake (VO2) and maximum workloads (Max Ex) of 90-100% of Max VO2. For each Pt, SMBF was determined at rest and Ex using 133-Xenon washout and a Cd/Te detector interfaced to a microcomputer. Heart rate (HR), VO2, femoral vein lactate (FVL) and pH (pH) were determined throughout Ex as follows:

<table>
<thead>
<tr>
<th>Submax Rest Ex</th>
<th>Max Ex</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>cc/min/100gm</td>
<td>2.21</td>
</tr>
<tr>
<td>ml/kg/min</td>
<td>4.66</td>
</tr>
<tr>
<td>mg/100ml</td>
<td>15.7</td>
</tr>
<tr>
<td>beats/min</td>
<td>2.27</td>
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<tr>
<td></td>
<td>4.58</td>
</tr>
<tr>
<td></td>
<td>14.5</td>
</tr>
<tr>
<td></td>
<td>7.34</td>
</tr>
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<td></td>
<td>115</td>
</tr>
</tbody>
</table>

No significant (P<.05) increase in SMBF occurred between rest and Ex. No significant increase in SMBF occurred between Submax and Max Ex. Therefore, in Pts with HF, Max SMBF was obtained at Submax Ex. Further increases in workload beyond 60% VO2 were achieved by increasing O2 extraction with lactate accumulation and severe acidosis. The pattern of increase in SMBF during graded Ex. This may reflect abnormalities in either the peripheral or central circulatory system.


The purpose of this study was to validate the tomographic LFA in patients (pts) with Wolff-Parkinson-White syndrome (WPW). Forty-four pts with WPW underwent both surgical division of accessory conduction pathway (ACP) and gated blood-pool emission CT were studied. Thirty-three pts showed ACP patterns on ECG during radionuclide studies. In 3 pts, pacing studies were performed postoperatively using pacing wires placed on the epicardium. The degree of fusion was changed using atrio-ventricular trigger. In one pt, simultaneous pacings were performed at two sites simulating multiple antegrade ACPs. We have previously described the algorithm of LFA (J Nucl Med 25: 917, 1984). The time-length curves from a center to ventricular edges were generated and Fourier transform was applied to calculate length-based phase (LP). The segment of minimal LP was compared with surgically confirmed site. Sensitivity of LFA for detecting ACPs was 28/33 (85%). The total 9/10 16/19 (4/8 ACPs) of ACP. The detectability of ACPs was as follows: Group PYP (CPM ± SEM) Function P N

CARDIOVASCULAR: MYOCARDIAL IMAGING

DEMONSTRATION OF Te-99m PYROPHOSPHATE UPTAKE IN REVERSIBLY INJURED NEONATAL MYOCYTES. A. J. Fishman, J. A. Scott, C. Rabito, H. W. Strauss, E. Haber, B. A. Khaw. Massachusetts General Hospital, Boston, MA.

The effect of ischemic injury to myocardium on Te-99m pyrophosphate (PYP) uptake by neonatal rat myocytes was investigated in primary cultures at 37 °C. One to 2 day old neonatal rat hearts were dispersed by trypsinization. After 48 hr in culture, the cells were beating at a rate of about 150/min. Three days later, culture plates were exposed to an atmosphere of 95% N2/5% CO2 for 4 hr in an anaerobic chamber to produce ischemic injury. Myocytes stopped beating in these cultures. The cultures were divided into 2 parallel groups; Group I was recultured under normoxia (95% O2/5% CO2). After 24 hr, the cells were beating normally. Then 10³ cpm PYP were added and incubated for 3 hr. Group II had PYP (10³ cpm) added immediately followed by exposure to the tracer under normoxia for 3 hr. Controls (Group III) were grown under normoxia and treated identically for PYP and reoxygenation condition. The myocytes were dissociated by mild trypsinization, washed with cold media, centrifuged and then counted in a gamma counter. The counts were then normalized to 5x10⁶ cells. PYP uptake in the three groups is as follows: Group PYP (CPM ± SEM) Function P N

Uptake of PYP in anoxic cultures also paralleled the uptake of propidium iodide, an indicator of increased cellular permeability. The results suggest that PYP is sequestered during reversible injury but not by neonatal rat myocytes which had recovered.
No. 479
MYOCARDIAL IMAGING WITH Tc-99m TERTIARY BUTYL ISONITRILE (T-BIN). MN Khalil, KM Patel, JV Thornback, MY Early, G Hartley, DM Taylor, JW Berry, FJB Hubner. Cardiology Department, Groby Road Hospital, Leicester, U.K.

We report our clinical experience with a new myocardial imaging agent; Tc-99m T-BIN in 15 patients with myocardial infarction (M.I.) and 45 with angina due to angiographically proven coronary artery disease. Imaging was performed in 3 projections after the administration of 200-400 MBq of Tc-99m T-BIN using a gamma camera with a converging collimator. In patients with M.I. defects in myocardial uptake were clearly shown at rest. The patients with angina showed reversible perfusion defects following intravenous injection at maximal treadmill exercise. Optimal images were obtained at 30 minutes for post exercise scans and at 4 hours for the delayed views. Hepatic to myocardial uptake rations were approximately 4:1 at rest and 2:1 after exercise. Separation between the liver and the heart was best demonstrated on the 45° LAO projection with 20° cranial tilt. 5 patients with M.I. and 15 with angina also had Tl-201 scans. T-BIN images were superior to those obtained with Tl-201 and perfusion defects were better seen on the T-BIN scans.

24 patients in the same study had ECG gated T-BIN cardiac scintigraphy. Regional wall motion could be seen and assessed using a cine display and defects in myocardial uptake were better seen.

In conclusion, besides its use as a myocardial perfusion imaging agent, Tc-99m T-BIN scan allowed assessment of L-V contraction when gated studies were performed. The results with T-BIN have been favourable and in our experience, superior to thallium-201.

No. 480

We corroborated scintigraphic findings with CPK-MB levels and clinical course in 152 patients who underwent coronary artery bypass surgery (CABG) between 1981-1985. No patients with concomitant valvular surgery or L.V. aneurysmectomy were included. The imaging was performed 1-4 days prior and 3-8 days after the surgery. The scintigrams were read by two observers and graded 0-4+, diffuse or focal, without knowing clinical details about the patients. A 2+ focal, 3+ or 4+ myocardial scintigram was considered positive for M.I.

Blood analysis of cardiac enzymes was obtained the day prior to surgery and serially at 8, 12, 24, 48, and 72 hours after surgery.

130 patients had peak CPK-MB below 50 IU/L. 128 of them had negative scintigrams. Of the two patients who had positive scintigrams with CPK-MB below 50 IU/L, one had M.I. clinically and the other had uneventful recovery. 22 patients had peak CPK-MB below 50 IU/L of whom 12 had positive and 10 had negative scintigrams. The post-operative course was uneventful in all the ten patients who had negative scintigrams.

We conclude that in our institution, patients with peak CPK-MB level below 50 IU/L are unlikely to have perioperative M.I. The CPK-MB can be falsely elevated as was in our two patients with negative scintigrams and uneventful clinical course. Scintigrams thus add specificity to the patients with elevated CPK-MB levels and are useful in diagnosing perioperative M.I.

No. 481

Doxorubicin hydrochloride causes severe cardiotoxicity often discovered by ventricular function studies only after irreversible cardiac damage has occurred. In-111 antomyosin antibody (AMAb) and Tc-99m-pyrophosphate (PYP) have been used to detect myocardial necrosis in patients with myocardial infarction. In the present study our goal was to determine whether myocardial necrosis that accompanied doxorubicin toxicity could be detected by In-111-AMAb.

Organ distribution of In-111 AMAb was measured in mature rabbits (12: control, 9: doxorubicin) that received weekly 2.5 mg/kg of doxorubicin intravenously for 4 weeks. At this dose, 70% of the animals could be expected to become cardiotoxic. All rabbits were injected with 40-50 μCi of In-111-AMAb 24 hr before sacrifice and the radioactivity in the heart and other organs was expressed as % injected dose/gm (%ID/gm). For In-111-AMAb the control myocardial uptake (mean ± SD) was 0.033 ± 0.021 and 0.022 ± 0.012 for the left and right ventricles, respectively, while in the doxorubicin treated group their values increased to 0.063 ± 0.035 and 0.062 ± 0.036 with a range of 0.027 to 0.126 %ID/gm (p<0.025). Similar results were obtained in septum and atrium.

We conclude: 1) In-111-AMAb myocardial uptake accumulates to a high degree in doxorubicin cardiotoxicity, and 2) the amount of uptake may reflect the degree of myocardial damage.

No. 482

Acute rejection (AR) is the most important complication in heart transplantation. Endomyocardial biopsy (EB) is considered the most reliable study for AR monitoring. The purpose of our investigation was to correlate a non-invasive procedure, Ga-67 imaging, with EB data in HT patients (pts). Seven male pts (41-54 years) were sequentially submitted to 41 Ga-67 studies between one week and 8 months after surgery. Images and EB were obtained 48 hr after Ga-67 injection. Pathologic findings were graded as 0=absent; 1=non-specific reaction; 2=AR in remission; 3=mild AR; 4=moderate AR; 5=severe AR. Cardiac Ga-67 uptake was graded as absent, mild, moderate and severe AR, the latter not found in our pts.

Ga-67 Biopsy

<table>
<thead>
<tr>
<th>Imaging</th>
<th>Absent (n=15)</th>
<th>Mild (n=19)</th>
<th>Moderate (n=7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>8</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>3</td>
<td>5</td>
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<tr>
<td>2</td>
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<td>0</td>
</tr>
<tr>
<td>4</td>
<td>0</td>
<td>0</td>
<td>5</td>
</tr>
</tbody>
</table>

Imaging sensitivity was 83% (19/23), with 27% false-negatives which included one AR in remission previously treated and 3 mild AR (pts not treated with uneventful course). Out of 7 studies with moderate Ga-67 uptake, 5 EB showed moderate AR and the pts were submitted to therapy. It is conceivable that Ga-67 imaging may play an important role as a screening procedure for EB in heart transplanted pts.

No. 483
REGIONAL DISTRIBUTION OF Tc-99m HEXAKIS-ALIPHATIC ISONITRILES IN ISCHEMIC HEARTS WITH AND WITHOUT REPERFUSION. S.A. Mousa, S.J. Stevens, and S.J. Williams. E.I. Du Pont de Nemours, Biomedical Products, N. Billerica, MA.

Many derivatives of Tc-99m-hexakis-aliphatic isonitriles show potential as agents for myocardial perfusion imaging. Three derivatives, [isonitrile = t-butyl (NEN-14); 2-isonitrilo-2-methyl isobutyrate (NEN-26); 2-
BUTYL ISONITRILE (Tc-99m TBI) AS A MYOCARDIAL IMAGING AGENT. P. Rigo, F. Gil is, R. Cantineau, University of Volume 27 • Number 6 • June 1986

No. 484

MYOCARDIAL UPTAKE AND RETENTION OF Tc-99m-HEXAKIS-ALIPHATIC ISONITRILES: EVIDENCE FOR SPECIFICITY. S. A. Mousa and S. J. Williams. E. I. DuPont de Nemours, Biomedical Products, N. Billerica, MA

The Tc-99m-hexakis-aliphatic isonitriles are a promising class of agents for myocardial perfusion scintigraphy (Holman, et al. 1984). A definition of the mechanism of extraction and retention of Tc-99m isonitriles by the heart will be valuable in understanding the diagnostic information these agents can provide. Studies in guinea pig heart slices demonstrate the uptake of Tc-99m-hexakis-butylisonitrile (Tc-99m-NEN-30) in the heart to be the most stable of any Tc-99m-isonitrile yet evaluated and suggest it to be a promising agent for diagnosis of ischemic heart disease in humans.

No. 485

PLANAR AND TOMOGRAPHIC EVALUATION OF Tc-99m TERTIARY BUTYL ISONITRILE (Tc-99m TBI) AS A MYOCARDIAL IMAGING AGENT. P. Rigo, F. Gils, R. Cantinieu, University of Liege, Institute of Medicine, Liege, Belgium.

Development of technetium labeled myocardial (M) blood flow tracers will enhance the role of M imaging. This procedure will indeed benefit from the higher photon flux, improved energy range and availability of technetium.

Tc-99m TBI is a compound. Preliminary experience in animal models and patients (pts) with M infarction has demonstrated good M uptake in relation to blood flow and definition of regional M infarction. In this study, we have evaluated its ability to document stress-induced regional M perfusion deficits in pts with CAD. Ten pts with stress-induced thallium (Tl) defects and CAD defined by angiography were studied (mean age: 53, range 51-72) at rest and stress. Exercise load and duration were comparable in all pts (mean 8.1 min and 106 watts on Tl and 8.3 min and 112 watts on TBI). Heart rate on TBI was slightly lower as 4 pts were treated with beta-blockers. In the interval (T1 130/min, TBI 126/min, N.S.). Tl defined ischemic or necrotic defects in 14 arterial territories (3 M, 11 ischemia). TBI demonstrated 11 of these. Although in comparison to the defects during one hour. Missed segments occurred twice in pts with multivessel defects and once because of hepatic superimposition. Tomography in 3 pts provided better M to background ratio in the thorax allowing early scanning (30min). Liver uptake remained a problem however.

We conclude that Tc-99m TBI is a promising new agent allowing definition of transient M ischemia. Early scanning with tomography and an analog with less hepatic uptake should be developed.

No. 486

VALUE OF INTERPOLATING SCAN AND OBLIQUE-ANGLE TOMOGRAMS FOR EVALUATION OF CORONARY ARTERY DISEASES IN MYOCARDIAL PERFUSION IMAGING. S. A. Mousa, M. Senda, Y. Yonokura, T. Tomaki, H. Saji, H. Koide and K. Torizuka. Kyoto University School of Medicine, Kyoto, Japan.

We recently pointed out the presence of low sensitivity areas or gaps between adjacent slices of the multislice positron emission tomography (PET) and introduced the "interpolating scan," which was performed as the object was moved half the slice interval, to fill them out and reconstruct oblique-angle tomograms (IEEE Trans Med Imaging MI-4:54-51, 1985). The goal of the present study is to evaluate the clinical usefulness of the interpolating scan and the oblique-angle tomograms for detection of disease coronary vessels. Stress myocardial perfusion studies using N-13 labeled ammonia were performed in 20 patients with coronary disease. The detectability of the diseased vessel observed as segmental perfusion defects for the right coronary artery (RCA) and the left anterior descending artery (LAD) was 57% and 89%, respectively, in single-position scans. The false negative defects were often located in the inferior and apico-inferior walls, which were almost tangential to the image plane and were considered to have fallen into the gaps. When the interpolating scan was utilized and the two sets of images were compared, the detectability was 72% for RCA and 94% for LAD lesions. Moreover, the interpolating scan also allowed to reconstruct long-axis and short-axis tomograms in high quality, which further improved the detectability (100% for RCA or LAD and 75% for LCX lesion) and helped understand the anatomical relationships to the coronary territories.

No. 487


We have previously demonstrated that 99mTc-EDDP (TC-LDL) was removed from plasma with kinetics that were identical to radioiodinated native-LDL. To further validate the utility of TC-LDL, we have compared the kinetics and biodistribution of TC-LDL with 131I-Tyramine Cellobose-LDL (T-TYR-LDL) in an intracellularly trapped ligand in normal rabbits (N) and rabbits fed a high cholesterol diet (HCR). TC-LDL and T-TYR-LDL were administered simultaneously into N and HCR. The fractional catabolic rate calculated from the plasma time-activity curves of TC-LDL...
were injected intravenously with 1-131 W3/13W (anti-rat... The present study showed that the serial quantitation of perfusion defect by 201-Tl SPECT reveals a significant...
No 492

REDISTRICT ABNORMALITIES IN EXERCISE THALLIUM IMAGES: UNRESOLVED ISCHEMIA VS INFARCTION? KG Cloninger, EG DePuey, EV Garcia, GS Robbin, WL Robbins, HJ Berger, A Mody, EE DePasquale. Emory Univ, Atlanta, GA

To determine if incomplete redistribution (RD) at 4 hrs in exercise tomographic thallium-201 (TL) studies is always due to scar, 154 patients (pts) were evaluated before and after a total of 162 successful percutaneous transluminal coronary angioplasty (PTCA) procedures. TL studies were analyzed using polar bullseye maps. For both immediate and delayed (DL) images, abnormalities were quantified as a TL score by calculating a standard deviation (SD) weighted sum of pixels > 2.5 SD below gender-matched normal limits. 146 of 162 studies were abnormal pre-PTCA. Of these 146, incomplete RD occurred in 113 (77%): 16 (12%) in pts with prior myocardial infarction (MI) and 97 (68%) in pts without MI. Post-PTCA, DL image abnormalities were normal in 1/16 (6%) with MI and 72/97 (94%) without MI (p<.05). Post-PTCA, DL images were normal in 1/16 (6%) with MI and 32/97 (33%) without MI (p>.05). Pre-PTCA, DL image scores were positively correlated with scores in the immediate post-PTCA images in pts with MI (r=.78) and those without MI (r=.65).

To determine if additional DL images could help differentiate scar from ischemia, an 8-24 hr DL image was obtained in 40 other pts with incomplete RD at 4 hrs. Of 28 pts with prior MI, 15 had no RD, and 13 had further RD at 8-24 hrs. In 12 pts without MI, 1 had no RD, 7 had further RD, and 4 had completed RD. Thus, 4 hr DL imaging defects frequently do not signify MI. Their severity is proportional to immediate post-max stress abnormalities. Additional imaging at 8-24 hrs is recommended in pts with incomplete RD and no prior MI.

No 493

A COMPARISON OF FATTY ACID AND TL-201 UPTAKE IN A CANINE MODEL OF MYOCARDIAL ISCHEMIA AND REPERFUSION. M.D. Devous, Sr., J.K. Payne. Nuclear Medicine Center, The University of Texas Health Science Center at Dallas, TX.

Relationships among the distributions of TI-201, [1-125-9-MPDA] and regional myocardial blood flow (RMBF, tracer microspheres) were compared in anesthetized open chest dogs following 90 min of left anterior descending coronary artery occlusion. Maximal count (CP) profiles from the mean of 3 maximum pixels along 60 radii at 6° intervals from the center of the LV. The half life (t1/2) of thallium (TI) after resting (RE) injection was not completely characterized in man and was comparable to similar data after exercise (EX).

We conclude that the t1/2 of TI is dependent upon status at injection and is multiphasic at RE. The variability of t1/2 between views suggests that 20 min after injection, maximum TI uptake had not occurred at RE, but washout of TI had already commenced after EX. The differences in t1/2 after rest and exercise injections must be considered in quantification and is not explained by less myocardial thallium at rest.

No 494

THE VARIABILITY OF THALLIUM HALF LIFE AT REST AS COMPARED TO EXERCISE. W.R. Freeman, M. Kanwar, P.W. Armstrong, St. Michael's Hospital, University of Toronto, Toronto, Ontario, CANADA.

The half life (t1/2) of thallium (TI) after resting (RE) injection has not been fully characterized in man and was comparable to similar data after exercise (EX).

We conclude that the t1/2 of TI is dependent upon status at injection and is multiphasic at RE. The variability of t1/2 between views suggests that 20 min after injection, maximum TI uptake had not occurred at RE, but washout of TI had already commenced after EX. The differences in t1/2 after rest and exercise injections must be considered in quantification and is not explained by less myocardial thallium at rest.

No 495

QUANTITATIVE STRESS-REDISTRIBUTION TI-201 SINGLE-PHOTON EMISSION TOMOGRAPHY (SPECT): DEVELOPMENT OF A SCHEME FOR LOCALIZATION OF CORONARY ARTERY DISEASE. M. R. Miller, C. M. Madsahi, DS Berman. Cedars-Sinai Med Ctr, Los Angeles, CA

To define the vascular territories (VT) on SPECT images, we studied 19 patients (pts) with angiographic single- vessel (SV) coronary artery disease (CAD) and positive exercise TI-201 SPECT, of whom 7 had left anterior descending coronary artery disease (LAD), 6 had left circumflex (LCX), and 6 had dominant right (R) CAD. Maximal-count stress circumferential profiles (CP) were generated from the LV short-axis tomograms. Perfusion defects, defined by the 50% counts below normal limits, were plotted onto a polar coordinate map, which was divided into the apex and 48 equal sectors. The probability (pr) of a sector to represent a particular VT was defined by the relative frequency by which it was involved in pts with CAD of the corresponding vessel. The 3 VT were defined by the sectors in which
the pr for the corresponding vessel was >.80. Defects in these regions were assigned to the given VT, whereas defects in the remaining regions of the myocardium (pr < .80 and hemodynamic isoenhancement) were assigned to VT but positive for CAD and were assigned to the VT from which they originated. Of the 19 pts, 16 (84%) were classified as SVD (all in the correct VT), while the remaining 3 were classified as double-vessel CAD due to extension of defect into another VT. The true negative rate for absence of CAD in the 9 coronary arteries was 92% for the LAD, LCX, and RCA. Conclusion: a scheme for localization of CAD perfusion defects to specific coronary arteries on SPECT images has been developed that allows for inter-individual anatomical variation and 2) offers promise for clinical characterization of patients with CAD.

No. 496

IN PATIENTS WITH HIGH-RISK CORONARY ARTERY DISEASE AND TI-201 ISCHEMIA, IS EXERTIONAL ANGINA MEANINGFUL? S. Reisman, J Maddahi, D Berman. VA Medical Center, Long Beach, and Cedars-Sinai Medical Center, Los Angeles, CA.

In light of recent reports suggesting a high frequency of asymptomatic ("silent") ischemia in patients with coronary artery disease (CAD), increasing attention is being focused on the clinical importance of chest pain symptomatology in patients with "high-risk" CAD, defined as left-main and/or triple-vessel CAD. Since the results of testing influence clinical decisions in this group, we analyzed the relationship between the presence or absence of exertional angina during treadmill testing and the extent and severity of exercise-induced ischemia, by evaluating 35 consecutive patients (pts) with TI-201 exercise-induced ischemia (28 reversible segments) and left-main and/or triple-vessel stenosis (50%). Three-view TI-201 scintigrams were divided into 15 segments. Severity of exercise-induced ischemia was represented by a TI-201 ischemic severity score (ISS) and extent of ischemia by # reversible TI-201 segments. Exertional angina during treadmill testing was present in 34 pts (62%) (Gpl) and absent in 21 pts (38%) (GpII).

<table>
<thead>
<tr>
<th>ISS</th>
<th>% R Segs</th>
<th>Ex Dur</th>
<th>HR</th>
<th>Max STi</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gpl</td>
<td>7.2+4.6</td>
<td>6.2+2.3</td>
<td>3.1+2.2</td>
<td>2.0+1.5</td>
</tr>
<tr>
<td>GpII</td>
<td>9.0+3.4</td>
<td>2.1+2.1</td>
<td>1.2+1.1</td>
<td>2.0+0.9</td>
</tr>
</tbody>
</table>

R segs = reversible segments; Ex-exercise; Dur-duration (minutes); HR = peak heart rate; Max STi = maximum ST depression (mm); # = significance.

We conclude that in pts with high-risk CAD and TI-201 ischemia, silent exertional ischemia is common and does not indicate a less ischemic group. Thus, the presence of absence of angina during treadmill testing may not be reliable for guiding medical or surgical intervention in this patient group.

No. 497

THALLIUM SCINTIGRAPHIC AND CORONARY ARTERIOGRAPHIC CORRELATES OF PROLONGED POSTEXERCISE ST SEGMENT DEPRESSION. S. Reisman, A Rozanski, J Maddahi, D Berman. VA Med Ctr, Long Beach, & Cedars-Sinai Med Ctr, Los Angeles, CA.

To determine the significance of prolonged post (p) exercise (Ex) ST depression (ST4), we studied 81 patients with 21 mm ST4 during Bruce protocol treadmill exercise. We determined Ex TI-201 scintigraphy and coronary angiography. Three-view TI scintigrams were divided into 15 segments (Ex). The extent of myocardial TI ischemia was determined by the number (#) of reversible segments. Forty-six patients had "normalization" of ST4 to <1 mm within the first 5 min pEx (Gpl) and 35 patients had prolonged 2 mm ST4 for 20 min pEx (GpII). Results:

<table>
<thead>
<tr>
<th>Gpl</th>
<th>Ex Segs</th>
<th>Ex</th>
<th>Max Ex STi</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gpl</td>
<td>9.0+3.4</td>
<td>2.0+1.1</td>
<td>1.2+1.1</td>
</tr>
<tr>
<td>GpII</td>
<td>9.0+3.4</td>
<td>2.0+1.1</td>
<td>1.2+1.1</td>
</tr>
</tbody>
</table>

G1 = 6.9+3.4, p<.05. GpII = 6.9+3.4, p<.05. Significant perfusion deficits were more common in GII vs GpII (69% vs 41%, p<.05).

No. 498


There is no specific diagnostic test for traumatic myocardial contusion, an injury associated with cardiac conduction abnormalities and a risk of life-threatening arrhythmias. Therefore, the current standard practice at our institution is to admit all patients with significant blunt chest trauma to a cardiac monitoring bed for three days of observation.

The current study evaluated TI-201 single photon emission computed tomography (SPECT) in the diagnosis of cardiac contusion. Forty-eight patients admitted to our institution with a diagnosis of possible myocardial contusion were prospectively studied with TI-201 SPECT scans, serial cardiac isoenzymes, and continuous EKG monitoring. Twenty-five patients had clearly abnormal or equivocal scans, most of these having a characteristic perfusion deficit in the apex and anterior wall and/or adjacent septum, two had serious arrhythmias and seven had conduction abnormalities. Of the 23 patients with clearly normal scans, none had serious arrhythmias and only three had conduction abnormalities. A larger percentage of patients with positive scans had elevated cardiac isoenzymes. Our study demonstrates that TI-201 SPECT scanning may prospectively identify that subgroup of trauma patients at risk for developing serious arrhythmias from cardiac contusion, and may therefore obviate the need for expensive continuous cardiac monitoring in a significant number of trauma patients.

No. 499


Physical fitness awareness has resulted in more graded exercise EKG tests (GXT) on relatively young asymptomatic subjects. Since the incidence of significant coronary artery disease in this group is well below the false-positive (FP) rate of 10-12%, most positive tests will be FP and a back-up test is essential to separate true-positive (TP) from FP. We prospectively performed GXT on 80 healthy asymptomatic volunteers. No positive GXT occurred in 34 who were less than 40 years old. In 53 between ages 40 and 70 there were 7 positive GXT with average ST segment depression of 2.6 mm. Pre-test probability of CAD based on age and sex was 8.5 ± 2% with post GXT probability increased to 33 ± 6% using Bayes' analysis with sensitivity of 0.65 and specificity of 0.88. Normal TI-201 GXT exercise studies were subsequently found in patients with positive GXT. A normal TI-201 test reduced likelihood of CAD back to 8.0 ± 2% based on sensitivity of 0.85, specificity of 0.90. We conclude that: 1) TI-201 is useful applied to asymptomatic positive GXT responders. 2) GXT and TI-201 tests should be sequential, not simultaneous (which would double the FP probability). 3) Routine GXT appears to be
of insignificant value below age 30 since post test probability of CAD is less than 10% even after positive GXT result. 4) Statistical calculations for this subgroup should be based on data obtained from asymptomatic populations rather than data obtained from patients referred for symptoms.

No. 499.5
COMPARISON OF TI-201 SINGLE PHOTON EMISSION COMPUTERIZED TOMOGRAPHY (SPECT) AND PLANAR IMAGING FOR EVALUATION OF CORONARY ARTERY DISEASE. J. Maddahi, KF Van Tracion, C Wong, J. Garwits, F Prigent, C. Youngkin, D. Berman. Cedars-Sinai Medical Center, Los Angeles, CA

Although TI-201 SPECT offers theoretical advantages over conventional planar imaging (PL) imaging, systematic comparison of optimized quantitative SPECT and PL for assessment of disease in individual coronary arteries is not available. Thus, in 33 patients with angiographic coronary artery disease (>50% stenosis), 2-3 mCi of TI-201 was administered at peak treadmill exercise. Sequential SPECT and PL images were obtained in all pts alternating the order of imaging. With SPECT, 30-32 projections (30 seconds each) were obtained over 180°. From circumferential count profiles of all short-axis and axial portion of vertical long-axis tomograms were plotted onto a polar coordinate map, were compared to a previously established normal SPECT data base. In various vascular territories were automatically determined. With PL, 3-view images were obtained and quantitatively analysed for presence of perfusion defects and/or Tl-201 slow washout. Sensitivity and specificity of SPECT and PL for identification of disease in each of the three coronary arteries were as follows: (*p<.01 vs. PL)

<table>
<thead>
<tr>
<th></th>
<th>SPECT</th>
<th>PL SPECT</th>
<th>PL SPECT</th>
<th>PL SPECT</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAD</td>
<td>72%</td>
<td>69%</td>
<td>76%</td>
<td>41%</td>
</tr>
<tr>
<td>SPECT</td>
<td>75%</td>
<td>75%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Specificity</td>
<td>5%</td>
<td>62%</td>
<td>75%</td>
<td>75%</td>
</tr>
</tbody>
</table>

In the 14 pts in whom PL preceded SPECT, the superiority of SPECT for detection of LCX disease was maintained (.83 vs. .50). We conclude that SPECT is superior to conventional planar imaging for detection of disease in the LCX territory.

No. 500
HIGH DIAGNOSTIC ACCURACY OF 180° EXERCISE THALLIUM TOMOGRAPHY IN EIGHTY CONSECUTIVE PATIENTS EVALUATED FOR CHEST PAIN SYNDROME. M.T. Wilson, C.P. Herbst, R.D. Burrow, O.J. Beckett, B.H. Sung, C.R. Corn, and E.W. Allen. VAMC and Oklahoma University Health Sciences Center, Oklahoma City, OK.

Due to recent controversy about reliability of 180° emission computerized tomography (ECT), we evaluated this technique by calculating sensitivity (SEN), specificity (SPEC) and diagnostic accuracy (DA) for the detection of coronary disease (CD) in both women (W) and men (M). We studied 82 consecutive patients (51W and 61 M, with history of chest pain (CP) by symptomatic limited treadmill exercise, electrocardiography (EKG), stress and 4 hr redistribution 180° ECT Imaging. CD was documented in 69 Pts: 51 by coronary angiography (CA) and 17 by myocardial infarction. Seventeen were normal (6W, 6M) with either CA (2W, 3M) or low probability profile. Results in percent for each diagnostic modality, mean age, peak rate pressure product (RPP) and treadmill time obtained were:

<table>
<thead>
<tr>
<th></th>
<th>SEN SPEC</th>
<th>DA AGE RPP/100</th>
<th>TMT secs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td>93.67</td>
<td>86.48</td>
<td>213.459</td>
</tr>
<tr>
<td>Men</td>
<td>96.75</td>
<td>93.53</td>
<td>203.399</td>
</tr>
</tbody>
</table>

Three CA pts were not detected by ECT; 2 had 50% single vessel disease, one anterior and one posterior; one had 2 vessel disease. There were 4 (2W, 2M) false positives; locations were 3 inferior and 1 anterior. Conclusions: 1) Reliability of 180° data sampling ECT to detect CD in W and M was comparable. 2) Both had high sensitivity and diagnostic accuracy. 3) In our hands this technique has proven to be a reliable tool for diagnosis of coronary artery disease.

No. 501
DYNAMIC SINGLE PHOTON EMISSION COMPUTED TOMOGRAPHY OF TI-201 WITH EXERCISE LOADING. Y. Yonekura, H. Koide, T. Mukai, N. Tamaki, Y. Konishi, T. Fudo, and K. Torizuka. Kyoto University School of Medicine, Kyoto, Japan.

Single photon emission computed tomography (SPECT) with Ti-201 has been reported to provide accurate means for diagnosis of coronary artery disease (CAD). The purpose of this study is to examine the serial changes in regional myocardial activity of TI-201 injected during exercise loading in CAD using a multidetector SPECT system.

Four cases without coronary stenosis (N) and 17 patients with CAD including 9 cases with prior myocardial infarction (MI) were studied. TI-201 was injected during submaximal exercise loading with a bicycle ergometer. Serial dynamic SPECT scan was performed every 5 min until 30 min after injection, followed by additional 3 scans for 10 min at 1 hr, 2 hr and 3 hr after injection. These SPECT images were corrected for the acquisition time, but no corrections were made for photon attenuation and scattering. -H revealed uniform distribution throughout the study, and rapid washout was observed from the early period in 3/5 cases (10 to 24 % for initial 25 min). CAD showed various patterns of abnormal distribution and washout.

In addition, the changes in regional distribution of TI-201 were observed during the early period. These preliminary results indicate the significance of the early washout during the 30 min after injection of TI-201, and careful consideration should be taken in calculating the washout rate by a conventional SPECT system with a rotating gamma camera.

Monday 999
COMPUTERS AND DATA ANALYSIS

No. 502

The accurate estimation of the input function, C(t), is essential in the quantitative determination of the rate constants in the deoxyc glucose method. The conventional strategy for designing the plasma sampling times in the deoxyc glucose method is based on the intuitive notion of taking more samples when the rate of change of the input function is large and less when the rate is small. In this work a plasma sampling schedule is designed based on achieving the maximum possible accuracy of the input function parameters in the presence of measurement noise.

The sampling schedule which minimizes the variance-covariance of the estimated parameters of the input function is deemed to be the optimal sampling schedule. The optimal sampling time schedule designed was found to be a sample clusters focused at specific times. The validation of this optimal sampling schedule was tested in simulation. It was found that this sampling schedule allows a more accurate characterization of the parameters of C(t) than the conventional sampling schedule; an improvement of up to 33 percent in the average standard deviation of a parameter (1 - SD(optimal)/SD(intuitive)) was observed in the estimation of the parameters of C(t). This optimal sampling schedule was used in rats to validate its practicality. Using a similar
No. 503

EVALUATION OF ROUTINE TELEPHONE TRANSMISSION OF NUCLEAR MEDICINE STUDIES. G.M. Kolodny, I. Tal, J.A. Parker, H.D. Royal and J.A. Orlin. Beth Israel Hospital, Boston, MA.

We have developed software to send nuclear medicine studies via telephone. We can rapidly review studies from satellite hospitals, arrange joint conferences with widely separated medical centers and take call from home. We use IBM -PC/XT based computers with 512x512 pixel displays, 16 bits deep, which can read 8" floppy disks from either our Technicare, Elscint or DEC computers. We communicate at 9600 bps with synchronous half duplex modems over regular dial up telephone lines. A special long training sequence is used for each turn around of the line and fallback to 7200 or 4800 bps is automatically performed if line quality deterioration occurs. In every transmission we use a long training sequence followed by an add one cycle to a matrix element; and a Bessel function optimizer written in Fortran. The benchmark results favored the Data General processor by factors of 2 to 4, particularly for the on-the-fly application. However by packing the list mode data from 32 bits/event to 24 bits/event, it was possible to achieve 590,000 events/second for essentially all of the processors tested. For our application, we selected a network of Data General MV series processors based on the benchmark performance and the general software tools provided with the system.

No. 504

DESIGN, DEVELOPMENT, AND TESTING OF A HIGH PERFORMANCE, MICROCOMPUTER BASED, SOLID STATE AUTORADIOGRAPHIC IMAGE ANALYZER. J. L. Lear, J. S. Plotnick, and S. Rumley. Stanford University School of Medicine & VA Medical Center, Palo Alto, CA.

We designed and developed from the ground up, a microcomputer based, solid state, digital image analyzer for quantitative autoradiography. We measured dynamic ranges and signal/noise characteristics of detectors used in existing digitizers, video camera systems (VC) and scanning microdensitometers (SM), and found them to be less than optimal for the gray scale ranges typically found in autoradiographs. We then tested two types of solid state arrays, linear silicon diode arrays and charge coupled device (CCD) arrays and found that CCD arrays had the most appropriate sensitivity for fast scanning. We next developed control circuits which could move a 1024 element linear CCD array so as to digitize an image into 1024 x 1024 pixel elements. Amplification circuits were developed to match the CCD to the video camera so as to obtain 256 true intensity levels and interfaces were developed to transmit the data through a standard bus to an IBM AT central microcomputer. Programs were written in C for processing requirements of single and multiple tracer concentration measurement.

No. 505

DESIGNING A COMPUTER SYSTEM FOR A TIME-OF-FLIGHT POSITRON EMISSION TOMOGRAPH. T.K. Lewellen, R.H. Harrison, University of Washington, Seattle, WA.

The University of Washington is installing a Scanditronix time-of-flight PET gantry. However, the data processing portion of the system has been developed in our laboratories. The basic design is a distributed computer network using 32 bit minicomputers instead of "hardwired" electronics. The use of a network of 32 bit processors was chosen to allow the full use of the distributed computing power for data analysis and display when acquisition was not in progress. Three performance benchmarks were developed and tested on many processors including Data General MV series, DEC VAX and microVAX systems, Perkin Elmer, and a variety of 68000 processors. The benchmarks were 1) a list mode acquisition simulation with a bit register tested for a status bit, the 32 bit event put into a list mode buffer, and the buffer transferred to disk when full; 2) an on-the-fly simulation with a 32 bit register tested for a status bit, the event read and 16 bits isolated and used for a table look up followed by an add one cycle to a matrix element; and 3) a Bessel function optimizer written in Fortran. The benchmark results favored the Data General processor by factors of 2 to 4, particularly for the on-the-fly application. However by packing the list mode data from 32 bits/event to 24 bits/event, it was possible to achieve 590,000 events/second for essentially all of the processors tested. For our application, we selected a network of Data General MV series processors based on the benchmark performance and the general software tools provided with the system.

No. 506

HIGH QUALITY SCINTIGRAPHIC IMAGE RECORDING ON PAPER USING A LOW COST LASER PRINTER. B.R. Line, J.C. Goble, J.A. Cooper. Albany Medical Center, Albany, NY.

Reports of nuclear medicine studies may be greatly enhanced by using line graphics and image data to visually transmit clinical findings and analysis results. Low cost, 300 dot per inch resolution laser printers can be used to achieve this end, but software to merge text and graphic data is not currently available, and procedures to provide an acceptable gray scale from single intensity laser dots are poorly defined.

We have developed a software driver for an inexpensive laser printer that is controlled by high level command protocols. It formats text, line graphics and gray scale images into a single report. We have also investigated the factors influencing perceived gray in laser generated paper based images. Gray levels were generated by varying position and number of dots written into 2 by 2 up to 8 by 8 dot matrices. Perceived gray is found to be related to both dot packing density and dot pattern. Best packing strategies are produced by maximizing distance between dots and by using similar dot patterns for neighboring gray levels. Despite the greater number of patterns possible with larger matrix sizes, 4 by 4 matrices with 16 gray levels provide the best compromise between required processing time and image appearance. A sigmoid relationship is evident between perceived gray and dot density which vary in proportion to the square of the difference between the number of dots written and unwritten in a given matrix. Image appearance is noticeably improved by correcting for this relationship and by assigning image values falling between defined gray levels according to distance weighted random probability.

This type of report generation system will provide an inexpensive means of transmitting high quality images and graphic results to referring clinicians.

No. 507


We have previously described the use of first
harmonic Fourier analysis for the identification of the site of electrical activation by gated blood pool imaging. One potential limitation of the method is the use of a single harmonic (cosine) to represent the time-activity curve of each pixel. Accordingly, we have now used a more advanced analysis after non-stationary temporal Wiener filtering of gated blood pool studies. This Wiener filter has a low pass filter, whose cut-off frequency is dependent on a given pixel's signal-to-noise ratio. In our studies, the filter passed 2-5 harmonics (typically 2-3).

We applied both single harmonic Fourier analysis and first derivative analysis after Wiener filtering to 21 studies acquired during pacing in 8 patients with coronary artery disease and episodes of sustained ventricular tachycardia. Both single harmonic Fourier analysis and first derivative analysis resulted in a 71% accuracy in predicting the site of the pacing electrode. We conclude that factors other than the cosine approximation, such as anatomic overlap and patient pathology, limit the accuracy of activation site identification.

No. 508


Estimation of rate constants of glucose metabolism pixel by pixel from serial PET images at 4 min intervals for 60-120 min scan of FDG was studied. The kinetic model of FDG is based on the three compartments with four parameters. PETs were reconstructed employing corrections for attenuation, scatter and dead time of counting. Curve fitting was performed by Newton-Raphson method providing the mapping of each parameter with the relative accuracy (95% confidence limit). Arterial blood sample curve was approximated by one straight line and sum of three exponential curves. Estimation of all rate constants and cerebral metabolic rate for glucose (CMRG) of each pixel could be performed in a few seconds on PDP 11/60 computer. Correction of blood volume (BV) effect was done by subtracting BV image by CO-15 from serial FDG images. While the rate constant maps were quite noisy because of random fluctuation of data, the accuracy of the parameters increased remarkably by using the few pixels. The dephosphorylation rate (k_p) could not be estimated sufficiently from 1 hr measurement. Estimation of k_p required 2 hr scan data. The values of all constants decreased slightly for 3-parameter fitting both for 2 hr and for 1 hr measurement, and k_p, k_s and k_g values decreased 15-50% by BV correction. In healthy subject, each constant almost coincided with the normal value. These maps provide a useful mean for studying the glucose transport system in various organs and diseases.

No. 509


Accurate description of the arterial time-activity curve (ATAC) is of paramount importance in quantitative determination of the regional cerebral blood flow (CRBF) using positron and tomography. One-shot intravenous injection of 0-15 labeled water. Frequent manual sampling from the arterial catheter does not permit sampling in less than 5 sec interval and runs the risk of missing the arrival time or the peak count, which may induce errors of 5-10% in CRBF values. The present study acquired system step response providing accurate arterial time course, which successfully filled out the gaps of the manual sampling. Moreover, water and blood showed different viscosity effect on the step response, suggesting that the system characteristics should be acquired using blood or fluid of similar viscosity.

No. 510

CORRELATION OF INCREASED PET SCANNER RESOLUTION ON NEUROLOGICAL DATA VARIABILITY. S.C. Strother*, T. Peters*, C.J. Thompson*, H. Peel, Neurological Institute, Montreal, Canada, and *Memorial Sloan-Kettering Cancer Center, New York, NY, USA.

Increased image resolution is assumed to be advantageous for PET studies of the brain. This may not be true because most brain structures are not simple homogeneous objects, but multiple, randomly oriented substructures repeatedly packed into larger heterogeneous regions (e.g., white matter, grey matter, cerebrospinal fluid). We studied the contrast recovery coefficient (CRC) behavior of single repeat structures, different object profiles and region-of-interest analysis techniques with a range of image resolutions. The resultant curves show the importance of the number of dimensions for which structural variations are considered
and suggest two important analysis regions for the delimiting region size (S)/resolution (FWHM) ratio: S/FWHM < 1 (R1) and S/FWHM > 1 (R2). As PET resolution volumes (RV) move from 3-7 mm towards 5 mm, the low but stable CRC’s of R1, which are relatively insensitive to the arrangement and shape of the underlying anatomical sub-units, become the higher but more variable values of R2.

The increased variability of regional values, due to sensitivity to the underlying anatomical variation with smaller RV’s, may decrease our ability to identify consistent functional activation patterns in all but test reject scanning protocols. We suggest that RV’s ≥ 1.0 mm³ may be nearly optimal for some tasks: in particular, for establishing activity distributions that best reflect functional, and not anatomical, normal range variations in populations.

No. 512

We have tested a new portable non-imaging device (VEST) which continuously records a beat-to-beat left ventricular (LV) time activity curve and ECG signal. To validate the measurement of LV function in ambulatory subjects with the VEST, 7 normals and 26 cardiac patients were studied with sequential gamma camera and VEST measurements. The VEST detector was placed over the region of LV. Serial beat-to-beat data were averaged over 15 seconds with the VEST and the following parameters derived: ejection fraction (EF), relative end-diastolic volume (%EDV), cardiac output (CO) and heart rate. The variability of the averaged EF over 2 minutes sitting quietly was < 3.5% (SD) in all patients. EF calculated by the VEST (v) was compared with that by the gamma camera (g) both at rest and during each stage of bicycle exercise.

(REST) EF(v) = 0.87 x EF(g) + 3.59; r = 0.92, SEE = 3.3, n = 33
(exercise) EF(v) = 0.99 x EF(g) + 0.85; r = 0.80, SEE = 9.0, n = 29

Repeated VEST study after complete removal and repositioning of the device resulted in a correlation of 0.98 for resting EF. ZEDV change from lying to sitting calculated by the VEST was correlated with that by the gamma camera (r = 0.84).

We conclude that the VEST provides reproducible and accurate measurement of LV function in ambulatory subjects.

No. 513

A single large computer system was developed to provide simultaneous viewing, acquisition and processing of patient (pt) data, pt data base management, pt image archival, pt scheduling (automated and manual), report generation, word processing and general ledger operations. The department consists of 11 imaging devices and a pharmacy lab. Average daily imaging of 50-65 pts generates about 2 Gb/annum of data.

A local area network was developed, consisting of a DEC VAX 11/750 as a central node and 12 stand-alone microprocessors for acquisition, processing and display. The VMS Operating System is adequate for system management. An in house software package written for the VAX is used for pt data base management, scheduling and report generation. A software package developed by the microprocessor manufacturer is effective for image processing. All pt data and demographics are stored. With data compression techniques, 8 weeks of image data is available on-line. Older studies are purged to mag tape and a tape index file is maintained. Demographic data is available on-line and is key in the location of pt studies.

An optical disk subsystem will permit a 24 month image data base to be available on-line. Scheduling software will provide the automatic retrieval of all previous studies on scheduled pts and VMS utilities permit operator retrievals.

Monday, 3:30-6:00

No. 514
FULLY AUTOMATED DATA PROCESSING OF PET STUDIES OF DOPAMINE (D2) RECEPTORS. M. Clausen, A.N. Bice, M.J. Stumpf, J.M Links, H.N. Wagner, Jr. The Johns Hopkins Medical Institutions, Baltimore, MD.

Data processing and quantification in PET studies of neuroreceptors is time consuming. To minimize this problem we have developed a fully automated, independent computer program for use in analysis of 11C-N-methylspiperone (NMSP) PET images.

With the NMSP tracer, dopamine (D2) receptor rich areas of the brain yield a linear relationship between ROI/cerebellar ratios and time, reflecting the nearly irreversible binding of the tracer. This fact serves as a basis for the functional images produced by our program.

11C-NMSP tracer specific characteristics were used to define sequences of automatic program actions. First the program determined cerebellar ROIs in the early (post-injection) PET frames. This was performed by multiplying vertical profiles of the appropriate transaxial image with a ramp function that increased progressively from the anterior to the posterior part of the brain. The image row corresponding to the maximum value of the weighted vertical profile was used together with an edge detection method to define the cerebellar ROI. Automatic ROI definition also was performed for caudate, putamen, frontal and temporal lobe regions.

Functional images of the slope of ROI/cerebellar ratios versus time, intercepts and linear correlation coefficients of such plots were produced. The images produced are convenient for quick assessment of approximate basal ganglia D2 receptor density, left-right receptor asymmetries and deviations from normal receptor binding kinetics.

No. 515

An observer study was performed to determine the optimum filter function for image processing. The images used in the study were reconstructed from simulated projection data. The simulated object was a cylinder of uniform activity distribution containing a cold, spherical lesion, 2 cm in diameter. The data was simulated in a manner which closely approximates acquired data, incorporating the effects of attenuation, collimator and scatter response functions, and noise characteristics typical of clinical SPECT studies. The projections were processed before reconstruction with either the Hanning or Butterworth filters with varying...
cut-off frequency, or the Metz filter with varying power factor. The observers were tested on their ability to detect the lesion in a 2AFC paradigm.

For each filter we have plotted percent correct responses vs. cut-off frequency (vs. power factor for the Metz filter). The results indicate a broad optimum for the Hanning and Metz filters. The Butterworth filter, however, displayed a well-defined optimum near 0.15 cycles/pixel at a pixel size of 6.4 mm. At its optimum, the Butterworth scored higher than either Hanning or Metz. All filters scored significantly better than no filter. We have proposed a model to explain the results based on the frequency response of the filter functions.

No. 516
AXIAL SAMPLING DENSITY REQUIREMENTS IN POSITRON EMISSION TOMOGRAPHY. E.W. Grochowski, M.R. Faler, S. Pelletier, and B.D. Pate. UBC/TRIUMF PET Program, Vancouver, B.C., Canada.

This study was directed at evaluating the effects of increased spatial sampling density in the axial direction on the accuracy of inter-plane interpolated data in positron emission tomography. With multislice PET scanners, many image slices in the imaged volume (e.g. coronal and sagittal sections) can be calculated by interpolating interleaved transverse section images which are in turn acquired by translating the subject axially between scans. It is important to consider the accuracy of data reconstructions of this approach.

Simulation studies were performed using the parameters of the UBC/TRIUMF PET VI tomograph which collects 7 axial slices simultaneously, with a center-to-center separation of 14.2 mm and a central slice thickness of 11 mm FWHM. The simulations involved the reconstruction of data along the axial direction from computer generated random signals, filtered, and sampled at densities corresponding to data taken at 2, 3, and 4 chair positions. Using a cubic spline interpolation kernel, the reconstruction error was found to be 12.2%, 3.3%, and 1.3% RMS for 2, 3, and 4 chair positions, respectively.

The costs of sampling at a higher axial densities are: 1) increased dead time as the chair is being moved; 2) lower statistics per acquired image slice, given the same number of counts in the study; and, 3) increased data storage requirements. The simulations indicate that a satisfactory trade-off between increased clinical scanning complexity and reconstruction accuracy occurs at 3 chair positions.

No. 517
A NUMERICALLY STABLE CIRCULAR HARMONIC TRANSFORM ALGORITHM FOR APPLICATION TO PET AND X-RAY CT. W.C. Hawkins, P.K. Leichner, N.C. Yang, T.L. Frenkel, and D.M. Loudenlager. The Johns Hopkins Hospital, Baltimore, MD.

The circular harmonic transform (CHT) solution of the 2-D Radon transform has only recently emerged as a computationally efficient method of image reconstruction. The algorithm is based on finding the fundamental solution of a system of non-homogeneous difference equations, and overcomes the poor spatial and contrast resolution associated with CHT algorithms. When compared to ramp-filtered backprojection or fan-beam convolution, the CHT algorithm is more robust to ringing and systematic errors in the projection data. The CHT algorithm can be applied to positron ring data without interpolation. For fan-beam data, a wide variety of geometries can be accommodated by interpolation of the projection sinogram in the angular direction only, with exact matching in the radial coordinate. For narrow-angle fan-beam data, however, the condition of exact matching requires that the dimension of the Tschebyshev radial transform become excessively large. Using Mellin transforms, we show that the signal energy of the 2-D Fourier-Tschebyshev transform of the sinogram is concentrated in well-defined sectors in transform space. The angle defining the sectors depends in a simple way on the fan-beam angle of the field-of-view. This result is used to reduce the dimension of the Tschebyshev radial transform, and to optimize the calculation of the sectors' orthogonal transforms of the CHT algorithm.

No. 518
OBJECT DEPENDENT INTERACTIVE VISUAL OPTIMIZATION OF SPECT PRE-RECONSTRUCTION FILTERING. M.A. King, S.J. Glick, B.C. Penney, R.B. Schwinger, and P.W. Doherty. University of Massachusetts Medical Center, Worcester, MA.

Starting with images of a liver/spleen phantom, a count-dependent Metz filter has been developed for use in two-dimensional pre-reconstruction filtering of single photon emission computed tomography (SPECT) studies. However, it has been noted that alteration of the filter parameters from those determined for the liver/spleen phantom was required to obtain the most visually pleasing images for different organ systems (objects). Through implementation on a hardware configuration which includes an array processor (AP400), a "real-time" interactive visual optimization of the Metz filter for the image of interest has been achieved. The program filters the first SPECT acquisition image according to the initial Metz filter formed for its count level. This filtered image, and the Metz filter employed in filtering it, is overlayed on a plot of the logarithm of the image power spectrum. The user is then shown to interactively vary the filter parameters of the Metz filter by changing the position of a "joystick." The "joystick" is set so that when it is centered in its X and Y range, the initial Metz filter is formed. Visual feedback from the filtered image, and plots of the filter and the image power spectrum are used to obtain an "optimal" filter. Preliminary results have indicated that pre-reconstruction filtering with this method produces visually superior SPECT images. It also allows for adapting the filter to the preferences of the individual reader, and serves as a useful teaching tool for the effects of filtering.

No. 519
EXAMINATION OF ASSUMPTIONS FOR LOCAL CEREBRAL BLOOD FLOW STUDIES IN POSITRON EMISSION TOMOGRAPHY. R.A. Koepe, G.D. Hutchins, R.D. Hichwa. Cyclotron/PET Facility, University of Michigan, Ann Arbor, MI.

We have examined the validity of two common assumptions of the Kety-Schmidt model for ICBF estimation as it is applied to positron emission tomography (PET). These assumptions are: 1) since an ICBF tracer must be freely diffusible, there is no effect due to blood-borne radioactivity, and 2) the arrival time of arterial input function is homogeneous throughout the brain. Both theoretical computer simulations and actual PET studies using 0-15 water indicate these assumptions can sometimes cause significant errors in the estimated flow values.

Even though complete equilibration between tissue and venous blood occurs, arterial blood remains at a different concentration. Thus, the early PET data following a bolus injection will have a considerable contribution from arterial-borne radioactivity. The effect of this blood-borne radioactivity is readily observed in the vicinity of the carotid arteries during the first 40 sec following injection. Blood flow images calculated using a dynamic protocol are noticeably
changed when the first 40 sec of data are omitted from the calculation. Flow estimates in cortical regions not near major arteries were decreased by ~5% which is in agreement with theoretical predictions.

The temporal shift of the arterial input curve was incorporated as an additional parameter in the model. Results indicate that arterial arrival times can differ by as much as 1 sec to various regions of the brain. This translates to changes in flow values of approximately 4-8%.

No. 520

Purpose: To perform quantitative measurements of distribution of radioactivity in SPECT by correcting for attenuation and using the method for dose planning for internal radiotherapy with radionuclides. The method is not depending on the shape of the object or the distribution of attenuating tissue.

Method: An algorithm for correction of attenuation has been developed and quantitative emission images from SPECT have been obtained. The algorithm is based on an iterative method where measured projections are individually corrected for attenuation by calculating projections from the emission image that are corrected for attenuation. The attenuation map is obtained from transmission studies using a flat radioactive source or from Computed Tomography. Using attenuation maps obtained from reference patients stored in a computer library, the method can be efficient and fast and will be useful for the clinical routine.

Conclusion: The code has been developed and has shown an improvement in quantification of radioactivity in a human head phantom. The relative distribution of pixels in a region of uniform radioactivity has been reduced from about 17% for the un-corrected image to 5% for the corrected image. The time required for correcting an image has been reduced from 12 minutes to about 1.5 minutes, for a PDP 11/34 computer with Floating Point Processor. This indicates the possibility of obtaining corrected sections other than transversal.

No. 521
A COMPARISON OF PET IMAGES OF CBF ESTIMATED BY THE INTEGRATED PROJECTION TECHNIQUE WITHOUT VS. WITH FIXED DISTRIBUTION VOLUME. DK Mahoney, SC Huang, ME Phelps. UCLA School of Medicine, Los Angeles, CA.

The integrated projection technique (IP) yields estimate images of both CBF and distribution volume (Vd) from algebraic formulas based on reconstructed images of un-decay- and non-decay-corrected tissue activity time-integrals. Although IP executes faster than non-linear regression, the speed of CBF estimation could be increased by modifying IP so that Vd is fixed to a globally uniform value beforehand and only CBF is estimated. This study examined the effect of fixing Vd on the estimation of CBF with IP.

We processed central-brain-slice data from four adult patients injected with 0-15 water and scanned with the NeuroECAT. After computing by IP a CBF and a Vd image for each patient, we calculated the mean value within the tissue in each Vd image. We re-processed the data twice using IP with two fixed global Vd values: the mean Vd value described above; and, a commonly cited value of 0.8 ml/g. To compare each fixed Vd CBF image to its corresponding variable-Vd CBF image, we computed the mean and standard deviation of the tissue values in each image.

CBF images calculated from IP with fixed Vd have lower mean values than corresponding images with variable Vd. Paired t-tests for the differences between mean for any patient implied that the differences were significant at the 0.05 level of significance. This result, along with other reports that the original IP underestimates CBF on boundaries between gray and white matter, suggests that fixing Vd in the integrated projection technique will lead to significant underestimation of CBF.

No. 522
BATES REGRESSION COMPUTATION (BR) OF LOCAL CEREBRAL METABOLIC RATE OF GLUCOSE (LCMRG) IN STROKE. PD Wilson, RA Hawkins, SC Huang. Univ. of Maryland, Baltimore, MD. and University of California, Los Angeles, CA.

LCMRG is typically estimated from FDG PET scans using a single scan (SS Method) which is cheaper and easier to conduct than the accurate computation via individual rate constants estimated from dynamic scans repeated up to 3 hours (Direct Method). But Hawkins et al showed that in ischemic tissue the SS Method produces estimates about 50% too low. Earlier we reported simulation studies indicating that BR should give more accurate estimates than SS in ischemic tissue.

We now report comparison of BR and SS to Direct Method in ischemic and contralateral normal regions of 5 stroke patients. We used BR with repeat scans up to T, and SS with scan at T, for T=30,45,60,90,120 min. The table gives mean and (RMSE) of % errors relative to Direct Method.

<table>
<thead>
<tr>
<th>Patient</th>
<th>SS</th>
<th>BR</th>
<th>DIRECT(N/I)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>3.76</td>
<td>3.14</td>
<td>1.21</td>
</tr>
<tr>
<td>Patient 2</td>
<td>3</td>
<td>1.55</td>
<td>1.82</td>
</tr>
<tr>
<td>Patient 3</td>
<td>2</td>
<td>-6</td>
<td>15</td>
</tr>
<tr>
<td>Patient 4</td>
<td>-100</td>
<td>-84</td>
<td>-11</td>
</tr>
<tr>
<td>Patient 5</td>
<td>-88</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

We conclude that BR may be superior to SS in normal tissue and should be markedly superior in ischemic tissue. BR should be useful in other LCMRG abnormalities and also in studies where the scanner is repositioned for additional slices, resulting in missing dynamic scans.

Monday, 3:30-6:00
COMPUTERS AND DATA ANALYSIS: QUANTITATION

No. 523

Radioimmunoimetry requires accurate quantitation of source activities and volumes. Correction for internal photon absorption, elimination of scattered radiation, and normalization of camera collimator spread with depth are the most important aspects in quantitation of nuclear medicine images. Most existing methods for image quantitation do not address all of these problems. Our procedures handle these aspects effectively.

Experimentally derived image files are used to produce point spread functions (PSFs) of scattered and unscattered photons in water at various distances from the camera. These PSFs are then used to compute the scatter fractions in images. Both scatter removal and collimator spread normalization are done by deconvolution of observed images with functions generated from these PSFs. After scattered radiation is removed we simply apply a factor, exp(u*d), to each pixel in the region of interest for attenuation correction; with u given as the linear attenuation coefficient of the primary photons in water and d given as the mean

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attenuation distance. For dual energy gamma emitters such as In-111 the value of u is a weighted average. Normalization of collimator spread with depth is necessary for source volume determination. Equal sized images were made from sources of the same size, irrespective of the source-to-detector distance. Our experiments with the liver, spleen and kidneys in an Alderson Torso Phantom resulted in errors < 9% in absolute quantitation of In-111 activities. Thus, these procedures allow effective absolute quantitation.

No. 524

AN ARTIFICIAL INTELLIGENCE APPROACH TO INTERPRETING THALLIUM-201 3-DIMENSIONAL MYOCARDIAL DISTRIBUTIONS.

S. Garcia, N. Esequerra, E. DePuey, W. Robbins, and H. Berger, Emory Univ. and Georgia Tech., Atlanta, GA

To overcome the subjectivity associated with identifying the presence and location of coronary artery disease (CAD) from stress Tl-201 myocardial distributions, we developed an expert system based on artificial intelligence (AI) tools to totally objectify this interpretation. In reviewing previous studies where a comparison existed with coronary angiography, we developed heuristic rules which best correlated the presence and location of perfusion defects (PDs) on 180° SPECT studies with documented CAD. The PDs were identified from polar maps and as pixels below gender-matched normal limits. Using AI tools, we structured 30 rules as the knowledge base of this expert system. This LISP driven, microprocessor-based expert system, tailored after MYCIN, acts as an inference engine where the location, size and shape of each of the PDs identified from bullseye maps, as well as pt-related information, is used to "fire" the rules to produce new facts or draw inferences. For each input parameter and for each rule, a certainty factor is assigned which is traced to infer the certainty of the identification and location of CAD. The entire interpretation takes place in less than 10 secs. This system is being tested and refined using a training set of 25 pts and will be validated against a prospective group of pts with angiographic correlates. This expert system, which has the ability to learn new rules and justify its interpretations, offers a tool for totally objectifying the interpretation of Tl-201 distributions. Importantly, this is the first report of the use of AI tools for interpreting medical images.

No. 525

A NEW TECHNIQUE FOR THE ANALYSIS OF DUAL RADIOPHILIC STUDIES.


Images of two radionuclides recorded simultaneously demonstrate differences in resolution, sensitivity and attenuation between the two energies. Also one image will compensate for these differences and minimise the attenuation at the two energies. Also one image will also show differences in resolution, sensitivity and attenuation between the two energies. This technique has been applied in both phantom and clinical studies involving dual radionuclide subtraction and demonstrated excellent scatter prediction with significantly reduced artifacts.

No. 526

QUANTITATION OF PERFUSION DEFECTS BY 201-TL SPECT.
Preliminary Results in Patients with Acute Myocardial Infarction.

G. Karcher, M. Amor, A. Bertrand, P. Zannad, F. Maurin, F. Aug, G. Ethovnot - C.H.U. Nancy-Brabois - France

Since 201-Tl myocardial distribution could only be assessed on a relative basis and since it is non homogeneous even in normal subjects (relative hypofixation in inferior and basal septal walls), we developed a quantitative analysis by 201-Tl SPECT which allows the myocardial distribution to be studied with respect to the myocardial distribution of normal subjects. From short-axis, long axis and 4-chambers slices, both the volume containing the heart and the long axis are determined. A radial analysis of each short-axis slice is performed by calculating the maximum count value along 64 radii. The distribution of 201-Tl over the defect size and thus for the follow-up of therapy.

No. 527

RECOVERY COEFFICIENTS FOR QUANTITATIVE IMAGING OF SMALL OBJECTS BY 180° AND 360° SPECT.

S. Loncarevic, A.N. Bice, M. Clausen, and H.N. Wagner Jr. The Johns Hopkins Medical Institutions, Baltimore, MD.

For quantitative analysis of SPECT images it is important to estimate the loss of quantitation (recovery coeff., RC) for objects comparable in size or smaller than the system resolution. A computer program was developed to simulate 180° and 360° SPECT acquisitions of long cylindrical sources in air to investigate the behavior of the RC as a function of acquisition parameters and source position in the field-of-view (FoV). The simulation involved randomly selecting point sources within the object and calculating each point source's contribution to every angular projection. This contribution was estimated from measured Gaussian point spread functions (PSF) of the Toshiba GCA-90B rotating camera with a LEAP collimator. PSF's were measured for source-detector distances of 0-50 cm. Cylindrical objects, 1-6 cm in diam., were simulated using a radius of rotation of 25 cm and a"" sampling. For the 360° acquisition the RC depends primarily on object size, not on FoV location. For 180° acquisition, the RC changes significantly with object location and acquisition starting angle. For a 2 cm diameter located 9 cm off the axis-of-rotation (AOR) in the LAD direction, the RC is 39% larger than that at the AOR for a RAO-LPO acquisition. Other 180° sampling arcs can produce a loss of quantitation that is greater off the AOR than on the AOR. This is due to the camera response dependence.
No. 528

PURE TUBULAR RENOGRA M CURVES OBTAINED BY FACTOR ANALYSIS OF I-131 HIPPURAN STUDIES. D.G. Pavel, E. Olea, K. Zolniczycyk, J. Sychra, University of Illinois Hospital, Chicago, IL.

Pure tubular renogram (R) curves can not be obtained in routine, due to simplistic, empirical, background (B) subtraction. This is due to complexity of surrounding structures and to kidney anatomy. Factor Analysis (FA) provides theoretically the ideal solution but only for single kidney (K) patients. In order to prove the theory and feasibility for 2 K patients we studied bilaterally normal renal cases, using LFOV camera and 20 (1 min) frames. After delineation in a classic fashion of ROI-s for each K and of 2 B areas, standard R-s were obtained and used for comparison. FA by Bazin-Di Paola algorithm, on whole field of view, by requesting 3 and 4 factor (F) searches. The results were used to reconstruct sequences of 20 frames based on all 3 or respectively 4 F and then, separately, based only on the typical tubular factor found. The same ROI-s were used on all sequences. The reconstructions can be achieved based on the factors preserve the original image information while showing a filtering effect and a slight loss in B; the total count loss within the ROI-s is negligible; 2) the isolated tubular factors show significant change in shape, characterized by sharper peak and steeper rate of decrease; these changes are pronounced than the effect of standard B subtraction on the original curves; 3) the best tubular R appears to be the one resulting from a 4 factor search and shows that it has been cleaned up of surrounding B as well as of intrinsic vascular B and of pelvis interference; 4) normal kidneys generate perfectly superimposable curves; 5) factor images also enable easy and accurate ROI delineation. Conclusion: Pure renogram curves can be obtained from each kidney without a priori bias, B subtraction and interpolation. The method is simple and reasonably fast on standard computers.

No. 529

ESTIMATION OF RENAL VOLUME WITH SPECT; PHANTOM STUDY Validation. W. Robeson, I. Zanzi, M. Lesser, P. Ley, and D. Marqouleff. North Shore University Hospital, Cornell University Medical College, Manhasset, N.Y.

On source distance. The simulation method is extendable to arbitrary source shapes in attenuating medium. The method is also useful for investigating inter-octant volume estimation inaccuracies and object distortions.

No. 530

TARGET DETECTION USING SINGLE PHOTON EMISSION COMPUTED TOMOGRAPHY. T.R. Simon, B.S. Walker, J. Triebel, J.E. Dowd. Univ. TX, Dallas VAMC, Dallas, TX.

Getting the best data for a given acquisition time and tracer dose becomes progressively challenging with more acquisition options. The type of filter (F) and number of projections (P) were analyzed for ability to identify hot and cold targets in images of a specially constructed set of phantoms with targets arranged in either a circular or rectangular array. The phantoms were charged with technetium-99m perchlorate. Two observers independently scored images acquired with 15 to 120P over 360 degrees in imaging series with 3-24 million total counts back-projected with Ramp, Hamming, Hann, Parzen and various Butterworth F. The targets were hot crosses and cold bars 3-9 mm in diameter. Targets were considered "detected" if not >2 contiguous pixels were missing in the processed image. Hot and cold target detection showed opposite trends: Cold targets were better recognized with more counts per P while hot targets benefited from more P. Hot target detection at 1SP was unacceptable. As expected more total counts in a series uniformly improves both hot and cold target detection through the range studied. We conclude that for the studied variables: (1) targets in a rectangular array are better detected than those in a circular array; (2) the type of back-projection filter is important with the best results obtained using a Hann, Hamming or high order Butterworth and (3) the number of P should be traded off against the number of counts per P with careful consideration toward purpose since hot object detection benefits from a different strategy than cold target detection.

No. 531

QUANTITATIVE SINGLE-PHOTON EMISION TOMOGRAPHY. D. Snyder, M. Miller, T. Miller, and C.-J. Chen. Washington University, St. Louis, MO.

A mathematical model for data acquired in single-photon emission computed tomography (SPECT) is derived for the quantitative reconstruction of radioactivity distributions. The model accurately accounts for: (1) the nonuniform attenuation of photons in body tissue; (2) the depth-dependent point-spread function of gamma-ray cameras used as a radiation detector; and (3), the statistical nature of the radioactive tracer dose becomes progressively challenging with the number of counts back-projected with the quantitative reconstruction of radioactivity distributions is based on the maximum-likelihood method of statistics and incorporates three of the aforementioned effects: photon attenuation, measurement errors due to the point-spread function of the gamma camera, and the statistics of the measurements themselves. The algorithm has been implemented using the iterative, expectation-maximization procedure of Dempster, Laird, and Rubin. Our treatment of the effects of attenuation and point-spread is fundamentally different from methods used in other published SPECT algorithms in that it arises from an accurate physical model rather than from an ad hoc averaging of data acquired in opposing views. We also describe how a "noise-like" artifact, which has been seen in positron-emission tomography as a series of randomly distributed peaks and valleys distributed through the image field when maximum-likelihood approaches have been used, is an intrinsic effect that is removed via the use of Grenander's method of sieves. We discuss the often advocated policy of avoiding this "noise" artifact by arbitrarily terminating the iterative maximum-likelihood procedure after 30-50 steps.

No. 532

A RENAL VASCULAR TRANSIT TIME DISTRIBUTION METHOD FOR USE WITH TECHNETIUM-99m COMPOUNDS. C.A. Westervelt, G.R. Olendried, and P.T. Kirchner. University of Western
Ontario, London, Ontario, and University of Iowa, Iowa City, Iowa.

A integral method has been developed for the analysis of the early or vascular portion of the renal time activity curve generated from scintillation camera frame data produced after peripheral venous injection of Tc-99m chelates. The kidney is modeled as three parallel capillary channel networks. A background subtracted aortic input function is produced and this curve along with the renal curve data are noise reduced by an appropriate asymmetric smooth. The integral from 0 to t of this input function is related to the earliest portion of the renal curve to determine the renal arterial delay time and a signal proportionately constant. This information is then used to synthesize the cumulative renal feed function which differs from therenal function only when tracer begins to leave the kidney. The difference between these latter two functions is the renal vascular output function. The output function is stripped of renal compartmental information by comparison of the early linear portion of this function with the identical portion of the cumulative feed function. The mean of the transit time distribution of the renal vascular output function is isolated for each of the first two compartments (mean ± 1 SD = 6.8 ± 2.4 and 12.8 ± 3.2 sec, respectively for 40 normal kidneys studied with Tc-99m MDP). The magnitude of the renal plasma flow is derived for all three compartments (mean ± 1 SD = 67±9%, 17±10%, 16±9% respectively) where the third compartment contains tracer which resides in the kidney for an extended period of time.

No. 533

Mass attenuation and mass energy absorption coefficients of human tissues are important in dosimetry calculations. They can be calculated with a sum rule by weighting the same coefficients of the individual elements with percentage chemical compositions and adding them together. For energies greater than 60 Kev, the molecular binding effect causes errors of less than a percent. For certain energies, the coefficients of the individual elements have been published and tabulated. But for energies in-between (gamma ray energies of most clinically used radionuclides), we used a cubic spline interpolation method to calculate the coefficients of blood, bone, brain, fat, heart, kidney, liver, lung, muscle, pancreas, and spleen for Co-57, Co-60, Ga-67, Ge-75, Tc-99m, In-111, In-113m, T-132, In-131 and Cs-137. Compared with some existing experimental values, the coefficients agreed within 0.0% to 4.5%. Different values of chemical compositions of the same tissue from different reports were compiled and compared, and the resulting coefficients agreed within 2%. Therefore, the coefficients are insensitive to the chemical compositions at these gamma ray energies.

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DOSIMETRY/RADIObIOLOGY

No. 534
ABSORBED DOSE IN SKIN FROM CONTAMINATION OF IN-111 IN-OXINATE WHEN WORKING WITH Y-90. LABELING WITH Y-90. Gustav Grafström, Bo-Anders Jonsson and Sven-Krik Strand, Radiation Physics Department, University of Lund, Lund, Sweden.

The radioisotope 111In-oxinate is used in labeling of leukocytes, granulocytes, platelets and antibodies. Because of its liquid state there is always a risk of contamination during the handling procedure. As the oxinate is soluble in fat, the contamination may penetrate the skin. Emission of low-energetic electrons during the decay would cause high absorbed dose. The aim with this investigation was to evaluate the "normal" grade of contamination and the absorbed dose enclosed.

The degree of contamination during different operations of handling was investigated by determination of the activity on protection gloves used by personnel at isotope-laboratories. Measurable activity remained after all handling procedures, ranging from 0.1 to 100 kBq.

Leakage in different latex protection gloves, with or without simulation of excessive sweating, showed fractions up to one percent of contaminated activity.

The magnitude of the renal plasma flow is derived for all three compartments (mean ± 1 SD = 67±9%, 17±10%, 16±9% respectively) where the third compartment contains tracer which resides in the kidney for an extended period of time.

No. 535

It is important in radiation therapy to deliver cell killing doses to all of the cancer cells. In therapy using beta emitters, the equilibrium dose rate does not apply to small sources or at the edges of tumors due to the finite range of the beta rays. The purpose of this paper is to present the spatial distribution of the absorbed dose per microcurie hour (AD/uCiH) for Y-90.

Computer simulations were performed to calculate the spatial distribution of the AD/uCiH for Y-90 sources of different volumes and spatial distribution. The sources were placed in a uniform absorbing media. The AD/uCiH was calculated using convolutional techniques and the absorbed-dose distribution from Berger (MIRD # 5).

For spherical sources containing homogeneously distributed Y-90 the maximum AD/uCiH, the AD/uCiH at the edge of the source, and the average in the object are CRU. VOL. MAXIMUM EDGE AVERAGE

<table>
<thead>
<tr>
<th>OBJ. VOL</th>
<th>MAXIMUM</th>
<th>EDGE</th>
<th>AVERAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0</td>
<td>1.11</td>
<td>0.46</td>
<td>0.76</td>
</tr>
<tr>
<td>1.0</td>
<td>0.4</td>
<td>0.2</td>
<td>0.95</td>
</tr>
<tr>
<td>1.0</td>
<td>1.64</td>
<td>0.69</td>
<td>1.12</td>
</tr>
<tr>
<td>1.0</td>
<td>1.88</td>
<td>0.75</td>
<td>1.32</td>
</tr>
<tr>
<td>1.0</td>
<td>1.96</td>
<td>0.83</td>
<td>1.45</td>
</tr>
<tr>
<td>1.0</td>
<td>1.97</td>
<td>0.88</td>
<td>1.56</td>
</tr>
</tbody>
</table>

The above calculations show that the absorbed dose for small sources can be significantly less than the equilibrium dose rate suggests. Thus, it is important to calculate the dose for representative small tumors or at the edge of large tumors to insure that a sufficient absorbed radiation dose is delivered to all of the tumor cells to achieve a cure.

Monday, 3:30-6:00
Exhibit Hall


Despite careful history taking and pregnancy testing, therapeutic radiodine is occasionally administered to women who turn out to be in the earliest stages of pregnancy. Because of concerns about fetal radiation,
genetic counseling, and possible therapeutic abortion, reliable dose estimates are needed. Iodine-131 iodide therapy has been widely accepted as the first-line treatment for metastatic disease, but radiation dose estimation (with any degree of accuracy) for the fetus, during the early stage of pregnancy, appeared to be difficult. Dosimetry for the two-week old fetus by several experienced investigators varied widely between 2.7 and 5.4 cGy/Gy (maternal thyroid uptake was 24% at 24 hour, and total body retention was 25% and 13% after 1 and 2 days). This led to the present reevaluation of fetal dosimetry. A 1.3 week old male fetus was implanted to the inferior vena cava with a mass less than 10 grams. Calculations were based on MIRD recommendations, other relevant publications, available experimental data, and kinetic considerations for iodine-131. Fetal radiation dose was mainly contributed from circulating hormone, whole body iodide level, and concentrations of radioactivity in the urinary bladder and the GI tract. Calculations were also made for uterus as a reasonable equivalent organ. Fetal dose in the above case, with the present approach, was approximately 12 cGy/Gy (0.43 Rad/MCi), narrowing down the wide range of 2.7-5.4 cGy/Gy. This dosimetry model employs a dynamic system with limited data, but offers higher accuracy.

No. 537

We assessed radiation doses to tumours in order to evaluate new metabolic radionuclide agents.

Seven children from 4 to 18 years old received 14 therapeutic doses of I-131-mDB for metastatic neuroblastoma; 2 adults received 4 treatments for malignant pheochromocytoma. The infused doses ranged from 1.4 to 5.5 MBq/kg and to 1.1 to 3.5 mg/m² of MIBG. A double head gamma camera with a 464° Na(II) crystal and a high sensitivity collimator was used, linked to a computer system (Sopha Medical). We obtained the activity present in a tumour using manually drawn ROI on the image representing the geometrical mean of the anterior and posterior views. Whole body scans were recorded from 1 to 14 days after injection. CT and NMR images were used to determine the volume of tumoral targets. The effective half-life of MIBG after the last scan was extrapolated exponentially.

After calibration with I-131 sources (0.2 to 740 MBq) placed at various depths in a phantom filled with water at a height of 10.15 and 20 cm, estimated error was ± 15%. Computed tumour doses varied from 3 to 1056 Gy. We report here the results in 2 cases. In a case of an orbital metastasis of a neuroblastoma, the biological half-life was 9.3 days, the uptake represented 11% of the injected dose for a tumour volume of 50 cm³; the resulting radiation dose was 1056 Gy. In the case of hepatic metastases of malignant phaeochromocytoma, the biological half-life was 29 days with an initial uptake of 15%, and one third of the liver was estimated to be involved by the tumour; the dose was 246 Gy.

No. 538
THERMAL EFFECTS OF HIGH-FIELD (1.5 TELSA) MAGNETIC RESONANCE IMAGING: CLINICAL EXPERIENCE BELOW AND ABOVE A SPECIFIC ABSORPTION RATE OF 0.4 W/kg. FG Shellock, DJ Schaefer and JF Crues. Department of Diagnostic Radiology, Cedars Sinai Medical Center, Los Angeles, CA and General Electric Company, Milwaukee, WI

The U.S. Food and Drug Administration has issued guidelines to ensure the safe operation of magnetic resonance imaging (MRI) systems which include limiting the radiofrequency (RF) radiation exposure to a whole body average specific absorption rate (SAR) of 0.4 W/kg. This recommendation may be unnecessarily restrictive, therefore we determined the thermal effects of MRI in patients subjected to RF exposures below (SAR < 0.4 W/kg, range 0.1 to 0.4 W/kg, N = 23, Group I) and above (SAR > 0.4 W/kg, range 0.5 to 1.3 W/kg, N = 28, Group II) the suggested SAR. Body and skin temperatures were obtained immediately before and after MRI. A high-field MRI device (Signa MR System, General Electric) was used in this study and scans were obtained with conventional RF pulse sequences.

No. 539
BIOLOGICAL DISTRIBUTION AND DOSIMETRY OF TC-99M-MAA. G.H. Simmons, J.J. Coupal, F.H. DeLand, J.S. Blake. Veterans Administration and University of Kentucky Medical Centers, Lexington, KY.

Tc-99m-MAA is used extensively for lung perfusion studies, yet existing human data are insufficient to accurately calculate the absorbed dose to individual organs. The objective of this study is to gather biodistribution data sufficient to enable the calculation of average organ doses in humans with normal lung function to an accuracy of 15%. Two approaches for quantitating the data were investigated. Absolute efficiency measurements were performed on 10 volunteer subjects using Tc-99m-HAM which is trapped in the lung capillaries with greater than 98% efficiency on the first pass. Efficiency factors for other organs of interest were measured using the REMCAL phantom. This method was judged unsatisfactory because of the large dispersion in the measured lung efficiencies, especially among females (51% r.m.s.). In the other method conjugate counts were performed over a 24 hour period on 20 subjects following injection of Tc-99m-MAA. Quantitation was achieved by assuming 100% of the injected activity to be in the lungs on the first count. Blood was drawn at the time of each count, and urine was collected for 48 hours, enabling a balance determination to account for all injected activity. Particle size, tagging efficiency, and integrity, radiochemical purity, and the number of MAO particles injected were measured for each subject. The average lung dose was determined to be 0.23 ± 0.024 rads/MCi. Doses to other organs as well as biological rate constants were also calculated.

No. 540
RADIATION DOSE CHARACTERISTICS OF AN IMPROVED Os-191/ Ir-191m GENERATOR SYSTEM. H.G. Stabin and E.E. Watson. Oak Ridge Associated Universities, Oak Ridge, TN; F.P. Knapp and T.A. Butler, Oak Ridge National Laboratory, Oak Ridge, TN; C. Brihaye and M. Guillaume, Universite de Liege, Belgium.

Short-lived radionuclides have great potential for use in radionuclide angiography because studies can be repeated frequently with little interference from previous radiation doses. We investigated the dose delivered by an Os-191m-Ir-191m generator system developed at ORNL and the Universite de Liege in Belgium, shows 1r-191m yields of up to 20% with Os-191m breakthrough of around 0.002%. Detailed review studies were performed in female Fisher rats for extrapolating radiation dose.
estimates to humans. Organ distribution, retention, and excretion data were collected for up to eight days; results were fit to one or two compartment exponential intravenous and intratumoral curves using linear and non-linear least squares techniques. The Ir-191m radiation dose estimates were on the order of 10^6 mGy/MBq. The Ir-192 and Os-191 contaminants contributed most of the radiation dose to the major organs. The highest dose estimate to any organ, including contaminants, for an administered activity of 5300 MBq of Ir-191m was near 100 μGy (representative of the dose to the liver, kidneys, spleen, and thyroid). Most of the estimates were less than 50 μGy. The dose estimates for this generator system will be compared to estimates for other agents currently used in radionuclide angiotherapy.

Work was performed for the USDoe under contract DE-AC0576OR00033 and Interagency Agreement No. FDA 224-75-3016.

No. 541

DOSIMETRY OF TANTALUM-178 AND TUNGSTEN-178 IN ADULTS AND CHILDREN. R. E. Zimmerman, B. L. Holman, and R. D. Neirinckx. Joint Program in Nuclear Medicine, Department of Radiology, Harvard Medical School and Brigham and Women's Hospital, Boston, MA.

Dosimetry calculations have been performed for the isotope Ta-178 and its parent W-178. Tantulalum-178 is a short half-life (9.3 min) generator-produced, low energy radionuclide for imaging heart function in first pass studies using gas imaging detectors. It decays from the parent W-178 (T1/2 = 2.23 d) by complex electron capture with subsequent gamma emission and internal conversion. Approximately 1% of the decays are by positron emission. The principal radiations for dosimetry considerations are the Auger electrons, X-rays, positrons and K-radiation. The number of internal conversion electrons, X-ray abdundances and Auger electron yields were calculated from nuclear data for Ta-178 and W-178. Biokinetic data were obtained from phosphate buffered Ta-178 eluant and were matched for age were used as controls (N). All patients and controls.

After thyroid blockage by Lugol's solution, 18.5 Mbq I-131-MIBG were injected to 35 patients for detection or follow up of MTC. Whole body scintiscan and 10 to 20 minutes activity recording of the neck, chest and abdomen were obtained at 24 and 48 hr.

MIBG scintigraphy was negative in patients with normal calcitonin levels (<0.1 ng/ml-n=9). It was negative in patients with sporadic and isolated MTC (n=1, despite elevated calcitonin and obvious tumor masses). It was positive in 2 patients with isolated MTC and unsatisfying familial screening. In familial or MEN cases (n=9), 3 patients with calcitonin between 1 and 6 ng/ml had negative scan. 6 patients with higher calcitonin level had positive scan, demonstrating uptake in thyroid tumors (4 cases) and liver metastasis (2 cases).

In conclusion, MIBG uptake in MTC is essentially detectable in familial disease or MEN syndrome with markedly elevated calcitonin. It could be a specific feature of MEN syndrome.

No. 543


Salivary gland function was studied in 20 patients with tumors, stone or other afflictions of the major salivary glands. Ten mCi of TC-99m pertechnetate was administered intravenously and the patient was imaged beginning immediately in the anterior position for 60 minutes. Salivary gland evacuation was stimulated 40 minutes after injection by administering the patient granular citric acid. The entire study was acquired by computer in list mode with 60 one minute frames. The time to maximum uptake and excretion fraction of the tracer were calculated for the parotid and submandibular glands. Contra-lateral glands and normal volunteers were used as controls.

The excretion fraction after citric acid stimulation for normal parotid and submandibular glands was greater than 75% and 55% respectively. Radiotracer excretion after citric acid stimulation was rapid, and peak excretion effect (defined as minimum counts in the ROI following stimulation) was achieved by 4 minutes. Obstruction of salivary ducts by tumor or stones resulted in a greatly diminished excretion fraction (range 3% to 45%).

We conclude that quantitative assessment of TC-99m pertechnetate kinetics before and after stimulation of salivary glands aids in the assessment of gland function and in detection of duct obstruction.

No. 544

SCINTGRAPHIC EVALUATION OF GASTRIC EMPTYING IN DIABETIC PATIENTS WITH CARDIAC AUTONOMIC NEUROPATHY. J. L. Urbain, M. Moulart, M. Buyschaert & S. Pauwels, University of Louvain Medical School, Brussels, Belgium.

The radionuclide technique was used to assess whether, in diabetic patients, cardiac autonomic neuropathy (C.A.N.) is associated with delayed gastric emptying. Twelve patients with CAN (C.A.N.) were compared to 9 patients without CAN (C.A.N.-). Nine healthy subjects matched for age were used as controls (N). All patients and subjects were asymptomatic and without any organic gastrointestinal disease. Measurement of variation in heart rate during deep breathing was used as index of CAN.

Gastric emptying of solids (GES) was determined after ingestion of Tc-99m-HSA labelled eggs. Anterior and posterior images were obtained every 20 min for 120 minutes and data were corrected for radioactive decay and changes in depth.

ENDOCRINE

No. 542


It was recently reported that MIBG could accumulate into various tumors growing from the APUD system, especially MTC. The aim of this cooperative study was to assess MIBG as a scintigraphic marker for MTC.
THE EFFECT OF THE MENSTRUAL CYCLE ON DOPAMINE RECEPTOR BINDING OF C11-3-N-METHYLSPERIPERONE.
D.F. Wong, G. Wend, H. Zacur, D.S. Goldberg, J. Williams, L. O'Tu­
ama, E. Broussolle (*), R.F. Dannals, J.M. Links, H.M. Wa­
ger, Jr. The Johns Hopkins Medical Institutions, Baltimore, MD.

In a previous report of the decline of dopamine receptor binding of C11-3-N-methylspiperone in the caudate nucleus as a function of age, the decrease was statistically different in men than in women. (Science 226:1393-1396,1984.) To determine whether hormonal effects could be important, we examined women at different stages of the menstrual cycle. All had normal menstrual cycles, were not receiving exogenous estrogens, and had a normal gynecologic history. The phase of the menstrual cycle was assessed by history, basal body temperature and serum and urine hormonal values. Each subject was studied with C11-3-N-methylspiperone at two different phases of the menstrual cycle. In 6 subjects in whom there was no more than 1 cycle between the two PET studies, there was a significant increase in the rate of binding of the C11-3-N-methylspiperone to the dopamine receptors during the pre-ovulatory period. The increase in receptor binding correlated with increasing serum estrogen levels. Previous studies in animals have suggested that estrogen administration can increase dopamine receptor density. The percent differences in each study was on an average 20±6% , and was signific­ant at p < .05 using a sign test.

*ADAMHA visiting NIDA Addiction Research Fellow.

Monday, 3:30-6:00
Exhibit Hall

GASTROENTEROLOGY: ESOPHAGEAL AND LOWER GI

No. 547
RADIONUCLIDE ASSESSMENT OF ILEO-ANAL ANASTOMOSIS EMPTYING: PRELIMINARY RESULTS. R. Taillefer, J. Heppell, V. Derbe­kian, P. Belliveau, S. Dubé. Hôpital Hôtel-Dieu and Royal Victoria Hospital, Montréal, Canada.

The aim of this study was to assess and compare with a radionuclide enema the emptying of two types of reservoir constructed with an ileo-anal anastomosis. Reservoirs were made of either two ("J" shaped pouch) or three limbs of ileum ("S" pouch). This prospective study includes 24 patients (11 with "J" pouch and 13 with "S" pouch) and 10 subjects with normal ano-rectal function as controls. One mCi of 99mTc-sulfur colloid was added to 300-350 cc of beaten eggs. The mixture was then cooked until firm in consistency. With a syringe and rectal tube, the semi-solid marker was instilled per anum in the neo­rectum until a sensation of fullness was reached. Ileal pouch counts (posterior view) were measured (2 min. ac­quisition) using a scintillation camera and computer pre and post spontaneous evacuation. The emptying was defi­ned as the difference in counts divided by pre-evacuation counts. The results are as follows:

<table>
<thead>
<tr>
<th>Group</th>
<th>Nb emptying</th>
<th>Range (mean ± SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>J pouch</td>
<td>10</td>
<td>90 ± 42</td>
</tr>
<tr>
<td>S pouch</td>
<td>11</td>
<td>70 ± 62</td>
</tr>
<tr>
<td>Mean</td>
<td>13</td>
<td>60 ± 72</td>
</tr>
<tr>
<td>SD</td>
<td></td>
<td>21-89%</td>
</tr>
</tbody>
</table>

The "J" and "S" pouches emptied less than controls. There appears no significant difference in the reservoir emptying of both pouches. More data is necessary however to confirm this latter finding.

The radionuclide study provides quantitative evaluation of ileo-anal reservoir emptying. As well, it helps in the follow-up and identification of patients who would benefit from rectal intubation.

No. 548

A noninvasive method of TL-201 per-rectal administra­tion was performed to observe the changes in portal­systemic circulation after sclerosing therapy (ST) and/or splenic artery embolization therapy (SAET) in patients with esophageal varices. One mCi of TL-201 chloride was given rectally and scintigram and heart/liver uptake ratio (H/L) at 60 min. after administration were investigated before and after ST (22 studies in 16 patients) and SAET (8 studies in 8 patients). After successful ST there was 5.1% of decrease as the mean change rate of H/L, but many of the studies showed little...
or no change in H/L. A marked decrease of H/L together with marked scintigraphic change was observed in two cases. One of them showed the recurrence of esophageal varices later. A marked increase of H/L was observed in one case in which the recurrence of esophageal varices was not found for two years. After SAET H/L dropped in most of the cases. We conclude 1) In cases showing highly decreased H/L after GT, portal-systemic shunting greatly depended on esophageal varices and they have a high risk of the recurrence of esophageal varices. 2) In cases showing little change or increase in H/L after GT, portal-systemic shunting did not depend on esophageal varices, but other shunting routes. 3) Reduction of splenic blood flow decreased H/L. This method was found to be useful in evaluating the pathophysiological changes of portal circulation after treatment.

No. 549
ESOPHAGEAL DYSMOTILITY IN PYLORIC OBSTRUCTION BEFORE AND AFTER GASTRIC DECOMPRESSION. S.H. Yeh, K.S. Liu, T.C. Yeh, S.C. Hu, and L.C. Wu. Veterans General Hospital and National Yang-Ming Medical College, Taipei, Taiwan.

This study assessed esophageal dysmotility in pyloric obstruction and the effect of gastric decompression on such a dysfunction by radionuclide transit (RT) studies. Data were acquired in list mode after an oral dose of 0.5 mCi Tc-99m sulfur colloid in 10 ml of water in the supine position. A computer routine modified from Klein (J Nucl Med 25:957, 1984) was used to calculate: (A) total mean transit time (TMTT) in sec, (B) residual fractional after the first swallow (RF), (C) retrograde index (RI), and (D) regional transit times (RTT).

Ten patients with pyloric obstruction (secondary to longstanding chronic duodenal ulcer in 8, gastric erosion in 1 and stricture after surgery in 1) underwent RT studies before and 7.1 ± 4.5 days following gastric decompression (GD). GD decreased both TMTT (mean ± s.d., 9.7 ± 1.9 sec to 7.7 ± 1.9 sec, p < 0.05) and RF (0.41 ± 0.19 to 0.19 ± 0.18, p < 0.02). RTT's also significantly decreased, especially for the proximal third (5.8 ± 2.1 sec to 3.6 ± 1.9 sec, p < 0.05). However, RTT and RTT's (mid and distal) were still significantly higher after GD than in normal subjects (n = 25; TMTT = 5.8 ± 0.6 sec, p < 0.001). In contrast, proximal RTT and RTD did not differ in pts after GD and in normal subjects (p < 0.2 in both). RI was unchanged by GD. In 10 pts of this study, 9 had moderate to severe symptoms of esophageal dysfunction, and all of them after GD were symptomatically improved or relieved together with improved motility.

In summary, esophageal dysmotility occurs in the great majority of pts with pyloric obstruction, and can be mitigated by gastric decompression.

Monday, 3:30-6:00
Exhibit Hall

GASTROENTEROLOGY: GASTRIC

No. 550
DUAL RADIOISOTOPE STUDIES OF BILE AND FOOD FLOWS IN THE PATIENTS WITH UPPER ABDOMINAL RECONSTRUCTIVE SURGERY. T. Aburano, A. Tada, N. Tonami, K. Hisada, I. Konishi, Y. Takeshita, I. Miyazaki, and M. Matsuhashi. Kanazawa University Hospital, Kanazawa, Japan.

The presence of bile is necessary in the digestion and absorption of fat. The dual nuclide studies of bile (Tc-99m IDA) and food (In-111 DTPA) flows were done in 20 patients with upper abdominal reconstructive surgery, such as gastroenterostomy and/or biliary enteric anastomoses, in order to evaluate the relation between bile and food flows. Five hundred micromicros of In-111 DTPA dissolved in 200 ml of fat-rich liquid meal was orally administered 20 to 30 min. after intravenous injection of 5 mCi of Tc-99m diethyl IDA. Both images of Tc-99m and In-111 over upper abdomen were simultaneously taken every 5 min. for 2 hours.

In 21 patients with Billroth II reconstruction, only five (24%) showed the good mixture of bile and food. The remained sixteen showed the poor mixture of those, mostly due to the prolonged retention of bile in the afferent loop and the rapid transit of food into the efferent loop (14 patients). Moreover, five showed the enterogastric reflux of bile. On the other hand, in 7 patients with Billroth I reconstruction, six (86%) showed the good mixture of bile and food, although one showed the poor mixture of those due to the markedly prolonged transit of food.

These findings suggest that the reconstruction with Billroth I method may be better than the one with Billroth II method in order to keep the good physiologic relation between bile and food flows in the patients following upper abdominal surgery.

No. 551

A new In-111 labeled solid meal (ILSM) was prepared by chelation with chelex resin bead (CRB). The effect of grinding of normal chelex resin bead (NCRB) on In-111 chelation and retention in solid meal with and without microencapsulation with silicone was evaluated in an in vitro system. NCRB (30-70 µm) was ground in a mortar-pestle to form ground chelex resin bead (GCRB). Fine particles were removed by resuspension in distilled water and centrifugation (1750 g, 100-150 µCi of In-111 Chloride was diluted with 0.1 N HCl and mixed with 1 gm of NCRB and GCRB in triplicate. Unbound In-111 was removed by centrifugation (1750 g). Some samples were coated with 0.5 ml of silicone oil (SO) and heated for 30 minutes. The In-111 labeled control and SO coated NCRB and GCRB were mixed with eggbeater (Fleischmann) and ILSM was prepared by heating until solid. The meals were digested with HCl-pepsin (1.2 mg/ml of 0.1 N HCl) for four hours in a stirrer-bath (37°C). Aliquots were collected at intervals for determination of In-111 loss from ILSM. The CRB labeling efficiency and In-111 loss at 4 hours are tabulated:

<table>
<thead>
<tr>
<th>CRB</th>
<th>In-111 In-loss (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-111 NCRB</td>
<td>98 ± 1</td>
</tr>
<tr>
<td>In-111 NCRB (SO)</td>
<td>96 ± 2</td>
</tr>
<tr>
<td>In-111 GCRB</td>
<td>96 ± 1</td>
</tr>
<tr>
<td>In-111 GCRB (SO)</td>
<td>96 ± 1</td>
</tr>
</tbody>
</table>

These results suggest that In-111 GCRB was retained in solid meal at higher level than NCRB and coating does not significantly increase retention.

No. 552
PH DEPENDENCE OF IN-111 ALGINIC ACID ANTICANGASTROESOPHAGEAL REFLUX BARRIER. L.C. Knight, A.H. Maurer, I.A. Ammur, J.A. Siegel, B. Krevsky, R.S. Fisher, L.S. Malmud. Temple University Hospital, Philadelphia, PA.

Alginic acid (AA) combined with antacid is used for the treatment of symptomatic gastroesophageal reflex. Prior studies with strontium-87m-labeled AA demonstrated that one mechanism of action involves the formation of a barrier (raft) which floats on the surface of gastric contents. In this study a new In-111 AA was used to study the effect of gastric pH on raft formation. In-111 AA was prepared by adding InCl3 to a suspension of Mg alginate in 0.04 N HCl. After centrifugation and washing, a mixture of those due to the prolonged retention of bile in the afferent loop and the rapid transit of food into the efferent loop (14 patients). Moreover, five showed the enterogastric reflux of bile. On the other hand, in 7 patients with Billroth I reconstruction, six (86%) showed the good mixture of bile and food, although one showed the poor mixture of those due to the markedly prolonged transit of food.

These findings suggest that the reconstruction with Billroth I method may be better than the one with Billroth II method in order to keep the good physiologic relation between bile and food flows in the patients following upper abdominal surgery.
Liver blood flow was found to be 63.1±10 in 27 patients with compensated cirrhosis; 43.1±5 in 49 patients with decompensated cirrhosis. The flow data agreed well with values recorded with an invasive method (Stapf, plenography). r=0.88 in 12 patients in a direct comparison and also with invasive methods in earlier investigations of our group and with those reported in literature.

The method is suitable for estimation of the recent status of the liver and controls, for prognosis of surgical procedures in shunt operations and liver transplantsations.

Monday, 3:30–6:00

Exhibit Hall

GASTROENTEROLOGY: HEPATIC

No. 553

DIFFERENTIATION OF PRIMARY SCLEROSING CHOLANGITIS (PSC) FROM PRIMARY BILIARY CIRRHOSIS (PBC) BY Tc-99m-IDACINDIGRAPHY. S. Krishmurthy, C.T. Krishmurthy, E.B. Keefe, and D.A. Lieberman. VA Medical Center and Oregon Health Sciences University, Portland, OR.

PSC and PBC are chronic cholestatic diseases that share many clinical and biochemical features. This study was undertaken to test if these two diseases could be differentiated reliably from each other by Tc-99m-IDACindigraphy. Thirteen patients with documented PSC and 10 with PBC were studied with Tc-99m-DISIDA. Analogue images were obtained at 2 minute intervals for 60 minutes with simultaneous computer data collection at 1 frame/min. Clearance t-1/2 was calculated for 3 regions of the liver. Single photon tomographic images (SPECT) were obtained between 60 and 90 minutes. The regional retention of radiotracer was noted on the SPECT images. The analogue and SPECT images were interpreted independently by 2 physicians who were unaware of the specific diagnosis.

Scintigraphically PSC was characterized by single or multiple band constriction of CBD, beaded appearance of CBD or LHD, cystic duct destruction, and marked variation in regional hepatic clearance time. The anterior segment of the right and medial segment of the left lobe were involved more frequently than others in SPECT images. PBC was characterized by hepatomegaly (predominantly left lobe); normal RHD, LHD, CBD, and cystic duct with diffuse retention of isotope in the liver. It is concluded that the distinct morphologic and physiologic alterations of PSC and PBC can be differentiated reliably by scintigraphy.

No. 554

MEASUREMENT OF REGIONAL LIVER BLOOD FLOW BY INHALATION OF XENON-133. A. Kroiss, L. Peschl, H. Benko, A. Neumayr, and KA Rudolfstiftung, Vienna, Austria.

Liver blood flow was measured by the Xe-133 inhalation technique with an Anger camera and an on-line computer system. In the same position Tc-99m colloid was then applied for edge detection of liver and spleen and to exclude overlapping areas from calculation. The activity of expiratory air (expiration-tube) was used as the arterial input function and a ROI was placed over the spleen representing the portal vein input function. Liver blood flow was estimated with a modification of Obrietz's algorithms.
PS/AL, GMS/L and PS/PL identified hepatocellular disease as a group distinct from other groups. Use of the total organ count produced parameters of better discrimination to detect hepatocellular disease than did parameters which used the mean count of the organ.

PS/AL >1.00, GM S/L >1.10 or PS/PL <<0.00 are strong numeric indicators of hepatocellular disease.

No. 557
QUANTITATIVE ASSESSMENT OF LIVER TRANSPLANT FUNCTION BY DECONVOLUTIONAL ANALYSIS. R. Reichle, D. Campbell, E. Tagge, S. Warber, J. Juni. University of Michigan Medical Center, Ann Arbor, MI.

A quantitative non-invasive technique to determine hepatic function in liver transplant patients is desirable. We have assessed liver function by deconvolutional analysis (DCA) of disofenin scans in an acute swine transplant model and in human liver transplants. By correcting for the effects of systemic circulation of a bolus injection, DCA simulates a bolus injected directly into the hepatic vascular supply.

Three normal and 11 unrelated donor transplant (within 2-60 days post-transplant) for a total of 16 studies. Changes in XE's showed a striking inverse relationship with MTT's, however, showed no such relationship.

Quantitative assessment of liver transplant function by DCA clearly identified acute liver dysfunction associated with transplantation and appears to correlate with and predict clinical course in preliminary patient studies.

Monday, 3:30–6:00
Hematology

No. 559
EFFECT OF SPLENO-RENAL ANASTOMOSIS ON SPLENIC SIZE IN HEPATOSPLENIC SCHISTOSOMIASIS. M. Abdel-Razzak, A. Nasef, and A. El-Aggan. Kasr El-Aini Faculty of Medicine and A.C. Medical Center, Cairo, Egypt.

Short operations have been used in the management of portal hypertension that ultimately develops secondary to periportal fibrosis characteristic of hepatosplenic schistosomiasis. Out of the shunt operations, splenorenal anastomosis is considered the procedure of choice since it selectively decompresses the portal bed without draining the mesenteric blood from the liver. Because of its decompressing effect, splenorenal anastomosis is expected to diminish the splenic size.

To test the validity of this assumption, the size of the spleen was determined from the anterior, lateral and posterior projections of hepatosplenic radiocolloid scans obtained before and after splenorenal anastomosis in 5 patients suffering from hepatosplenic schistosomiasis. Postoperative scans were obtained at periods ranging from 2 to 80 weeks.

Following the operation, the clearance rate of radiocolloid from the circulation became faster. However, the size of the spleen did not change significantly. Accordingly, splenic enlargement in schistosomiasis should be due to cellular hyperplasia, rather than venous congestion.

Monday, 3:30–6:00
Exhibit Hall

Gastroenterology: Pancreas

No. 558
IMAGING OF HUMAN PANCREAS WITH 1-123 Labeled HIPDM AND SINGLE PHOTON EMISSION COMPUTED TOMOGRAPHY (SPECT). K. Yamamoto, Y. Kuge, H. Saji, E. Aoki, N. Hayashi, and Y. Fujiyashiki, University of Miami, Miami, Florida and Aristotelion University, Thessaloniki, Greece.

The pancreas accumulation of radioiodinated HIPDM (N,N,N'-trimethyl-N''-(2-hydroxy-3-methyl-5-iodobenzyl)-1,3-propanediamine) in mice and rats has been reported (J Nucl Med 26:765-9,1985). In this study, we have tried to assess the localization of 1-123 labeled HIPDM in the human pancreas.

2-3 mCi of 1-123 labeled HIPDM was given to the normal volunteers intravenously. The planar scintigram was obtained at 1, 3, 5 and 20 hours after injection. SPECT was performed at 1, 3 and 5 hours after injection using the rotating gamma camera with medium energy collimator and it took 32 min to get projection data over 360°.

The pancreas was visible in the planar image from 3 hours and more clearly visualized at 20 hours later, but the radioactivity ratio of pancreas to liver was much lower than those of mice and rats. Only a little activity was seen in the kidneys and the intestinal tracts throughout the study.

SPECT could avoid overlapping the radioactivity in the liver and the spleen with that in the pancreas, and thus good positive images of pancreas could be obtained at 3 hours after injection of 1-123 HIPDM in spite of slightly lower radioactivity in the pancreas as compared with in the liver and the spleen.

In conclusion, 1-123 labeled HIPDM was expected to have the clinical usefulness as the pancreas imaging agent, especially if imaged using a SPECT system.

Monday, 3:30–6:00
Exhibit Hall

No. 560
RED BLOOD CELL VOLUME (RBCV) AND BLOOD VOLUME (BV) IN THE MALE ALBINO (NZW) RABBITS. N.D.Karatzae, K.I-Kalaras. University of Miami, Miami, Florida and Aristotelion University of Thessaloniki, Greece.

The estimation of RBCV and BV in experimental animals is important in studies of pharmaceuticals distribution. Since the standard values of them with Tc-99m in the rabbit has not yet been published we measure RBCV and BV in 64 male albino New Zealand rabbits 2.0-4.0 kg body weight (BW) (x±sd: 3.12 ±0.37 kg). Two ml heparinized (20 u/ml) venous blood from the rabbit's ear was added to 10 ml saline for injection and the standard. Blood was drawn 10 min after injection from the other ear (2 ml) and duplicate samples of 0.5 ml were counted. Venous hematocrict was 38.2±0.97. The labeling efficiency was 96.4±3.8 (sd.). The BV were 156.12±24.27 (sd.) or BV = 1013 ml/kg BW x (x±sd: 3.12 ±0.37 kg).

Monday, 3:30–6:00
Poster Sessions

No. 561
EFFECT OF SPLENO-RENAL ANASTOMOSIS ON SPLENIC SIZE IN HEPATOSPLENIC SCHISTOSOMIASIS. M. Abdel-Razzak, A. Nasef, and A. El-Aggan. Kasr El-Aini Faculty of Medicine and A.C. Medical Center, Cairo, Egypt.

Short operations have been used in the management of portal hypertension that ultimately develops secondary to periportal fibrosis characteristic of hepatosplenic schistosomiasis. Out of the shunt operations, splenorenal anastomosis is considered the procedure of choice since it selectively decompresses the portal bed without draining the mesenteric blood from the liver. Because of its decompressing effect, splenorenal anastomosis is expected to diminish the splenic size.

To test the validity of this assumption, the size of the spleen was determined from the anterior, lateral and posterior projections of hepatosplenic radiocolloid scans obtained before and after splenorenal anastomosis in 5 patients suffering from hepatosplenic schistosomiasis. Postoperative scans were obtained at periods ranging from 2 to 80 weeks.

Following the operation, the clearance rate of radiocolloid from the circulation became faster. However, the size of the spleen did not change significantly. Accordingly, splenic enlargement in schistosomiasis should be due to cellular hyperplasia, rather than venous congestion.
5.00% ± 0.43% (ad.) ml/kg of the BM of the rabbits. The above values with Te-99m do not differ significantly from those of the standard Cr-51 procedure and permit repeating RBCV measurements in shorter intervals as compared to Cr-51.

No. 561


Kinetic observations were done in two patients with eosinophilia and the kinetic patterns were compared with those of neutrophils. About one hundred million of cells of eosinophils or neutrophils were collected and they were labelled by In-III-oxine or -tropolone with 300-500uCi of radioactivity.

Two cases of reactive eosinophilia with the count of 56,700 and 47,500/uL of blood were used for this study. The disappearance of labelled eosinophils from the circulation followed a single exponential curve after the initial fluctuation. The pool sizes and turnover rate were calculated from the recovery and disappearance rate according to the formula of Mauer for granulocyte kinetics study. Various indices of eosinophils kinetics were compared to those of neutrophils in neutrophilia (DDP-32 study) and in chronic myeloid leukemia with almost same sizes of circulating pool.

Disappearance rate of eosinophils was slower than that of neutrophils in CML and was fastest in neutrophilia. Size of total blood pool of eosinophils was much smaller than that of neutrophils in CML and was almost equal in neutrophilia. Turnover rate of eosinophils was smaller than that in neutrophilia and was remarkably larger in CML. Migratory pattern of labelled eosinophils in the body was observed by scintillation camera. Radioactivity accumulated in the spleen and it gradually increased until 24 hours while there were no change of radioactivity in the lung, liver and bone marrow. Specificity of eosinophils kinetics were clearly demonstrated from these findings.

No. 562

IN VIVO KINETICS OF AUTOLOGOUS RED CELLS PRESERVED 49 DAYS AT 4°C IN PAGGSS AND IN ADSOL-Al. O. Messian, Centre de Transfusion, Le Chesnay, France.

Extending the storage period of red blood cells (RBC) at 4°C will help to improve the supply and simplify the development of autologous transfusion programs. Measurement of the in vivo recirculation of preserved RBC has been a controversial subject over the last years.

In order to give an accurate 24 hours recirculation percentage we used a double label technique with 51 Chromium containing Tween-80 (INO) and Indium-III-tropolone (INT).

The T 50 % was 16.9 ± 3 days and the T50-24 H was 75.2 ±6.5 % with Chrome only and 78.2 ±6.5 % with Chrome and INT. The double label technique appeared to be easy to use and demonstrated some degrees of early exoergerated post transfusion destruction after 49 days of storage (11 % for two patients in ADSOL-Al). PAGGSS appeared to maintain the viability of stored RBC at a satisfactory level by present standards. From our results, we believe that further studies should be done including late kinetics measurements for evaluation of new RBC products.

No. 563

IN VITRO EVALUATION OF GRANULOCYTE LABELING WITH In 111 CHELATED TO THREE DIFFERENT AGENTS. L. Mortelmans, A. Verbruggen, M. Bogaerts, C. De Bakker, W. De Roo, U.Z. Gaithusberg, Leuven, Belgium.

We have studied the influence of granulocyte labeling with commercially available In-111-Oxine or - Tropolone (Trop) or home made In-111-Merc (JNM 26: 518-525, 1985) on the cell structure by electron microscopy (EM) and on the cell function by measuring myeloperoxidase content and release, superoxide production, random migration (RM), chemotaxis (CHEM), phagocytosis (PHAG) and bacterial activity (BACT).

(i) The granulocytes were labeled with 400 uCi of In-111-Oxine in saline or In-111-Trop or -Merc in plasma.

(ii) The influence of the chelating agents without addition of the tracer was tested (n=4) in the following range (ug/ml final solution): 5-10 (Oxine), 10-160 (Trop), 1-4 (Merc).

(iii) The test was repeated for the same concentration range with addition of In-111.

In ADSOL-Al the 24 hours survival percentage was 79.5 ±8 %.

In PAGGSS these values were 79.5 ±8 % with Chrome only and 72 ±6.5 % after correction. PHAG and BACT were normal in the full range. With addition of In-111, CHEM and RM were unaffected up to 80ug/ml by Trop and markedly suppressed by Merc and Oxine.

In our experience, only labeling with In-111-tropolone assures morphologically and functionally intact cells with a reasonable labeling efficiency.

Monday, 3:30-6:00

Immunology/Infectious Disease

No. 564


Leukocytes were separated by three techniques: Ficoll-Hypaque (FH), volex sedimentation (VS), and VS-hypotonic lysis (VSHL) (method of Karesh et al JNM 26: 518-525, 1985). The cells were labeled with Indium-111-oxine containing Twem-80 (INO) and Indium-111-tropolone (INT). All studies were done on normal volunteers.

The harvested granulocyte (PMN), platelets (PLT), and red blood cells (RBC) per ml of whole blood and the ratio of Chemotactic migration to Random migration (CM/RM) (using the granulocyte chemotaxis response to E. coli in agarose plates) are tabulated below (mean ± SD):

<table>
<thead>
<tr>
<th>Method</th>
<th>PMX106</th>
<th>PLT106</th>
<th>RBC106</th>
<th>CM/RM</th>
</tr>
</thead>
<tbody>
<tr>
<td>INT FD</td>
<td>2.04+0.8</td>
<td>7.04+0.3</td>
<td>1.30+0.7</td>
<td>1.70+0.8</td>
</tr>
<tr>
<td>INT VS</td>
<td>2.47+0.7</td>
<td>5.62+0.4</td>
<td>6.29+2.3</td>
<td>1.30+0.3</td>
</tr>
<tr>
<td>INT VSHL</td>
<td>2.80+0.9</td>
<td>1.50+0.9</td>
<td>1.10+0.5</td>
<td>1.40+0.3</td>
</tr>
<tr>
<td>INT VSL</td>
<td>2.10+0.4</td>
<td>6.44+0.4</td>
<td>4.59+1.0</td>
<td>1.40+0.2</td>
</tr>
<tr>
<td>NO VSL</td>
<td>2.20+0.4</td>
<td>3.80+0.6</td>
<td>0.9+1.4</td>
<td>1.40+0.2</td>
</tr>
</tbody>
</table>

In a separate animal study, the leukocyte survival times were found similar among all techniques. With VSHL there were significantly fewer RBCs and PLTs approaching the results of FH. CM/RM response is not significantly changed by hypotonic lysis. Trypan-
blue exclusion testing showed 100 percent cell viability in all experiments.

In conclusion, VSHL separation technique is a simple method of obtaining a relatively pure granulocyte preparation with no sacrifice of viability or function.

**No. 565**

**GASTROINTESTINAL ACTIVITY IN IN-111 LEUKOCYTE IMAGING: CLINICAL SIGNIFICANCE IN PATIENTS WITH FEVER OF UNKNOWN ORIGIN.** F.L. Datz, D.A. Thorne, P.E. Christian. University of Utah School of Medicine, Salt Lake City, UT.

We undertook a study to determine the frequency and clinical significance of In-111 labeled leukocyte activity in the GI tract of patients with fevers of unknown origin. 312 In-111 studies involving 271 patients were retrospectively reviewed. A total of 59 cases (19%) showed bowel activity. These scans were correlated with necropsy findings, laboratory data, radiographic studies and clinical course. Of the 59 cases with gastrointestinal uptake, only 45% (27 studies) were due to infectious or inflammatory causes which caused the patient's fever (true positives). 55% (32 studies) were false positives. True positives included abscesses communicating with the bowel (8), pseudo-membranous colitis (6), inflammatory bowel disease (6), GI infections (2), necrotic bowel (2), vasculitis (2), and typhilitis (1). The false positives included swallowed leukocytes secondary to endotracheal, Dobhoff, and other tubes (10), pneumonia and empyema (5), sinusitis (2), esophagitis (1), pharyngitis (1) and parotitis (1). Other causes were related to bleeding and included ulcers (3), diverticulitis (2), gastric leiomyosarcoma (1), aortoduodenal fistula (1), and other causes (3). No cause for bowel uptake was found in 2 patients.

Gastrointestinal activity on In-111 leukocyte scan in patients with fever of unknown origin correlates with true causes of the patient's fever in only 45%. The remaining 55% are false positives due primarily to swallowed leukocytes and GI bleeding.

**No. 566**

**GALLIUM-67 IMAGING IN THE DIAGNOSIS AND FOLLOW-UP OF BLASTOMYCOSIS.** M.C.P.Giorgi; W.P. Pinto; G. Del Negro; E.E. Camargo.- Centro de Medicina Nuclear, Sao Paulo, Brazil.

Gallium-67 imaging is very sensitive for detection of extrapulmonary blastomycotic diseases. The purpose of our study was to investigate the usefulness of Ga-67 imaging to evaluate the extent of blastomycosis, a granulomatous disease, and to follow its response to therapy. Twelve patients (pts) with active blastomycosis (11 male; 4-57 years) were studied. Clinical and laboratory data indicated lesions in the lungs (11 pts), lymph nodes (6), skin (5), subcutaneous layer (1), bone (1) and rectum (1). Pts were imaged at 24 and 48 hr after intravenous injection of 111 MBq of Ga-67 citrate. All of the above lesions were detected in all pts. Moreover, hepatic (3 pts) and cerebral (1) lesions were also found but not demonstrated by other studies. Abnormal parotid uptake was found in 5 pts without clinical evidence of parotitis. Bony lesions were found in 2 pts and confirmed in one of them on bone scintigraphy but not on x-ray. Chest X-ray (CRX) and Ga-67 imaging correlated well, except for 2 pts in whom CRX underestimated the extent of the disease. Follow-up imaging on 3 pts after therapy showed decreased uptake in the lungs and other sites, despite an equivocal CRX in one pt. Gallium-67 imaging is a useful tool for detection and follow-up of blastomycotic lesions, particularly those non-detectable by other diagnostic modalities.

**No. 567**


Using preparative scale technologies which minimize polymer content and maximize Tc-99m specific activity, metallothionein (MT) conjugates of a mouse monoclonal antibody (B72.3) reacting with human breast adenocarcinomas and rectal adenocarcinomas have been prepared in a lyophilized instant-kit format. After reconstitution and transmission via Tc-99m glucoheptonate, the Tc-99m-MT-IgG or F(ab')2 conjugates were purified by gel permeation HPLC. Radiolabeled conjugates retained full immunoreactivity compared to radiiodinated MAb in a direct tumor membrane microtiter plate binding assay. Athymic mice bearing subcutaneous target LS174T, or non-target HCT-15, human colon tumors were injected with either Tc-99m-MT-IgG or MT-F(ab')2 conjugate and the corresponding radiiodinated control. Biodistribution and imaging were evaluated between 1-24 hours. The blood clearance of I-131 B72.3 and Tc-99m-MT-B72.3 were similar. The ratio of Tc-99m-MT-B72.3 to I-131-B72.3 in the liver was 1.4 at 24 hours. Tc-99m-MT.B72.3 imaged all LS174T tumors between 375-835 mg at 4-6 hours post injection. Comparable studies using Tc-99m-MT-F(ab')2 are in progress. Biodistribution, pharmacokinetics, tumor targeting, and imaging for both conjugates will be presented and compared.
macrophages obtained from a Fisher 344 rat with In-111 oxine, and evaluated their invivo distribution patterns in rats bearing transplanted mammary adenocarcinoma (upper flank). A group of the tumor bearing rats was treated with focal hyperthermia (Ft) of 43°C for 20 mins at the tumor site. For controls, groups of untreated tumor bearing rats (UTB) and sham-heated (SH) tumor bearing rats were used. At 1 hr after hyperthermia treatment, a dose of 2x10^6 In-111 macrophages per 100 g weight was injected i.v. in each rat and distribution calculated as %ID/g tissue was evaluated at 2, 24, 48 and 72 hours post injection. Significantly different uptake patterns were observed in the FH group when compared to the control groups. At 2 hrs the uptake of the labeled macrophages was higher in the UTB controls than in the FH and SH groups. Splenic uptake at 24 hrs and hepatic uptake at 72 hrs was higher in the FH rats than in the SH and UTB controls. Uptakes in the tumor tissue was higher in the FH rats than in the SH group but lower than in UTB controls from 24 to 72 hrs post injection. The differences in tissue distribution of the In-111 macrophages in the FH group, especially in the spleen, liver and tumor indicates functional effects exerted by hyperthermia probably caused by splenic processing of macrophages prior to redistribution.

No. 572


Multilamellar liposomes (mLV) are lipid vesicles prepared from a 7:3 mixture of Dimyristoyl phosphatidylcholine and Dimyrystoyl phosphatidylglycerol. The mLVs were labeled with Tc-99m pertechnetate reduced with stannous chloride. A dose of 150 mg/m2 labeled with 8-10 mCi Tc-99m was injected intravenously. These liposomes are normally cleared by the reticulo-endothelial system (RES) and may be used for delivery of certain drugs for targeted treatments. We used Tc-99m labeled liposomes to study the distribution in four patients with malignancy and systemic fungal infection including candidiasis and aspergillosis with the intention of using liposomes encapsulated amphotericin B in their therapy. Images were recorded immediately, at 4 and 24 hrs post intravenous injection of Tc-99m mLV. Regions of interest over the areas of infection and the liver, spleen, kidney, bone and cardiac blood pool were taken from the digital images. There was increased localization of these labeled liposomes in the nasopharynx and in the lungs of the two patients with fungal infection in these areas respectively. In the patients with liver infection, there was nonuniform distribution of radioactivity in the liver of one patient and in the other there was general increased liver uptake when compared to the normal values which we had established on other patients with cancer and with Hodgkin's disease. This study suggests that Tc-99m liposomes may be useful in the investigation of patients with severe systemic fungal infection requiring anti-fungal therapy.

No. 571

RADIOLOCALIZING MONOCLONAL ANTIBODIES AGAINST CONCEALED EPITOPES ON CARCINOEMBRYONIC ANTIGEN (CEA) F. J. Primus, R. M. Sharkey, C. Ballance, E. Kelley, D. Varga, and D. M. Goldenberg. Center for Molecular Medicine and Immunology, Newark, NJ.

Soluble tumor-associated antigens may be less desirable targets for antibody-directed tumor imaging or therapeutic agents due to combination of antibody with circulating antigen. We have prepared monoclonal antibodies to CEA that have different binding activities in immunoassay in which incubation buffer ionic strength was varied. The activity of one antibody, NP-2, was markedly reduced when ionic strength was raised whereas the activity of another, NP-3, remained unaltered. Radiolabeled NP-2 and NP-3 were similar in their localization of human colon tumor xenografts growing in hamsters which had undetectable circulating antigen. Injection of radio labeled NP-2 into cancer patient having CEA titers exceeding 200 mg/ml did not result in the formation of antibody-CEA complexes as measured by molecular sieve chromatography. However, CEA-containing NP-3 radioantibody complexes appeared in patients injected with NP-3 antibody. The amount of complex formed was related to circulating CEA titer, with levels around 200 mg/ml producing complexes consisting of up to 70% of the circulating radiolabeled antibody. Enhanced clearance of the NP-3 radiolabeled antibody was also observed in some patients, especially those having elevated levels of immune complexes. These results suggest that certain monoclonal antibodies to CEA that have the unique property of reacting with a site on this antigen that is hidden while in the blood, such as NP-2, could be more useful for tumor imaging and therapy since they would avoid neutralization and altered metabolism by circulating antigen.

No. 570


Multilamellar liposomes (mLV) are lipid vesicles prepared from a 7:3 mixture of Dimyristoyl phosphatidylcholine and Dimyrystoyl phosphatidylglycerol. The mLVs were labeled with Tc-99m pertechnetate reduced with stannous chloride. A dose of 150 mg/m2 labeled with 8-10 mCi Tc-99m was injected intravenously. These liposomes are normally cleared by the reticulo-endothelial system (RES) and may be used for delivery of certain drugs for targeted treatments. We used Tc-99m labeled liposomes to study the distribution in four patients with malignancy and systemic fungal infection including candidiasis and aspergillosis with the intention of using liposomes encapsulated amphotericin B in their therapy. Images were recorded immediately, at 4 and 24 hrs post intravenous injection of Tc-99m mLV. Regions of interest over the areas of infection and the liver, spleen, kidney, bone and cardiac blood pool were taken from the digital images. There was increased localization of these labeled liposomes in the nasopharynx and in the lungs of the two patients with fungal infection in these areas respectively. In the patients with liver infection, there was nonuniform distribution of radioactivity in the liver of one patient and in the other there was general increased liver uptake when compared to the normal values which we had established on other patients with cancer and with Hodgkin's disease. This study suggests that Tc-99m liposomes may be useful in the investigation of patients with severe systemic fungal infection requiring anti-fungal therapy.
Collimator modules similar to the proposed design were evaluated to provide a reference for overall sensitivity of the system. A mathematical model was developed to simulate the projection data acquired in our proposed system for controlled studies of various parameters which include ring radius, number of detectors, collimator response, quarter ray offset, photon attenuation, and noise. Tomograms were reconstructed from the projection data with standard fan beam algorithm. Several variations of system design were evaluated based on their input collimator resolution and output tomographic resolution.

From the simulations we conclude that a system with 72 or 80 detectors on a 34 cm diameter ring will be needed to achieve 8 mm FHWM resolution at the center of the reconstruction volume. The corresponding sensitivity should be about 2.5 to 3 kcps/uc/ml for a 13 mm thick tomographic slice.

No. 576
PORTABLE, CEREBRAL BLOOD FLOW MEASUREMENT SYSTEM FOR REAL DIAGNOSTICS. G. Entine and T. Tiernan, Radiation Monitoring Devices, Inc., Watertown, MA; D. Stump, L. Rinsland, Bowman Gray School of Medicine, Winston Salem, NC.

It is becoming widely recognized that in situ analysis of regional cerebral blood flow (rCBF) patients undergoing surgery or in intensive care can provide important diagnostic information needed to decrease the potential of brain damage in these critical situations.

Under an NIH sponsored program, we have conducted research to construct a very portable rCBF diagnostic system which uses miniature, solid state radiation detectors and sophisticated high speed microprocessor systems to provide for statistical analysis. The instrument can be brought directly to a patient and perform safe, rapid, evaluation in the often cramped confines of the neurological and cardiac bypass operating room, the intensive care unit and the emergency room.

Preliminary clinical studies have been done in these areas on a variety of patients. In particular, measurements taken on twenty patients undergoing bypass surgery indicated that, contrary to expectations, the cerebral vascular system is not completely autoregulating the blood flow during these procedures. The data suggests that the flow is almost entirely dependent on the setting of the external pump and the general body vascular chemistry and condition. This situation may relate to the significant fraction of bypass patients which experience a post-operative brain deficit.


In-field acceptance testing using the protocol adopted by the National Electrical Manufacturers Association (NEMA, U.S.A.) Standards Publication NU1-1980 was initiated five years ago. Of the first 23 cameras to undergo on-site acceptance testing using our implementation of the NEMA standard, 22 failed to meet the manufacturers' specifications. Four manufacturers are represented in those cameras tested to date. Parameters found to depart from the specified performance were field uniformity, energy resolution, intrinsic spatial resolution, system resolution, multiple window spatial registration, intrinsic count rate performance, and system sensitivity. Most problems were rectified by subsequent adjustment.
DESIGN AND PERFORMANCE OF A SMALL CLINICAL CYCLOTRON

A clinico-based cyclotron system for delivery of short-lived positron-emitting isotopes has been designed to meet the following objectives: 1) Automated, unattended operation. 2) Compact, self-shielded configuration for minimal facility requirement. 3) Economical, high-yield target reactions.

Tests on the completed cyclotron have demonstrated that it easily and stably delivers 50-100kA through a 1 cm collimator at the target entrance. This is more than enough beam to produce required quantities of positron-emitting isotopes and allows for simultaneous irradiation of two separate targets.

Carbon-11, Nitrogen-13, Oxygen-15, and Fluorine-18 have been economically produced in clinically useful quantities. For example, continuous flow Oxygen-15 is produced at a rate of 20 mCi per minute at a cost of $1 per minute for enriched target material.

Initial test of the prototype system shield have demonstrated that the cyclotron can be installed in a facility without additional shield construction.

IMPROVEMENT OF SPATIAL RESOLUTION AND VARIANCE OF RCBF IMAGE BY A RING DETECTOR SPECT (HEADMITE II).


Dynamic SPECT with inhaled Xe-133 has been used to map regional cerebral blood flow (rCBF). This method, however, has several problems such as uncertainty of rCBF value and poor spatial resolution, especially in deep region of the brain. The rCBF images are influenced by Compton scattered photons, the timing to start data acquisition, and inhalation techniques. The image quality is mostly affected by the energy window of the pulse height analyzer (PHA). The amount of scattered radiation is approximately proportional to both the depth of radiation source and the width of energy window. Fraction of scattered radiation is, for example, 4% for 2cm source depth/73-110keV (-10-+35%) window and 63% for 12cm depth/57-110keV (-30-+35%). This fraction is severely affected by lower level of the energy window. Therefore, an asymmetric window should be adopted for Xe-133 rCBF study. According to our experiments, the window of -30-+35% was the best for this purpose. The time difference between the start of inhalation and the start of data acquisition also affects the rCBF. The best results are obtained when the effective data acquisition starts at 6 seconds after the rising point of the end-tidal curve.

No. 578

by the manufacturer, although several required a number of months to correct.

Even though each of the manufacturers represented by the cameras tested subscribed to the test procedures of the NEMA standard, we found different interpretations being applied by the various manufacturers to specific measurements. Due to these differences the prospective purchaser should use caution when intercomparing the published NEMA performance measurements for scintillation cameras.

Our experience over the last 5 years has proven the practicability and value of performing in-field NEMA testing on scintillation cameras. It has also shown that very few cameras initially meet all of the published NEMA performance specifications after installation by the manufacturer.

No. 579

No. 580

No. 581

QUANTITATIVE DIGITAL AUTORADIOGRAPHY J. L. Lear, K. Mido, J. P. Plotnick, and R. A. Muth. Stanford University School of Medicine / V. A. Medical Center, Palo Alto, CA

Quantitative autoradiography requires a method of obtaining precise and accurate densitometric measurements of the images created by exposure from tissue sections. Existing image analysis systems, such as scanning densitometers or video cameras interfaced to microcomputers, use detectors which were designed for purposes other than autoradiography and their performance is therefore not optimal for digitizing the gray scales typically found in autoradiographs.

We therefore developed a solid state, digital image analyzer from the ground up specifically optimized for quantitative autoradiography of images used in cerebral blood flow and metabolism studies. The system uses a linear array of charge coupled devices (CCDs) which scan the images under the control of a DEC PDP 11/23+ computer and create a digitized matrix of 512 by 512 pixels with 256 true gray levels. Data is directly mapped into random access memory for processing and video memory for display on a monochrome monitor. Software was written in Forth for conversion of densitometric images to blood flow or metabolism images using appropriate kinetic equations. Cross contamination between different images obtained in multiple tracer studies can be subtracted on a pixel by pixel basis to yield pure tracer concentration images. Ratio images can be generated for detailed comparison of tracer uptake mechanisms.

 Autoradiographs of brain sections containing I-123 isopropyl iothalamate, C-14 iodoantipyrine, F-18 deoxyglucose, C-14 glucose, and TI-201 diethyldithiocarbamate were digitized with this scanner as well as with previously reported video and rotating drum densitometers. The CCD scanner provided 2-3 times the precision and 1.5-2.0 times the accuracy of the other systems for autoradiographic determination of tissue tracer concentration.

AN AUTOMATED HIGH-RESOLUTION SCANNER FOR COLLIMATOR PERFORMANCE EVALUATION. K. Rezai, W. Chang, S. Li, U. C. Ehrhardt, Un. T. F. Kirchner, University of Iowa College of Medicine, Iowa City, IA.

Collimator sensitivity and resolution values derived directly from gamma-camera-computer data are often too imprecise. We have developed a microprocessor-based scanning device capable of 3-dimensional mapping of a collimator's sensitivity and resolution at spatial sampling of 0.4 mm/pixel. The system runs automatically under software control and special display techniques facilitate global assessment of collimator performance vs depth or detailed analyses at a given depth.

A scanner, boaring a point source of activity, is driven by 2 precision motors in the X and Z directions within any number of planes (y axis) perpendicular to the face of the collimator. Positioning is accurate to 0.1 mm. Counts are recorded via a single channel detector in a 6502-based microcomputer, decay corrected, and stored in 2 bytes/pixel. The pixels X-Z dimensions in a plane are independently software selectable in the range of 0.4-10 mm. Output includes: 1) Color-coded display of counts/pixel in the entire field of view with highlighting of FWHM points. 2) Color-coded isoresponse contours at 5, 10, 50, 90, and 100%. 3) Pseudo 3-D display of line-spread functions. 4) Count profile at a given depth with FWHM and FWTM. 5) Numerical printout simulation tests. Software implementation makes the system versatile and upgradable. The scanner can be constructed from inexpensive hardware and interfaced to available detectors and computers in any nuclear medicine department. The system is a powerful tool in the design and testing of high-performance collimators for SPECT imaging.
No. 582

IAEA STUDY OF THE QUALITY OF NUCLEAR MEDICINE IMAGING IN DEVELOPING COUNTRIES - PRELIMINARY RESULTS. A. V. Wegst, University of Kansas Health Sciences & Hospital, Kansas City, Kansas, H. Bergmann, Il. Medizinische Universitätsklinik, Vienna, Austria, R. Gandria, M. Nofal, International Atomic Energy Agency, Vienna, Austria and G. Souchkewitch, World Health Organization, Geneva, Switzerland

The International Atomic Energy Agency (IAEA), in cooperation with the World Health Organization (WHO), initiated an imaging performance survey including countries in Latin America, Asia and the Pacific to gather information concerning the quantity and state of nuclear medicine imaging in those countries. The methodology was similar to that used by the College of American Pathologists and permits analysis by receiver operating characteristic (ROC) indices.

Identical transmission phantoms whose images resemble an anterior liver containing space occupying lesions were designed and built by the IAEA. Fifty phantoms were distributed with instructions for image acquisition for scintillation camera or rectilinear scanner to approximately 30 countries. Each laboratory was asked to complete a questionnaire concerning equipment, procedures and quality control (QC) to be returned with the image evaluation form and QC and phantom images. A coordinator was chosen in each country to direct the project.

One hundred fifty questionnaires from 10 countries have been analyzed to date. The ROC curves, area under the curves and other statistical parameters will be presented. Strict anonymity with regard to country and laboratory will be maintained. The study is being continued.

No. 583

MONOCLONAL ANTIBODIES

No. 584


Monoclonal antibody B72.3 is a murine IgGl that was generated using a membrane-enriched fraction from a human carcinoma metastasis. mAb B72.3 binds to a novel high molecular weight glycoprotein (TAG-72) with characteristics of a mucin. Immunohistochemical studies demonstrated that TAG-72 is expressed in approximately 85% of colon carcinomas, while it is not expressed or expressed in only trace amounts in normal adult tissue.

1-131 B72.3 IgG has proven useful for the radioimmunodetection of human colon carcinomas, both in athymic mice bearing xenografts and in clinical trials.

No. 585

RADIODETECTION OF METASTATIC MELANOMA (MM) USING IN-111-DTPA-ZME-018 MONOCLONAL ANTIBODY (MoAb). E. Cornelius, R. Neumann, S. Zoghbi, M. Ernstoff, J. Kirkwood and M. Unger, Yale University School of Medicine, New Haven, CT & Hybritech, Inc., San Diego, CA.

This was a phase I study of ZME-018 to assess safety, kinetics and imaging sensitivity over a dosage of 1-40 mg. 1.0 mg of MoAb was labeled with 5.0 mCi In-111, then mixed with a variable amount of "cold" MoAb. Kinetics are reported separately. 1/26 patients (pts) had mild wheezing and urticaria. Scans were done at 1 & 3 dys with computer stored blood activity. High activity interfered with tumor detection. 109/149 known metastases (mets) > 1 cm were detected (73%). Sensitivity related to MoAb dosage was: 1 mg, 2 pts, 3/11 (27%); 2.5 mg, 4 pts 2/2 (100%); 5.0 mg, 5 pts, 2/12 (17%); 10 mg, 5 pts, 18/27 (67%); 20 mg, 5 pts, 59/65 (91%); 40 mg, 5 pts, 25/32 (78%). 4 pts had previously undetected foci. In 2 pts with widespread mets, 55/55 (100%) & 2/24 (83%) of mets > 1 cm were detected, respectively; 19/19 & 15/15 additional mets seen on Ga-67 scans were also detected; and 2 & 32 previously unknown foci were seen. 11 pts had a Ga-67 scan within 1 mg; Ga-67 sensitivity was 78%, and for MoAb, 85%, 74/47 extracerebral mets < 1 cm were detected. Major false positives were axillae (17/21 pts) and female breast (3/9 pts). ZME-018 scintigraphy is safe as a 1 dose procedure. Results complement current imaging tests.

No. 586

1-23 F(ab')2 and Fab FRAGMENTS OF ANTI-CEA LABELED MONOCLONAL ANTIBODIES: BIOKINETICS IN PATIENTS WITH COLORECTAL CARCINOMA. B. Delaloye, A. Bischof-Delaloye, P. Buchgeher, V. von Fliedner and J.P. Mach. Nuclear Medicine Dpt, CHUV and Ludwig Institute, Lausanne, Switzerland.
In 31 patients pretreated with cold MAb. Thyroid and gastric mucosa were blocked. 6 and 24h after injection organ distribution was measured with respect to the remaining whole body (WB) activity by the ROI technique in averaging simultaneously obtained anterior and posterior data. Dual head camera, WB attachment. Plasma disappearance curves were bi-exponential with effective plasma T1/2(± SD) of 16±3.6h for MAb25 F(ab')2, 30.9±14.8h for MAb35 F(ab')2 and 9.5±1.9h for MAb35 Fab. These T1/2 were not influenced by serum CEA(1.0-2500 ng/ml). Organ distribution in % of remaining activity (±SD) for Fab(±12 25) F(ab')2 35 P(ab')2 35 Fab 35 Heart 6h 8.8±0.8 12.5±4.2 8.0±1.7 24h 8.0±0.5 13.7±1.9 5.6±1.3 Lungs 6h 10.8±2.4 9.6±1.8 10.3±1.3 24h 9.7±1.8 8.0±0.7 10.6±1.6 Liver/ spleen 6h 15.2±4.4 13.9±3.1 14.6±2.8 24h 15.9±2.0 16.1±3.7 14.9±2.0 Kidneys 6h 7.3±1.6 8.3±1.0 11.6±2.9 24h 7.5±1.7 6.1±1.2 9.1±1.5 24th urinary elimination was 20.1±11.6% for F(ab')2 and 44.5±12.1% for Fab. Because of low background Fab seem preferable for the use with I-123.

Poster Sessions

No. 587


In 31 patients (11F, 40-82, 26Y, 20M, 39-82, 26Y) plasma disappearance and in vivo distribution of I-123-F(ab')2 (n=17) and Fab(n=14) fragments of 2 monoclonal antibodies (MAb) were administered and scanning performed at the end of infusion, 4, 24, 48, 72, and 144 hours postadministration. Serum was taken to observe the disappearance rate of I-111 from the vascular compartment.

Comparison of two I-111 labeled monoclonal antitumor antibodies was performed with a greater concentration of 2ME-018 in the liver, spleen, gastrointestinal tract, and testicles than was seen for 96.5. Seventy-four of out 113 lesions were detected in the 42 patients (65%). Sixty-two of the lesions were detected for 96.5. Six patients with Stage III melanoma were administered 5 mCi In-111 labeled MoAb. The distribution of both I-111 MoAbs was dramatically affected by the MoAb mass administered. Fourteen lesions were detected by the 2 MoAbs that were not known prior to the study. Presumed false positive lesions occurred with 2ME-018.

In conclusion, I-111 MoAbs targeted against melanoma associated antigens appear to have clinical utility in the detection of metastatic melanoma.

No. 589

IN-111 MONOCLONAL ANTIBODY (MOAB) PAY-276 IMAGING AND KINETICS IN PHOSTATIC CANCER. R.E. Henry, P.R. Ahmann, J.A. Kotler, M.E. Ahmann, J.A. Green and M. Unger*. VA Medical Center and University of Arizona, Tucson, AZ. and Hybritech Inc.*. San Diego, CA.

In 21 patients (pts) with prostatic carcinoma (19 with metastasis) were infused with 5 mCi In-Ill labeled murine MoAb to prostatic acid phosphatase (PAP) in doses of 15(5pts), 5(3pts), 10(4pts), 20(5pts) and 40(4pts) mg over 1 h without significant side effects. Planar whole body and spot imaging was performed at 24 and 72 h post infusion. Liver and spleen activity was high at 24 h. Bone and marrow activity increased with time. The prostate imaged at 24 h in 9/15 pts with palpable mass. Abnormalities were seen best at 72 h when vascular activity had declined. In 17 pts with different bone scans, MoAb identified lesions as prostatic metastases in 46% of abnormal regions. Identification increased with dose: 22% with ≤ 5 mg and 58% with ≥ 10 mg. Bone lesion detection was difficult due to prominent marrow activity or small size of lesions as in ribs. MoAb identified pulmonary metastasis in 1 pt and unsuspected malignant pleural effusion in another. CT-confirmed pelvic adenopathy was not identified in 3/3 pts. Blood clearance was biphasic with T/2 of 24.3± 10.5 h for all antibody doses. Urine clearance was 29.1± 15.6% in 24 h and 38.8± 16.5% by 72 h. Anti-PAP MoAb has low sensitivity for imaging bone metastases compared to phosphates but is highly specific with potential to differentiate benign bone lesions in selected patients. Its potential for detection of soft-tissue metastases appears promising and merits further evaluation.

No. 590


In order to determine if the in vitro evaluation of a radiolabeled Mab reflects its utility for tumor imaging, in vitro and in vivo studies were performed using two human tumor cell lines, LS174T (colorectal) and A549 (lung), and the tumor specific Mab 86.2. FACS analysis showed that FITC-labeled Mab 86.2 bound to both LS174T (49.0% positive) and A549 (85.2% positive) cells. Further, 3X10⁶ of LS174T or A549 cells maximally bound 59.4± and 88.2± of 1-125-86.2, respectively. After a 24 hr. in vitro incubation of either In-111 or I-125 labeled 86.2 with cells, HPLC analysis of the culture media showed minimal antibody degradation and no evidence for the formation of soluble immune complex. Gamma scintillation images of athymic mice bearing s.c. LS174T xenografts showed significant tumor uptake.
of B6.2 labeled with either isotope. In contrast, A549 tumors imaged poorly or not at all. Biodistribution data indicated that In-111 and I-125-B6.2 cleared more rapidly from A549 mice than from LS174T animals. Thyroids of A549 mice accumulated I-125 rapidly. Abnormally elevated S I.D./g values of In-111 in both liver (35.25) and spleen (11.22) resulted after In-111-B6.2 injection into A549 mice. These contrasting findings between A549 and LS174T mice may be the result of more shed antigen or catabolism of antibody by A549 tumor.

The prediction from the in vitro data that A549 tumors would be an excellent in vivo target for labeled B6.2 was not fulfilled. The striking differences between distributions of isotopes observed in mice bearing tumors antigenic for the same antibody may have important implications for future in vivo studies.

No. 591


This study was taken to evaluate GA-67 labeled monoclonal antibody (MoAb) for the tumor imaging using human osteosarcoma as a tumor model. MoAb was efficiently labeled with GA-67 through the chelation of deferoxamine (DFO) employing three methods for the coupling of DFO and MoAb: glutaraldehyde method, pyridyl disulfide method and maleimide method, which introduced Schiff's base, disulfide bond and thioether bond, respectively.

All GA-67 labeled and radiiodinated MoAb showed similar specific binding reactivity in vitro to osteosarcoma cells. Transplanted tumors in nude mice were clearly visualized at 24 and 48 hours after the administration of GA-67 labeled MoAb prepared by the three methods as well as with I-131 labeled ones, while the coupling method between MoAb and bifunctional chelates influenced the localization of MoAb in tumor tissues and liver. Highest tumor-to-liver ratio and in vivo stability was observed by using labeled MoAb with thioether bonds, which was considered a choice of coupling procedure. Ga-67 labeled irrelevant MoAb or free Ga-67 did not localize in tumors.

Present study demonstrated that Ga-67 labeled anti-tumor MoAb appeared promising for the radioimmuno-imaging. These methods would be also applicable to the preparation of immunonconjugates for the selective and specific transport of anti-cancer drugs.

No. 592


One mg of ZCE-025 monoclonal antibody (i.oAb) directed against carcino-embryonic antigen (CEA) was labeled with 2 mg of In-111 using bifunctional UTP. One mg of unlabeled ZCE-025 was intravenously administered into 16 patients with metastatic carcinoma of the colon. Patients were divided into 4 groups (I to IV) and each group was given 2.5, 5, 10, or 20 mg of unlabeled MoAb with the labeled MoAb. Images were recorded at 24, 48, and 72 hours (h) and occasionally at 144h. Regions of interest over the liver, blood pool, spleen, bone, and kidney were used to analyze relative body distribution. Lesion detection was compared with clinical, CT, and other nuclear studies. Detection of metastatic lesions in the lungs improved with increased dose of unlabeled MoAb. No lung metastases were detected at less than 10 mg. Lymph node lesions were readily detected even with less than 10 mg of "cold" antibody. Lymph lesions appeared "cold" indicating the metastatic lesions take up less labeled ZCE-025 than normal liver. There was uptake in 2 sites of previous disease but no disease at the time of the study. Two other positive areas were not substantiated by other tests (null disease?). Non-tumor body distribution of the labeled MoAb showed greater liver concentration of doses below 10 mg than at higher doses of unlabeled antibody. Occasional uptake in breasts and lungs was observed with the higher doses.

ZCE-025 is a promising i.oAb for imaging metastatic colonic cancer, when used in conjunction with blocking MoAb. However, liver metastases are overshadowed by the normal liver uptake.
Poster Sessions

Proceedings of the 33rd Annual Meeting

No. 595


We used anti-a-fetoprotein (AFP) monoclonal antibodies (MAB) for imaging hepatocellular carcinoma (HCC). Two anti-AFP Mabs (AF01 and AF04) were produced (Bellet et al., Proc Natl Acad USA, 1984, 81: 3669-73). Isotype and affinity constant were respectively IgG2a and 1.6 x 10^{10} M^{-1}. 1qG1 and 0.8 x 10^{10} M^{-1}. After I-131 labeling the bound fraction was 9.8% by HPLC. Information was obtained from 18 patients bearing HCC. After control, 0.27 to 0.50 mCi of intact MAb (AF01, 7 cases; AF04, 5 cases) or Fab fragments (AF04, 6 cases) labelled with 70 to 115 MBq of I-131 were intravenously infused after thyroid protection. Emission tomography (PET) was performed 1 day and 2 or 3 days later and after a complementary injection of Tc-99m sulfur colloid (74 MBq), providing comparative distribution of I-131 and Tc-99m in each transverse slice. We obtained 3 negative results, 5 were doubtful (no contrast to normal liver), 5 positive (weak contrast to normal liver) and 5 strongly positive (tumour uptake without I-131 uptake on normal liver). The Mab uptake was higher around the tumour than in its center. There was no correlation between the outcome of PET and the blood AFP level which ranged from 25 to 147000 ng/ml. Patients receiving Fab fragments seemed to have better results.

The sensitivity of immunoscintigraphy for HCC is not sufficient for widespread clinical use but the method provides valuable information for the practicability of therapeutic use of radiolabelled anti-AFP MABs in HCC.

No. 596


28 patients (pts) with melanoma were studied after an i.v. bolus injection of radiolabelled F(ab')2 of 225.28S, a Monoclonal Antibody (MAB) reacting against an High Molecular Weight Melanoma Associated Antigen. Pts were studied during a 96 hr period using 2-3 mCi (30-50 mCi/mg) for In-111 and during a 24 hr period with 4-10 mCi (30-100 mCi/mg) using Tc-99m. 24/28 pts (85.7%) showed at least one pathological uptake. 32/52 (61.5%) tumor sites were clearly visualized. Using a retrospective approach a further 7 locations were evidenced. False negatives were connected with the organ, absence of antigen, and the tumor size and location with the lowest number of positives in skin lesions. 8 pts were studied one month from immunoscintigraphy after i.v. injection of 2 mCi of Thallium-201 Chloride (Tl), whose uptake in malignant tumors has been related to the pathological state (blood flow, cellularity, growth rate, transformation). 11/17 melanoma sites were clearly positive. In addition 3 pts underwent a 2nd Tl scan six months after the first one. A disagreement with previous data was demonstrated with uptake only in sites with a disease progression. The comparison Tl/Mab showed substantially overlapping results. These data suggest that the “in vivo” lack of arrival of the Mab to the Antigen could determine some false negatives in Immunoscintigraphy.

No. 597

DOSE-DEPENDENT DIFFERENCES IN BIODISTRIBUTION OF IN-111 LABELED MONOCLONAL ANTIBODIES (MoAb) D Munc, JA Carrasquillo, RD Neumann, JG Reynolds, P Abrams, K Foon, PA Bunn, JI Mulshine, R Schroff, C Morgan and SM Larson. National Institutes of Health, Bethesda, MD.

This study was done to determine whether increasing doses of MoAb result in biodistribution changes. All MoAb were labeled by a modification of the Krejcarack method (Hybrit, Inc.) with approximately 5 mCi of In-111 on 1 mg of MoAb. Dose escalation studies were done by adding increasing amounts of the same MoAb, un conjugated and unlabeled to provide total mg doses listed. Three MoAbs (igG2a) were evaluated: 9.2.27 directed at a high molecular weight antigen (Ag) of melanoma, 9.6.5 directed at p97 a melanoma associated Ag and T101 directed at a pan T-cell Ag present on cutaneous T-cell lymphoma (CTCL). 46 patients were studied with 1 to 100 mg of 9.2.27, 7 pts were studied with 1 to 3 mg of 96.5 and 11 pts were studied with 1 to 50 mg of T101. Digital acquisition of patient images up to 1 week post-injection had ROI analysis (CPM per pixel, geometric mean) performed. Pts receiving higher total doses had the least “nonspecific” organ uptake (liver, spleen and marrow). Ratios of blood pool to organ were significantly different at the various dose levels. Higher doses of 9.2.27 showed decreased activity in the spleen and marrow. Higher doses of 96.5 showed predominant less activity in the liver. Higher doses of T101 showed decreased activity in the liver, spleen and marrow. In conclusion, 1) each MAb has a characteristic pattern of distribution; 2) this distribution can be altered by increasing “carrier” amounts of the MAb.

No. 598


The aim of this study was to evaluate monoclonal antibodies (IgM), ST-439 and ST-433, raised against a gastric cancer (ST-4), xenografts, in the radioimmunodiagnosis for human colon and gastric carcinoma xenografts in nude mice.

Label-imaging and localization experiments were performed by IV injection approximately 40 mCi of I-125 labelled antibodies into nude mice bearing Co-4 (poorly differentiated colon carcinoma), and H-111 (well differentiated gastric carcinoma).

There was uptake of ST-439 (polymer) into the Co-4 at day 8, with tumor to blood ratio (T/B) 3.0, but tumors were not clearly visualized until 4 days post injection. By injecting ST-439 (monomer), tumors were better seen at day 3 (T/B=1.7), while average accumulation into the tumors equaled to 0.13% of the total injection dose (ID). Uptake into liver was 0.74% of the ID, probably due to the immunocomplex with the antigen in the blood. On the other hand, ST-433 was selectively accumulated into the H-111 with T/B as high as 7.8 at day 7, with no significant uptake into liver, spleen and kidney as well as stomach itself. Excellent images were obtained 1 day after the injection.

The efficacy of IgM antibodies for in vivo diagnosis and therapy has been questioned. ST-433 holds promise for the radioimmunodetection of colon and gastric cancer.

No. 599

A potential impediment of repeat immuno­scintigraphy or radiolimunotherapy is the development in patients of human antimouse antibodies (HAMA). To assess for the presence of circulating HAMA a simple screening assay was developed using I-125 B72.3 monoclonal antibody (MoAb) as tracer and protein A for separation of the HAMA. Patients evaluated for HAMA were those that had been studied previously for 8 weeks of a chemotherapeutic study using MoAb B72.3 (IgG), T101 (IgG2a), 9717/36 (IgG2a) and Fab fragments of antibodies 96.5 and 98.7 (IgG2a and IgG1, respectively). 23 of 50 patients who received one IV injection of IgG developed HAMA whereas none of the 12 patients who received a single Fab injection became positive. However, four of 7 patients who received multiple injections of Fab did develop HAMA. 6 of 20 patients who received IgG2a developed HAMA compared to 15 of 30 patients receiving IgG1. With subcutaneous (SC) injections 3 of 10 IgG2a patients and 1 of 6 Fab patients became HAMA positive. We conclude 1) that murine IgG is more immunogenic than Fab fragment, 2) that repeat administration of murine Fab fragment will lead to a high frequency of HAMA positivity, 3) both SC and IV injections of MoAb are immunogenic, 4) that HAMA frequently occurs after IV injection of murine IgG or Fab and is a significant problem in the use of these agents for immuno­scintigraphy or radiolimunotherapy.

No. 600

A PROSPECTIVE STUDY OF RECURRENCE IN COLON CANCER WITH 1-131 B72.3 MONOCLONAL ANTIBODY. N.Salvatore, S.Lastoria, L.Hanni, A.Remotti, D.Colcher, J.Schlam, S.M.Larson, L.Callegaro. 2nd Medical School, Naples, Italy, NIH, Bethesda, MD, SORIN Biomedica, Saluggia, Italy.

23 patients (pts) that underwent a total resection of a colon cancer were prospectively analysed using 1-131 labelled mononclonal antibody B72.3 (IgG) reacting against a tumor associated glycoprotein present in more than 95% of Human Colon Carcinoma. B72.3 was labelled via the Chloramine-T method (Specific Activity 5mCi/mg). Pts were studied at .6mg and 3 mCi at different times (24-48-72-96 hours) after an iv.bolus injection. A very low activity was seen in the liver. Nor other organs neither blood cells acquired the radioactivity. Blood Pool activity was present at all times. Tumor sites were demonstrated by Dupont* N. Billerica, MA 01862 and Albert Einstein College of Medicine*, New York 10461 and Albert Einstein College of Medicine*, New York 10461 also demonstrated.

We conclude that an In-111 labeled anti-CEA MoAb permits specific for azophenylarsanate (ARS). The ArM1 was purified by size exclusion chromatography to separate HgL (47E) from HL (53E). Micropore diffusion chambers containing immobilized ARS antigen on 75 mg of Sepharose beads were implanted s.c. in CDI mice to serve as "model tumors": Immunoreactivities of the 125 I (iodogen method) and 396-methionine labeled antibodies in vitro were comparable. The blood clearance of all ARS antibodies in mice was biphasic, an initial rapid decrease followed by a slower rate of disappearance. Blood clearance of murine IgG (liver, spleen, G.I.) clearance of 125 I-ArM1 (HgL) > 125 I-ArM16 > 125 I-ArM13 > 125 I-ArAr13.4. At 13 days, the ratios of antibody accumulation in ARS beads/blood were 1680, 80, and 65 for ArM1, ArM6, and Ar13.4, respectively. Percent I.D./gm ± S.E.M. were:

<table>
<thead>
<tr>
<th>ARS-Beads</th>
<th>Blood</th>
</tr>
</thead>
<tbody>
<tr>
<td>131I-ArAr13.4</td>
<td>43.7±4.0</td>
</tr>
<tr>
<td>125 I-ArM16</td>
<td>9.0±3.8</td>
</tr>
<tr>
<td>125 I-ArM1</td>
<td>11.8±1.7</td>
</tr>
</tbody>
</table>

Specific images of the ARS chambers were observed with all the ARS antibodies 2-5 days after injection. These results suggest that CH3 deficient antibodies may prove useful for tumor localization.

No. 601


Selective modification in antibody structure and may provide better diagnostic and therapeutic reagents. We compared the blood clearance, whole organ distribution, and in vivo targeting of two mutant IgG2b immunoglobulins Tarn61, end62 domain positives; ArM13, domain deficient and the parent Ar13.4 antibody all.

**Supported by CNR grant Special Project Oncologia.**

No. 603


The correlation between mononclonal antibody (MoAb) imaging and surgical specimens was studied in a group of 21 colorectal cancer patients. A high affinity MoAb to carcinoembryonic antigen (CEA) was used - each patient receiving 200 mg of protein labeled with 2.0 mCi of In-11l. Scans were obtained at 24 and 48 h and laparotomy was performed within 17 days of injection. Surgical specimens were assayed for CEA content, weighed and counted for activity. By immunoperoxidase staining, all tumors were CEA positive. Of the 10 primaries, 3 scans were positive (30%), 4 were equivocal (40%) and 3 were false negative (30%). 13 patients had hepatic metastatic disease, but only 5 scans (38%) were positive; i.e., showed an elevated count rate at the rim of the lesions and/or a cold nodule. Correlations of scan result, lesion size, CEA content (pg/mg) and tissue uptake in % injected done (ID) per Kgm were as follows:

<table>
<thead>
<tr>
<th>Site</th>
<th>Scan</th>
<th>Fraction</th>
<th>CEA(pg/mg)</th>
<th>% ID/Kgm (at 7d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colon</td>
<td>+</td>
<td>3/10</td>
<td>7.3</td>
<td>6.4</td>
</tr>
<tr>
<td>+</td>
<td>4/10</td>
<td>10.2</td>
<td>5.2</td>
<td></td>
</tr>
<tr>
<td>-</td>
<td>3/10</td>
<td>0.3</td>
<td>4.5</td>
<td></td>
</tr>
<tr>
<td>Liver + rim</td>
<td>2/13</td>
<td>9.5</td>
<td>16.4</td>
<td></td>
</tr>
<tr>
<td>Merts -nodule(s)</td>
<td>3/13</td>
<td>3.7</td>
<td>3.6</td>
<td></td>
</tr>
<tr>
<td>8/13</td>
<td>0.9</td>
<td>8.9</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

We conclude that an In-111 labeled anti-CEA MoAb permits correct localization of those colorectal lesions having high CEA content. Uptake by normal liver remains an appreciable problem, however.
Later with a gamma camera. In 12 patients, liver metastases were clearly shown in the liver scans. Large lesions in general appeared as cold defects in the early Ab images but lesions became equal to or higher than liver background clear late. Clear late liver involvement occurred in all lesions after subtraction of 99mTc sulfur colloid but not after human serum albumin. In surgical specimens from 5 patients 3 to 5 days after injection of labeled Ab, the tumor to liver ratio was 2.87±0.51 and tumor to blood ratio was 0.66±0.30. Patients excreted 12.32±15.3% of the dose in the 1st day and 60.8±4.35% in 3 days. One patient had liver biopsy on the 3rd day and resection on the 3rd day. The tumor to liver ratio was 2.37 in the early specimen but 0.8 in the resected specimen.

This preliminary study suggest that mouse monoclonal Ab HT 29-15 is potentially useful for radioimmuno-detection of metastases from colon CA.

Monday, 3:30–6:00

Exhibit Hall

NEUROLOGY: GENERAL

No. 604

ERROR IN PARAMETER ESTIMATES OBTAINED FROM Rb-82/PET STUDIES OF BLOOD-BRAIN BARRIER PERMEABILITY (BBB): EFFECT OF TISSUE HETEROGENEITY AND COUNT RATE. V. Dhawan. Memorial Sloan-Kettering Cancer Center, New York, NY.

Rb-82 bolus infusion in conjunction with dynamic positron emission tomography (PET) has been used to estimate the blood-to-brain and blood-to-tumor transport constants (Kj) for Rb. The accuracy of these estimates depends primarily upon PET measurements of regional tissue radioactivity. We have extended our previous error analysis (J Cereb Blood Flow Metabol 5 [Suppl 1]: S85-S86, 1985) to regions containing a varying mix of tumor and normal tissue. Effects of count rate were studied by changing the magnitude of the arterial input function, A(t). Brain radioactivity (A(t)) was calculated at one-minute intervals for 6 min for 8 different tumor-tissue mixes. The blood curve simulated a "slow" bolus infusion of 120 mCi of Rb-82. Appropriate noise was added to A(t), and the operational equation was then solved for Kj and blood water volume, Vb. Our analysis suggests that for a 10% error in A(t), Kj and Vb can be estimated with an accuracy of 5% for all tissue mixes. The error in Kj and Vb increased marginally (<5%) vs that for equivalent homogeneous regions. Substantially decreased count rate (one-half injected radioactive) increased the error in Kj to >40% for small regions (<2.5 cm^3). Based on this error analysis we conclude that accurate estimates of Kj and Vb can be obtained for heterogeneous tissue regions using our bolus injection protocol for Rb-82/PET studies.

No. 605

THE RATE OF VENTRICULAR ENLARGEMENT IN DEMENTIA OF THE ALZHEIMER TYPE (DAT) CORRELATES WITH RATE OF NEURO-Psychological DETERIORATION J. Luxenberg, H. Creasey, J. Haixby, M. Sundaram, S.I. Rapoport. Laboratory of Neurosciences, National Institute on Aging, National Institutes of Health, Bethesda, MD; Lidcombe Hospital, Lidcombe, New South Wales, Australia.

Twelve men with DAT (age 63±2 yrs, interscan interval 508±47 days) and twelve healthy male control subjects (age 65±4 yrs, interscan interval 1196±108 days) were studied with serial brain X-ray CT scanning. Ventricular volumes were calculated by summing ventricular areas outlined with a light-pen on an image analysis system, and multiplying by the interslice distance (7 for DAT patients and third ventricular (1.204±0.32 cc/yr) and lateral ventricular (13.3±2.0 cc/yr) enlargement; both values differed from Controls (p<0.02). The controls had significant third ventricular enlargement (0.3±0.1 cc/yr, p<0.01) but not lateral ventricular enlargement.

A composite neuropsychological score was obtained utilizing the Syntax Comprehension Test, Extended Range Drawing Test, Porteux mazes, and verbal and visual immediate memory from the Wechsler Memory Scale. In men with DAT, the rate of decline in neuropsychological scores correlated with both rate of third ventricular enlargement (r=0.67, p<0.05), and right lateral ventricular enlargement (r=0.83, p<0.003).

There was no overlap between the rates of lateral ventricular enlargement in controls and DAT subjects. Serial CT differentiates between normal aging change and pathological ventricular enlargement in DAT. The rate of ventricular enlargement in DAT correlates with the rate of neuropsychological deterioration.

No. 606


BBB permeability to Ga-68 EDTA was measured using NeuroCAT in 11 patients (pts) with primary or metastatic brain tumors and in 4 normal volunteers. 6-8 mCi of 68-Ga EDTA were injected as an i.v. bolus and 16 consecutive 300 sec scans were performed. Arterial blood samples were collected throughout the procedure. A 20 ml venous blood sample was obtained at 10-15 min and a PET scan of the syringe was performed later. Using Multiple Time Graphical Analysis (Patlak, 1983) Kl: unidirectional blood to brain transfer constant and Vp: estimate of cerebral blood volume were calculated. We used an input function both the arterial concentrations of the tracer and values obtained from a ROI taken on the superior sagittal sinus, using a correction factor derived from the scan of the syringe. Values of Kl were corrected for Vp. Full agreement was found between both methods (R=0.997). In normal subjects Kl was 0.0003 - 0.00008 ml/g/min and Vp= 3.4 - 0.7 ml/100g. Similar values were found in areas contralateral to a tumor. Tumor regions presented a net variability in Kl. While low grade astrocytomas did not show alteration of Kl and Vp, Kl was increased in malignant tumors up to twenty-folds.

No. 607

USING FLOOD PHANTOMS TO EVALUATE QUANTIFICATION IN PET: OBJECT SIZE EFFECTS. S.C. Strother*, A.C. Evans, C.J. Thompson. Montreal Neurological Institute, Montreal, Canada.

Typically a series of images from a decaying flood phantom (FP) are analyzed as plots of reconstructed image activity vs true activity (RIAyTA) to establish the linear operating range of a given scanner. However, random coincidence and deadtime errors may compensate for each other, and an independent measurement of one or the other is required [e.g. randoms (true activity)].

Such FP linearity of mean RIAyTA can be achieved without FP spatial uniformity when errors due to incorrect scatterers and/or attenuation corrections remain. A sensitive test of any spatial non-uniformity may be developed by noting that all the relevant error effects are circularly symmetric about the center of a centrally placed FP. By averaging circumferentially around annuli a few pixels wide we obtained radial uniformity profiles. The F-statistic from a one-way ANOVA of these
profiles is a sensitive measure of spatial uniformity. It was used to adjust an analytic scatter deconvolution filter. In particular, we measured the filter parameters required to optimally flatten images from 20 cm and 15 cm FP's using a narrow beam attenuation coefficient for water of 0.096. Applying the scatter filter, derived for a 15 cm FP, to a 20 cm FP produced systematic spatial variations of > 10%. In addition, the 15 cm FP scatter filter increased the mean image values from the 20 cm FP to >15% of those obtained with the 20 cm FP scatter filter. This demonstrates the need to explicitly adjust scatter corrections for object size effects.

The CSFSFR greater than 0.1 ml/min were obtained at 10°g and 15°g, the measurements were carried out on a shunt device connected to an infusion pump and a 16mm in diameter and 2mm in thickness, and a small straight bore collimator; 5mm in length, was attached to it. Total weight of the detector is less than 100g so that it can be easily attached to the patient's head. With this system, experimental measurements were carried out on a shunt device connected to a infusion pump and a computerized cadmium telluride(CdTe) probe system. The size of CdTe detector is 16mm in diameter and 2mm in thickness, and a small straight bore collimator; 5mm in length, is attached to it. Total weight of the detector is less than 100g so that it can be easily attached to the patient's head.

Proceedings of the 33rd Annual Meeting of the Society of Nuclear Medicine

Monday, 3:30–6:00
Exhibit Hall

NEUROLOGY: PET

No. 608
ASSESSMENT OF CEREBROSPINAL FLUID SHUNT FLOW RATES BY COMPUTERIZED SEMICONDUCTOR DETECTOR SYSTEM. Y. Suzuki, M. Matsunae, T. Murakami, T. Ueda and D. Satoh. Tokai University School of Medicine, Isehara-city, Japan.

Nuclear medicine techniques have been widely used for measurement of cerebrospinal fluid shunt flow rates (CSFSFR). However, the measurements are only feasible when the patients are in their supine position in most of the cases and real CSFSFR are hardly available during changing position, while CSFSFR will be greatly influenced by it. The purpose of this paper is to describe a flexible method of assessing CSFSFR with a computerized cadmium telluride (CdTe) probe system. The size of CdTe detector is 16 mm in diameter and 2 mm in thickness, and a small straight bore collimator, 5 mm in length, is attached to it. Total weight of the detector is less than 100 g so that it can be easily attached to the patient's head.

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No. 609
REPRODUCIBILITY OF METABOLIC PATTERN FOR BEHAVIORAL STATES STUDIED REPEATEDLY IN A SINGLE PET/FDG PROCEDURE. J.Y. Chang, R. Duara, W. Barker, J.Y. Chang, F. Yoshii and A. Apicella. Mount Sinai Medical Center, Miami Beach, FL.

PET/FDG studies in AD have shown hypometabolic areas and asymmetries in metabolism in temporoparietal regions. Normal subjects also show these features but to a lesser extent. The purpose of this study was to effectively distinguish normal subjects from mild cases of AD by using a behavioral task which would activate unaffected brain regions and increase the contrast between normal and abnormal regions. Six patients with mild AD and 3 normal controls were studied in the resting state and while performing a verbal memory test. The studies, in each subject, were performed in one extended procedure, using 2 injections of FDG and 2 PET scans in a 100 min. period (Chang, et al. J. Nucl. Med. 26, P103, 1985). The orbital-frontal and inferior temporal regions showed significant increases in metabolism in normals, with global glucose metabolic rates (mg/100g/min) from 7.52 to 8.34; only the left inferior frontal cortex and cerebellum were activated in demented subjects with metabolic rates increasing from 7.4 to 7.55. Hypometabolic deficits were generally more apparent during activation than rest in demented subjects. Mean % asymmetry during rest and activation were 5.1 ± 0.3 and 5.5 ± 2.0 in normals and 11.0 ± 7.9 and 11.1 ± 6.1 in demented subjects. Only in demented subjects were there any regions that showed significant increases in asymmetry during activation relative to rest (eg. medial temporal asymmetry was 4.6 ± 4.0% at rest and 8.6 ± 0.6% during activation, t = 3.0, P < 0.01).

We conclude that behavioral activation may be a useful way to enhance metabolic abnormalities in AD.

No. 610
THE USE OF A BEHAVIORAL "STRESS" TEST TO ENHANCE METABOLIC ABNORMALITIES IN ALZHEIMER'S DISEASE (AD). R. Duara, W. Barker, J.Y. Chang, F. Yoshii and A. Apicella. Mount Sinai Medical Center, Miami Beach, FL.

PET/FDG studies in AD have shown hypometabolic areas and asymmetries in metabolism in temporoparietal regions. Normal subjects also show these features but to a lesser extent. The purpose of this study was to effectively distinguish normal subjects from mild cases of AD by using a behavioral task which would activate unaffected brain regions and increase the contrast between normal and abnormal regions. Six patients with mild AD and 3 normal controls were studied in the resting state and while performing a verbal memory test. The studies, in each subject, were performed in one extended procedure, using 2 injections of FDG and 2 PET scans in a 100 min. period (Chang, et al. J. Nucl. Med. 26, P103, 1985). The orbital-frontal and inferior temporal regions showed significant increases in metabolism in normals, with global glucose metabolic rates (mg/100g/min) from 7.52 to 8.34; only the left inferior frontal cortex and cerebellum were activated in demented subjects with metabolic rates increasing from 7.4 to 7.55. Hypometabolic deficits were generally more apparent during activation than rest in demented subjects. Mean % asymmetry during rest and activation were 5.1 ± 0.3 and 5.5 ± 2.0 in normals and 11.0 ± 7.9 and 11.1 ± 6.1 in demented subjects. Only in demented subjects were there any regions that showed significant increases in asymmetry during activation relative to rest (eg. medial temporal asymmetry was 4.6 ± 4.0% at rest and 8.6 ± 0.6% during activation, t = 3.0, P < 0.01).

We conclude that behavioral activation may be a useful way to enhance metabolic abnormalities in AD.

No. 611
DISCRIMINATION OF FUNCTIONAL BRAIN RESPONSES BENEATH IMEGE RESOLUTION WITH POSITRON EMISSION TOMOGRAPHY. M.A. Mintun, P.T. Fox, and M.E. Raichle, Washington University School of Medicine, St. Louis, MO.

As positron-emission tomography (PET) is safely performed on normal subjects engaged in controlled sensory, motor or cognitive activities, it has unique potential for studying structure:function relations of the in vivo human brain. A major hindrance, however, to the utility of PET for functional brain mapping has been the limited spatial resolution of emission imaging relative to the size of brain structures. PET images typically have spatial resolution greater than 1.0 cm full-width at half-maximum (FWHM), prompting the inference that PET cannot establish structure:function relationships with accuracy better than one cm. We have now demonstrated, using both simulated and actual PET brain images, that a conventional PET device (PETT VI, 18 mm FWHM images) can specify the location of a region of functionally activated brain to within 1 mm and, therefore, can distinguish functionally activated foci separated by less than 3 mm. The fundamental constraint of this technique is that at least two studies (resting-state and
activated-state) must be acquired for each subject during a single scanning session. To enable a brief interval between studies we have chosen the measurement of cerebral blood flow using bolus, intravenous administrations of oxygen-15-labeled water. This allows a measurement time of less than one minute, and an inter-measurement time of 3-10 minutes. Subtraction of the resting-state image from the activated-state image results in a difference image which is used to find the loci of the activated focus. Such functional brain mapping within the image resolution therefore, is achieved by experimental strategy alone and does not require any physical modifications of the PET device.

No. 612
COMPARATIVE STUDY OF POSITRON EMISSION TOMOGRAPHY AND MAGNETIC RESONANCE IMAGING IN CEREBROVASCULAR DISEASE.
S.Nishizawa, M.Senda, Y.Yonekura, K.Nishimura, I.Pujisawa, S.Fukuyama, M.Ishikawa, T.Taki, M.Kawabe, N.Handa, and K.Torizuka. Kyoto University School of Medicine, Kyoto, Japan.

X-ray computed tomography (CT) frequently fails to diagnose cerebrovascular disease (CVD) without major atrophy. In order to evaluate the clinical role of positron emission tomography (PET) and magnetic resonance imaging (MRI) in CVD, we studied the patients with occlusion of internal carotid artery (IC) using PET and MRI. Regional cerebral blood flow (CBF), cerebral blood volume (CBV), oxygen extraction fraction (OEF) and cerebral metabolic rate of oxygen (CMRO2) were measured with inhalation of 0-15 labeled gases. For MRI, superconducting high magnetic field device, SIGNA, was used with pulse sequence of spin echo 2000/20-60 or 2000/40-80. In all cases, MRI revealed small multiple high intensity lesions in the white matter with higher contrast and detectability than CT. On the other hand, PET demonstrated decreased CBF with increased CBV and OEF not only in the white matter but also in the extensive cortical area.

No. 613
ASSESSMENT OF 11-C-L-METHIONINE TRANSPORT INTO THE HUMAN BRAIN WITH A SIMPLE DUAL-PROBE DETECTION SYSTEM.

Decreased transport into the brain of large neutral amino acids (LNAA) may be a major factor in the pathogenesis of certain neurodegenerative disorders (Ratzmann, Biochim. Biophys. Acta. 43:197, 1984). We have used a simple, inexpensive, high efficiency detection system (HEADS) to quantify LNAA uptake by the human brain. In studies of normal, fasted volunteer subjects, 360-410 uCi (1.5-24 ug) 11-C-L-methionine (MET) was injected i.v. and a 40 minute time activity curve of brain 11-C-L-MET uptake was acquired. All studies showed a rapid initial accumulation of brain 11-C-L-MET, which plateaued after 5 mins. A 11-C-L-MET study was performed 1 hour after the oral administration of 100 mg/kg L-phenylalanine (L-PHE). These studies showed a decreased 11-C-L-MET accumulation after the L-PHE challenge: mean ± S.D. δ = -32.5 ± 14.7%. Total serum LNAA levels (except L-tryptophan) were analysed before and after each 11-C-L-MET injection and showed: a) a greater than 10-fold elevation of serum PHE after loading; b) no change in other LNAA levels.

The HEADS system needs approximately 1/40th the tracer dose needed for PET imaging, thus allowing multiple studies without excessive radiation. Our results indicate that this simple detector system may play a useful role in the study of neurometabolic diseases such as phylketonuria or other conditions where brain amino acid transport is altered.

No. 614
BLOOD FLOW AND BBB INTEGRITY AS FACTORS IN MISONIDAZOLE UPTAKE IN CEREBRAL ISCHEMIA. D.W. Shaw, J.S. Rasey, A.M. Spence and K.A. Krohn. Univ. of Wash., Seattle, WA.

Our recent work (JNM 26:252, 1985) with misonidazole (MISO) in the gerbil stroke model was consistent with its preferential uptake by hypoxic tissue. However the pharmacology of drugs in the brain is complicated by factors in addition to specific metabolism by cells. Studies have been done to delineate the relationship between MISO uptake in cerebral ischemia and the concurrent regional cerebral blood flow (rCBF) and BBB integrity. The production of cerebral ischemia in the gerbil stroke model is linked with alterations in rCBF, blood volume and ultimately disruption of the BBB, any of which potentially alter tissue delivery and retention of MISO. MISO uptake appears relatively unaffected by changes in the BBB. Gross disruption with mannitol produced only small increases in MISO uptake, thought to represent relative ischemia produced with the transient increase in local cerebral glucose utilization, uncompensated by flow changes. In contrast there was 2-3 fold increased MISO uptake in the stroke model at 4 hours when there was only minor alterations in the BBB. This is consistent with MISO's octanol:water partition coeffient of 0.43. Studies in the gerbil stroke model utilizing IAP as a flow tracer demonstrated a variable correlation between MISO uptake rCBF, depending on the degree of stroke. Consequently MISO uptake per unit of flow was assessed and provided a more useful measure of hypoxia than MISO uptake alone. Tracer delivery in the most severely affected animals is limited by flow.

Monday, 3:30-6:00
Exhibit Hall

NEUROLOGY: RECEPTOR IMAGING

No. 615

CNS dopamine (DA) receptors have been classified into D1 and D2 subtypes based on their coupling to the enzyme adenylyl cyclase. We recently reported the visualization, in vivo, of D1 receptors in a monkey brain with Br-75-SCH 23390 analog and PET (Eur.J.Pharmacol. 108:327, 1985). Here we report the preparation of C-11-SCH 23390, presently the most potent and selective D1 antagonist, and evaluation of its utility for PET studies. In experiments involving two anesthetized rhesus monkeys each scanned twice on separate occasions after receiving 2-4 mCi C-11-SCH 23390 (dose=4-34 ug/kg), this drug entered the brain rapidly and was taken up, distributed, and cleared in a manner consistent with mediation by DA receptors. Fifteen minutes after injection, mean striatum/cerebellum (S/C) uptake ratio was 0.51 ± 0.54. Blocking experiments to characterize the localization of D1 receptors in the monkey brain and saturation experiments to assess receptor parameters were done. Preliminary results show that pretreatment with 56 ug/kg unlabelled SCH 23390 reduced the S/C ratio to 0.30 while after pretreatment with 10 ug/kg p-bromoisopropirolidin,
S/C ratio measured was not significantly different from control. These results demonstrate that PET, involving both C-11-SCH 23390 and current D2 radioligands, is a useful non-invasive tool in distinguishing subtypes of CNS DA receptors and may provide insights into the role of multiple DA receptors in normal and diseased physiology.

No. 616

C-11 carfentanil (CAR) can be used to measure opiate receptor (OR) binding in man by the use of PET (Frost, et al. JCAT, 1985). Three compartment (vascular, extravascular and receptor) analysis similar to that described by Mintun, et al. (Ann. Neurol., 1984), was carried out using CAR binding in the thalami (TH) and unmetabolized CAR in arterial plasma [Cp(t)] determined by HPLC. Four male and one female (ages 21 to 44) were studied on (w) and without (w/o) 1 mg/kg naloxone (NAL). The maximum occupancy of OR was < ca. 8%. The average percent CAR of total arterial plasma activity was 69 ± 14 (1r), 47 ± 9 and 26 ± 9 at 15, 30 and 60 minutes after injection w/o NAL, and the percent CAR was ca. 20% lower. There was a good fit to the data by the 3 compartment model to TH CAR binding and C(t) using nonlinear least square analysis w. and w/o NAL: The fit was significantly worse when the data w. NAL was fit to 2 compartments and when total plasma radioactivity was used in place of C(t). The binding potential (BP = Bmax/Kd) ranged from 12 to 34 (mean 21) in this group of normal subjects who were heterogeneous with respect to age and sex. BP was > 0 w/o 1 mg/kg NAL indicating that not all OR are occupied at this dose. These findings demonstrate that compartmental analysis can be used to obtain quantitative estimates of OR binding when plasma radioactivity is corrected for CAR metabolism.

No. 617

Seizure activity produces an increased release of endogenous opioid peptides and may result in an increased threshold for immediate repetition of a seizure. In laboratory animals chronic seizures produce an increase in opiate receptors in the brain, further enhancing the anti-seizure effect of endogenous opioids. C-11 carfentanil can be used to measure opiate receptor (OR) binding and was employed in the study of 3 patients with temporal lobe epilepsy. Three male patients were identified who had a predominately unilateral temporal lobe seizure focus based on EEG criteria and were candidates for temporal lobe resection. CAR binding was measured in the amygdala (AM), caudate, thalamus (TH), and frontal, temporal, cingulate and calcarine cortex (FCX, TCX, CNG, and CCX). Activity in FCX, which contains very few OR, was subtracted from activity in the other regions to obtain estimates of average specific OR binding 15-45 min. after CAR injection. The ratio (R) of OR binding during arousal to that in the control state was then computed. In 6/7 subjects R < 1 in most regions whereas in 1/7 R was uniformly > 1. The largest individual deviations of R from 1 tended to occur in AM, TH and CNG and ranged from 1.41 to 1.72 and 0.27 to 0.83. Activity was not significantly different 0-6 min. after injection indicating that blood flow and diffusion effects are not producing the observed changes in R at 15-45 min.

These results support the hypothesis that sexual arousal predominantly results in release of endogenous opioids which increase the occupancy of OR (R<1). However, there is evidence for decreased OR occupancy following arousal in some regions (R > 1).

No. 618

The opiate receptor (OR) and endogenous opiate peptides have been implicated as mediators of sexual behavior in laboratory animals and in man. C-11 carfentanil (CAR) was used to measure regional OR binding in 3 normal male volunteers and 4 patients with a history of deviant sexual behavior during a control resting state and following sexual self arousal. Arousal was initiated 10 min. prior to receiving CAR and continued for 15 min thereafter. Activity was measured in the amygdala (AM), caudate (CD), thalamus (TH), and frontal, temporal, cingulate and calcarine cortex (FCX, TCX, CNG, and CCX). Activity in CCX, which contains very few OR, was subtracted from activity in the other regions to obtain estimates of average specific OR binding 15-45 min. after CAR injection. The ratio (R) of OR binding during arousal to that in the control state was then computed. In 6/7 subjects R < 1 in most regions whereas in 1/7 R was uniformly > 1. The largest individual deviations of R from 1 tended to occur in AM, TH and CNG and ranged from 1.41 to 1.72 and 0.27 to 0.83. Activity was not significantly different 0-6 min. after injection indicating that blood flow and diffusion effects are not producing the observed changes in R at 15-45 min.

These results support the hypothesis that sexual arousal predominantly results in release of endogenous opioids which increase the occupancy of OR (R<1). However, there is evidence for decreased OR occupancy following arousal in some regions (R > 1).

No. 619

Lesch-Nyhan Syndrome is an X-linked metabolic disorder associated with compulsive self-injury in which there is autopsy evidence of reduced striatal dopamine and dopamine metabolites. Experiments in monkeys suggest that D1 blockade may reduce the self-injury. We have examined D1 and D2 dopamine receptors in the brain of a 21 year old male patient, using C-11 SCH 23390 and C-11 3-N-methylspiperone, respectively.

We have radiolabelled the D1 antagonist SCH 23390 and our animal studies have shown that C-11 SCH 23390 (SCH) is specifically bound to D1 receptors. In vivo rodent binding studies indicated that TH and CNG was reduced by 77% in caudate by the 01 antagonist cis-flupenthixol, but only 6% by the 52 antagonist cinanserine, and 27% by the D2 antagonist haloperidol. Similar blockade was demonstrated in baboon PET studies. The ligand localizes in striatum and dissociates after 90 min. in mice and 50 min. in baboon.

NMSP PET studies were conducted before and after a bone marrow transplant. Both studies showed low D2 binding. A D1 study done concurrently with D2 NMS PET suggested the relative D1/D2 ratio of the rate of binding to the receptors (k3) maybe as large as 3:1. The D1 ligand equilibrated with the receptor during the scan. Hence receptor density measurements are possible for both ligands. Autopsy studies at this age indicates a 1:1 ratio of D1/D2 receptor densities.
No. 620

The monoclonal antibody, 17-1A, to human colorectal carcinoma antigens is also immunoreactive to metastatic adenocarcinoma. Since it was uncertain whether this antibody would localize in brain metastases, radiolabeled 17-1A was intravenously administered to patients with confirmed metastatic adenocarcinoma of the brain. A bifunctional chelating group, DTPA, was attached to 17-1A, IgG using its cyclic anhydride. Approximately .8-1.0 DTPAs per molecule of IgG were attached. In-111 was then complexed to the DTPA conjugate in citrate buffer. Free uncomplexed In-Ill was removed using gel chromatography. Immunoreactivity was determined to be greater than 75% from in vitro binding studies. Patients were initially skin tested and then received intravenously 1.0 milliCurie of In-111 labeled antibody containing about 10-20% In-Ill DTPA. Imaging was initiated at 4-6 hours postinjection with Tater images obtained at 24-48 hours. The resulting scans indicated positive In-111 uptake in metastatic tumors from 24 through 48 hours. All tumors in the brain were clearly delineated in multiple spot images and correlated well with CT scanning. Other metastatic sites in the rest of the body were also visualized and confirmed by CT scans. These preliminary results suggest that certain monoclonal antibodies will selectively concentrate in brain tumors after crossing the blood-brain-barrier as demonstrated by imaging.

Monday, 3:30-6:00 Exhibit Hall
NEUROLOGY: SPECT

No. 621
BRAIN IMAGING WITH Tc-99m-d,l-HMPAO SPECT, CT, and NMR RESULTS IN EPILEPSY. R.J. Biersack, H. Stefan, K. Reichmann, B. Hohenermann, K. Kuhnen, A. Bockisch, H. Penin, F. F. Knapp, and W. Laimirre, Nuclear Medicine Division, University of Missouri, Columbia, MO.

This investigation was undertaken to compare brain SPECT by means of the d,l-isomer of Tc-99m labeled HMPAO with results of CT and NMR in patients (pts) with epilepsy. 18 pts were studied with ECT according to phase II and III protocols. Blood clearance was determined in 12 pts, and urinary excretion in 8 pts. ECG and CT results were available in all pts and NMR in 15 pts. Brain SPECT was performed with a rotating gamma camera 15, 60, and 180 min after iv injection of 10 mCi Tc-99m-HMPAO. No adverse reactions were observed in any of the pts. There were no significant changes in vital signs, blood count, blood chemistry, and urine analysis before and after injection. Blood clearance showed a rapid decrease (T/2 = 2.5 hrs). Urinary excretion amounted to 20 - 40 % within 24 hrs. The clinical results are summarized as follows:

<table>
<thead>
<tr>
<th>CT + SPECT</th>
<th>CT + SPECT</th>
<th>CT normal/ normal</th>
<th>CT abnormal/ SPECT normal</th>
<th>NMR + SPECT</th>
<th>NMR + SPECT</th>
<th>NMR normal/ normal</th>
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In the group of 15 pts who underwent SPECT, CT, and NMR the sensitivity for epileptic foci was: SPECT = 12/15, NMR = 12/15, and CT 4/15. Our data suggest that Tc-99m-HMPAO SPECT and NMR are likewise useful for the evaluation of pts with seizures.

No. 622

Although isopropyliodoamphetamine (IMP) labeled with I-123 has been suggested as an agent for measuring cerebral blood flow (CBF) and is currently being used in patients in combination with SPECT, its behavior has not been adequately investigated in pathological situations. In a series of rats (n=5) in which the middle cerebral artery (MCA) has been occluded we have compared local CBF using 14-C-iodoantipyrine (IAP) with 123-I IMP uptake utilizing a double label autoradiographic technique. 123-I IMP was injected 30 minutes following MCA occlusion. At variable times up to 30 min later, CBF was measured with IAP. Although CBF calculated using IMP was highly correlated with CBF using IAP in most of the brain tissue, there were regions in which a mismatch occurred. In the ischemic territory, blood flow measured with IAP dropped to 15-20% of control, whereas the corresponding IMP uptake was 40-50% of control. Therefore IMP is an inaccurate measure of local cerebral blood flow in ischemia. Very dramatic mismatches between IMP and IAP were also observed in regions remote from the ischemic tissue, primarily in the white matter where the IMP uptake was greater than in the surrounding grey matter even though blood flow with IAP showed a 1:3.5 white:grey flow ratio. The uptake mechanism for IMP is presumably different in ischemic tissue as well as in the white matter.

No. 623
ECT BRAIN IMAGING USING Tc-99m-HEXAMETHYL PROPYLENAMINE OXIME (d,l-HMPAO); CLINICAL STUDIES. R.A. Holmes, K.W. Logan, W.A. Volker, A. Singh, W.H. Olive, T.A. Laimirre, Nuclear Medicine Division, University of Missouri, Columbia, MO.

Tc-99m-d,l-HMPAO, a new radiopharmaceutical developed by Amersham International in collaboration with our laboratory is a lipophilic chelate that efficiently crosses the intact blood-brain-barrier and maintains a high concentration in the brain tissue for an extended period. Its distribution reflects cerebral blood flow and we have studied its ECT imaging characteristics in more than 30 patients with neurologic diseases. Counts for the ECT images were recorded stepwise (64 angles) around the circumference of the head after the IV administration of 20 mCi Tc-99m-d,l-HMPAO starting at 15 min and repeating the study 180-240 min post-injection. Tomographic images (1.5 cm thick) are reconstructed for transverse coronal and sagittal projections using commercial computer software. The highest regional activity is seen in the grey matter, cerebellum and basal ganglia. Three stroke patients with fluent aphasia demonstrated large focal defects in the right fronto-thalamic (Broca's) area that were not as clearly seen on their x-ray CT's. Two of 7 TIA patients demonstrated focal decreased perfusion at the brain base without concomitant changes on the CT. Three of 25 stroke patients with post-infarction "luxury perfusion" demonstrated greater CT lesion discordance with the hyperperfused area. Like iodoamphetamine a cerebellar medulloblastoma showed fixed reduced tumor uptake. Our results should provide additional impetus for wider application of this agent clinically.

No. 624

Although isopropyliodoamphetamine (IMP) labeled with I-123 has been suggested as an agent for measuring cerebral blood flow (CBF) and is currently being used in patients in combination with SPECT, its behavior has not been adequately investigated in pathological situations. In a series of rats (n=5) in which the middle cerebral artery (MCA) has been occluded we have compared local CBF using 14-C-iodoantipyrine (IAP) with 123-I IMP uptake utilizing a double label autoradiographic technique. 123-I IMP was injected 30 minutes following MCA occlusion. At variable times up to 30 min later, CBF was measured with IAP. Although CBF calculated using IMP was highly correlated with CBF using IAP in most of the brain tissue, there were regions in which a mismatch occurred. In the ischemic territory, blood flow measured with IAP dropped to 15-20% of control, whereas the corresponding IMP uptake was 40-50% of control. Therefore IMP is an inaccurate measure of local cerebral blood flow in ischemia. Very dramatic mismatches between IMP and IAP were also observed in regions remote from the ischemic tissue, primarily in the white matter where the IMP uptake was greater than in the surrounding grey matter even though blood flow with IAP showed a 1:3.5 white:grey flow ratio. The uptake mechanism for IMP is presumably different in ischemic tissue as well as in the white matter.
This study was performed to investigate the spatial and quantitative relation between CBF and the I-123 labeled amines, isopropyliodoamphetamine (IMP) and the diane, HIPDM.

The brain distribution in rats of I-123 HIPDM (N=5) and I-123 IMP (N=6) was determined with C-14 iodoantipyrine using quantitative double label autoradiography. Forty minutes after a bolus injection of I-123 amine, a CBF study with C-14 IAP was performed. The ratio of CBF between gray and white matter was 4 to 1. In the case of CBF in the brain stem, the distribution of the two agents is similar. However, in the cerebellum, the high contrast distribution of the I-123 amines is not related to the CBF pattern and is suggestive of the distribution of astrocytic neuronal amine.

The use of the I-123 amines for the investigation of cerebral perfusion with SPECT has rested on the assumption that the distribution of their uptake is proportional to CBF. Both SPECT and techniques using tissue sampling to compare CBF with the uptake of the I-123 amines do not possess the spatial resolution of autoradiography and would not reveal this disparity. This observation emphasizes that the binding mechanism of the I-123 amines is not completely understood.

No. 625
ASSESSMENT OF CEREBRAL PERFUSION RESERVE IN PATIENTS WITH CEREBRO-VASCULAR DISEASE BY SINGLE-PHOTON EMISSION TOMOGRAPHY. R. v. Kurmer, W. K. Kubler, H. Ostertag, German Research Center and Neurologic Department, University of Heidelberg, Heart Center MA, Bad Oeynhausen, FRG.

The ratio between cerebral blood flow (CBF) and cerebral blood volume (CBV) determined by positron emission tomography has been proposed as a parameter for the perfusion reserve in cerebro-vascular disease (CVD), but its assessment with SPECT is not yet established. We have chosen N-isopropyl-(I-123)-p-iodoamphetamine (IMP) and -iodoantipyrine (IAP) SPECT. The corresponding CBF/CBV data in 15% of the affected territories was 85±10% when related to the non-affected territories affected by CVD. In 16 patients with CVD, CBF and X-ray tomography were obtained using GE No. 625.

The ratio of CBF between gray and white matter was 4 to 1. In the cortex, thalamus and brain stem, the distribution of both nuclides was investigated in succession using corrections for the contamination of the Tc-99m tomograms by I-123. The ratio between I-123 and Tc-99m tomograms yielded the CBF/CBV distribution. Quantification was obtained by side-to-side comparison of both hemispheres and of segments containing the territories affected by CVD. In 16 patients with CVD, CBF of the affected territories was 85±10% (SD) when related to the non-symptomatic contralateral side (t=9.03). When the regions of interest defined within one slice encompassed the whole affected hemispheres, the average CBF was 9±5%, again related to the non-symptomatic side. The corresponding CBF/CBV data in 15% of these patients differed significantly (p<0.001) from CBF with 60±32% and 81±106. In unilateral strokes >50% (N=7), segmental CBF averaged 81±10.3% and CBF/CBV 49±15%. (p<0.001) relative to the contralateral side. The figures for the hemispheres were 92±5.8 and 75±12.5 (p<0.001), respectively. These clinical findings mirror the characteristics of cerebral blood flow autoregulation in decreased arterial perfusion pressure, namely the vasodilation of arteriolar resistance vessels and small veins. They thus substantiate the adequacy of the concept to determine CBF/CBV for the assessment of cerebral perfusion reserve and of the procedure chosen for imaging this parameter with SPECT.

No. 626

Fourteen patients with a variety of central nervous system disorders were examined with N-isopropyl I-123 p-iodoamphetamine (IMP) SPECT, MRI and XCT. IMP SPECT images were obtained using GE 400AC/T and MRI was performed with 0.35 or 0.5 Tesla super-conductive magnet. Regional IMP uptake was determined as standardized uptake ratio and the ratio of each cortical region to mean whole brain IMP uptake was calculated; ratios for frontal, parietal, occipital, cerebellar, thalamic, striate and cerebellar regions.

SPECT was most sensitive for the detection of lesions in all five cases with cerebral infarction. Crossed cerebellar diaschisis was only detected by SPECT in cerebral infarction (2/5), multiple sclerosis (1/1) and Alzheimer disease (1/1). In AD patients, MRI and XCT showed cerebral atrophy (3/7) and periventricular change (4/7), whereas SPECT revealed severe cerebro asymmetry (2/7) between right and left hemisphere and decreased activity of several cortical regions; parietal (6/7), frontal (4/7) and temporal (4/7) cortex.

These findings suggest that SPECT can detect earlier change of Alzheimer's disease than MRI or XCT. In one case of Creutzfeldt-Jakob (CJD) and SPECT showed diffuse decrease of activity in the cerebral cortex, although MRI and XCT suggested minimal atrophy of the cortex.

In conclusion, SPECT appears valuable for the detection of the disturbed perfusion area and remote effect in cerebral infarction and the early focal change in dementia.

No. 627

14 normal volunteers (mean age: 24.9 y), 30 patients with partial complex seizures (mean age: 31.3 years) and 12 patients with auditory or visual hallucinations (mean age: 41.8 years) were investigated by IMP-SPECT. Studies were performed with occluded eyes and without ear plugs in a silent dim lightened room. 18 ROI's in each hemisphere were drawn on 5 adjacent transversal SPECT slices. These findings suggest that SPECT can detect earlier change of Alzheimer's disease than MRI or XCT. In one case of Creutzfeldt-Jakob (CJD) and SPECT showed diffuse decrease of activity in the cerebral cortex, although MRI and XCT suggested minimal atrophy of the cortex.

In conclusion, SPECT appears valuable for the detection of the disturbed perfusion area and remote effect in cerebral infarction and the early focal change in dementia.

No. 628
RADIOACTIVE THALLIUM DISTRIBUTION IN THE BRAIN AFTER CSF INJECTION. D. V. Woo, J. Rubertone, J. Emrich. Hahnemann University, Philadelphia, PA.

The cerebral spinal fluid (CSF) which bathes the brain and spinal cord may be used to permit entry of drugs that do not readily cross the blood brain barrier. However, the actual circulation of such exogenous substances via the CSF is uncertain and unpredictable. Although cisternography with radioactive tracers is commonly used to evaluate CSF space, no radioactive drugs designed to be taken up by specific neurons after injection directly into the CSF have been recently studied and used in nuclear medicine procedures. We report preliminary studies which examine the uptake and distribution of selected radioactive cations in the brain and spinal cord after intrathecal injection. Radioactive Thallium-201 (T1-201) was stereotactically administered into either the lateral or fourth ventricle.
of adult rats. From 2 to 6 hours after injection, the brains were lightly fixed, sectioned on a freezing microtome, and apposed to autoradiographic film. The developed autoradiographs of brain sections indicated uptake correlating to specific nuclei. Significant uptake was also observed in the spinal gray matter. Increased uptake was seen in specific nuclear regions of the thalamus, hypothalamus, periaqueductal gray, and deep cerebellar and vestibular nuclei. Movement of tracer throughout the neuropil with time appeared to correlate well to known patterns of CSF circulation. Thallium uptake in specific neurons may reflect CSF flow as well as active transport processes. Therefore, these data suggest that TI-201 may be useful in delineating specific neuronal function via CSF circulation.

Monday, 3:30–8:00 Exhibit Hall

ONCOLOGY: GENERAL

No. 629

Regional cerebral blood flow imaging has been shown to be useful as an aid in the diagnosis of neurological and cerebral vascular disorders. As yet its role in the study of brain tumors is uncertain. TC-99m-HMPAO (a neutral, lipophilic complex) crosses the blood brain barrier and is fixed in brain tissue proportional to blood flow. We have studied the uptake and distribution of HMPAO in patients with various types of brain tumor, undergoing radiotherapy (RT). 4 patients have been studied and 16 scans performed to date. Each patient received a HMPAO/SPECT scan pre-, mid- and post-RT. X-ray CT scans were also performed and when possible Glucohep­tonate(GH)/SPECT scans. All patients received 750MBq TC-99m-HMPAO per study. Dynamic images were acquired for 4 min. post-injection, followed 10 min. later by a SPECT scan using the GE STARCAM system. For each study brain uptake curves were generated, tumor uptake was studied using ROI analysis and global HMPAO uptake was determined using a thresholding technique to exclude extracellular activity. 4/5 lesions, verified by CT and exhibiting positive GH uptake, demonstrated decreased HMPAO uptake prior to completion of RT. Initial analysis of RT significant changes in HMPAO uptake were noted corresponding to tumor areas and were quantified using ROI analysis. In 1 patient the tumor/normal brain uptake ratio increased from 0.73±0.02 pre-RT to 1.00±0.02 post-RT. Global HMPAO uptake measurements in 2 patients indicate 44±4% increase by the end of RT.

No. 630

Radiolabel uptake by human sarcomas after i.v. injection of N-13 L-valine (Val) and L-glutamate (Glu) was studied using a thresholding technique to exclude extracellular activity. 4/5 lesions, verified by CT and exhibiting positive GH uptake, demonstrated decreased HMPAO uptake prior to completion of RT. Initial analysis of RT significant changes in HMPAO uptake were noted corresponding to tumor areas and were quantified using ROI analysis. In 1 patient the tumor/normal brain uptake ratio increased from 0.73±0.02 pre-RT to 1.00±0.02 post-RT. Global HMPAO uptake measurements in 2 patients indicate 44±4% increase by the end of RT.

No. 631
Sr-89 THERAPY: STRONTIUM KINETICS IN METASTATIC BONE DISEASE. G.M. Blake, M.A. Zivanovic, A.J. McShan & D.M. Ackery. Southampton General Hospital, Southampton, U.K.

Strontium kinetics were investigated in a group of 14 patients receiving Sr-89 palliation for metastatic bone disease secondary to prostatic malignancy. Using Sr-85 as a tracer, wholebody strontium retention was monitored for a three month period following Sr-89 administration, and at 90 days was found to vary from 11 to 88% and to correlate closely with the fraction of the skeleton showing scintigraphic evidence of osteoblastic metastatic involvement. Strontium renal plasma clearance varied from 1.6 to 11.6 litres/day, and was significantly reduced compared with normal controls due to increased tubular reabsorption associated with the disturbance of calcium homeostasis. Gamma camera studies of strontium turnover in individual metastases gave retention curves that typically rose to a plateau at 10 days after therapy and then decreased very slowly. In contrast, retention curves for adjacent normal trabecular bone showed more rapid turnover, peaking at 1 day and subsequently decreasing following a power law function in time with index -0.2. Preliminary estimates of absorbed dose to spinal metastases following Sr-89 therapy determined at 2.2 MBq/kg body weight gave values between 1000 and 3000 cGy, with dose depending on the total extent of skeletal involvement and strontium renal plasma clearance amongst other factors.

No. 632

The purpose of this study was to determine the "ideal" time between gallium injection (inj) and imaging in patients (pts) with malignant tumors. Imaging, with computer acquisition, was performed on at least two different days in a total of 17 pts. The pts were scanned an average of 2.9 times. Analog images were based on a 500,000 count technique centered over the chest. Computer acquisitions were all within a time of 6 minutes. Regions of interest were selected over lesions and adjacent background areas. Target to non-target ratios (TNT) were measured. The TNT were normalized to the two day post inj values. In 5 of 12 pts the TNT at five days was greater than at three days. The TNT was greater at six days than at two days in eight of eight pts. We grouped two and three day measurements and compared them to four and five day, as well as six and seven day measurements. Results are shown in the following table.
No. 633

CORRELATION OF GALLIUM UPTAKE AND DEGREE OF MALIGNANCY IN NON-HODGKIN'S LYMPHOMA. D.C.P. Chen, C.L. Hung, A. Levine, and M.E. Siegel. LAC/USC Medical Center, Los Angeles, CA.

The gallium (Ga) uptake in the Non-Hodgkin's Lymphoma (NHL) is variable. With the new pathologic classification of NHL, the degree of malignancy can be determined. We performed a retrospective study to investigate the relationship between the grade of Ga uptake and degree of malignancy of NHL.

47 patients (29 male, 18 female, age range: 16-77 with mean age 44) with NHL had total body Ga scans 24-48, and/or 72 hrs. post IV injection of 3 mcI of Ga-67 citrate. The Ga activity was classified as grade 0: normal, grade 1: < sternal activity, grade 2: equal to sternal activity, grade 3: < liver activity, and grade 4: > liver activity. Function classification of these 47 NHL shows 25 high degree of malignancy, 5 medium degree, 12 low degree, and 5 miscellaneous.

In the high degree NHL, 20/25 (80%) had grade 4 gallium uptake, 2 (8%) had grade 3, 2 (8%) had grade 2, and 1 (4%) had normal activity. In contrast, low grade uptake (grade 0 through 2) was noted in 8/12 patients (75%) with low degree malignancy. Using the criteria of Ga activity above grade 2 as high uptake, we found that the positive predictive value of high Ga uptake for NHL classified as highly malignant was 85% and negative predictive value for low degree NHL is 73%.

In conclusion based on this preliminary data, there appears to be good correlation between Ga uptake and degree of malignancy of NHL. Further investigation is progressing to evaluate the potential clinical application of this finding.

No. 634


Metastatic carcinoma commonly involves the liver which has spurred the development of selective intrahepatic artery chemotherapy. We studied 28 consecutive patients referred for routine evaluation of hepatic artery infusion pump function. Most of the patients had no pre-test diagnosis of pump dysfunction or aberrant catheter placement.

One to three mcI of 99mTc microspheres were administered per pump port via trans abdominal injection, after the sterile cleansing of the abdominal skin site. A dedicated camera/computer acquisition began immediately post injection for 60 seconds (3 second frames) followed by an immediate hepatic view (500K counts). Next, multiple abdominal, thoracic and pelvic images with appropriate markers were obtained.

We found 15 out of 57 studies in 28 patients were abnormal. These abnormalities were: catheter migration, anomalous anatomy, arterial thrombosis, pump / or catheter malfunction and other organ perfusion.

We conclude that routine hepatic artery infusion studies should 1) be done on every hepatic artery catheter to confirm proper placement and 2) should be performed serially in patients to identify potential problems. These studies 1) discovered catheter or pump related abnormalities in 15 of 57 studies 2) can be performed simply and safely in a routine nuclear medicine laboratory and 3) can be done with 99mTc microspheres as well as 99mTc.

No. 635

POTENTIAL USE OF C-11 LABELED ALPHA-AMINOISOBUTYRIC ACID (AIB) FOR STUDYING ALTERATIONS IN AMINO ACID UPTAKE IN TUMOR ASSOCIATED CACHEXIA. P.S. Conti, H.F. Starnes, E.L. Kleinert, and M.F. Brennan. Memorial Sloan-Kettering Cancer Center, New York, N.Y. 10021.

Alterations in host metabolism associated with progressive tumor growth may be attributed to anorexia or some unknown direct effect on the host tissues not related to reduced dietary intake. Changes in amino acid uptake in tissues of rats bearing the Dunnng R3327 prostate tumor from 2-5 weeks post-implantation, in non-tumor bearing rats studied for 7 days, and in tumor control rats were studied with C-11 AIB at 45 minutes after injection (6 rats per group):

<table>
<thead>
<tr>
<th>Lesions Measured</th>
<th>243</th>
<th>465</th>
<th>667</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average T/NT</td>
<td>2.00</td>
<td>2.04</td>
<td>2.24</td>
</tr>
</tbody>
</table>

There was a 10% increase in contrast between baseline and late imaging, which was significant at the .05 level. Using both subjective evaluation of images and measurement of T/NT, we have found that many tumors are more clearly visualized beyond three days post inj. Late imaging may not be practical as a routine, but should be considered in selected cases.
GALLIUM-67 SCINTIGRAPHY IN GARDNER'S SYNDROME. R. Hardyoff, D. Ben-Dov, and A. Front. Lady Davis Carmel Hospital, Haifa, Israel.

Gardner's syndrome was described in 1953 as a disease entity associating familial polyposis with extracolonic manifestations. The latter consists of cutaneous and subcutaneous lesions, desmoid tumors, as well as osteomas and dental abnormalities. Desmoid tumors differ from most fibrous growth by their tendency to infiltrate into surrounding tissues, therefore difficult to treat surgically or medically. We used Ga-67 scintigraphy as an additional imaging modality in patients with Gardner's syndrome in order to evaluate its contribution to the management of these patients. Their extracolonic manifestations consisted of desmoid tumors, small bowel polyps and skull osteomas. Four patients were considered to be clinically disease-free. Two of them had a normal Ga-67 scintigraphy and two patients demonstrated abnormal uptake. One of them had an abdominal uptake which was subsequently found to be a desmoid tumor on an ultrasound study, and the second patient showed bilateral diffuse maxillary and mandibular uptake, which was thought to be due to osteomas, in spite of normal skull radiography. In two patients who had known desmoid tumors, an additional abnormality was found on Ga-67 scintigraphy. One patient with a giant abdominal desmoid tumor medically treated had three consecutive C-T and Ga-67 studies, which demonstrated a decrease in tumor size and uptake. It is concluded that Ga-67 uptake can differentiate between viable tumor cells and post treatment fibrosis, and is therefore a useful adjunct to the clinical and radiological follow-up of patients with Gardner's syndrome.

IMMUNOSCINTIGRAPHY (IS) OF MALIGNANT TUMORS. T. Yamada. Isotopen Diagnostik CIS, Frankfurt, and Dept. of Radiology, University of Frankfurt, and Dept. of Radiology, St. Mary's Hospital, Frankfurt, FRG.

I-131 labeled monoclonal antibodies (MAB) or its fragments are widely used for planar IS and high sensitivity is reported. High quality of images is obtained with I-125 labeled MAB or its fragments and ECT. In the present paper, sensitivity of PS and ECT was compared in vivo and in vitro with the use of I-131 labeled MAB fragments.

Twelve patients with malignant tumors or its metastases (colorectal carcinoma (CR) (n=4), ovarian carcinoma (OV) (n=4), breast cancer (BC) (n=2), and lung cancer (LU) (n=2)) were submitted to ECT gamma scanning specifically in oat cell bronchial carcinoma. For anatomical land marking one case with ovarian cancer. The visualization of malignant tumors was better than that of Ga-67 citrate, 81.4% (20/25). Ga-67 citrate more avidly accumulated than Tc-99m DMSA, except one with ovarian cancer. The visualization of malignant tumors appeared to be much better in the late Tc-99m DMSA image (3-6 hr).

In conclusion, our findings suggest that persistence of activity in the tumors cannot be ascribed to increased vascularity alone, but Tc-99m DMSA possibly has affinity for malignant tumor cells. The details of tumor affinity mechanism of Tc-99m DMSA still must be studied.

UNILATERAL BONE AGENT ACCUMULATION IN THE THORAX IN LUNG CANCER. Howard A. Levy and Chan H. Park. Thomas Jefferson University Hospital, Philadelphia, PA.

Soft tissue accumulation of bone imaging agents has been reported in lung cancer and in malignant effusions, but the incidence of this finding is unknown. The bone scans of 130 patients with proven lung cancer and available clinical and laboratory data were studied. 59/130, or 45% of these patients showed unilateral thoracic soft tissue accumulation (UTS) of MDP, and in every case, this was in the hemithorax in which the tumor was located. The remaining 70/130 or 55%, did not have UTS. There was no significant difference between the two groups as to age, sex, tumor cell type, use of chemotherapy, or performance of a thoracotomy. Pleural effusion (PEF) noted on chest roentgenograms or computed tomography was seen in 41% of patients with UTS, but only in 18% of those without this finding. 46/59, or 78% of the patients with UTS had received Radical or Chemotherapy therapy at the time of bone scan and compared to 6/71, or 8% who received RT but did not have UTS. 8/59, or 14% of patients demonstrated UTS but had not received RT, while 57/70, or 80% did not have UTS and were not treated with RT. The bone scans of 14 patients showed no UTS prior to RT, but did so after RT. 8/59, or 8.5% of patients with UTS had received RT to other parts of the body but not to the lung, as compared to 7/71, or 10% of those without UTS who received the same therapy. Of 47 patients with UTS who received RT, there were about as many patients without PEF, 28, as those with this finding. 20 UTS was seen in almost half of treated lung cancer patients, most commonly in patients with prior RT to the tumor.

GALLIUM IMAGING IN OAT CELL BRONCHIAL CARCINOMA. N Milroy, M L Smith, S W Banham and J H McKillop. Departments of Respiratory Medicine and Nuclear Medicine, Royal Infirmary, Glasgow, Scotland.

Galium scanning has been extensively investigated as a means of pre-operative mediastinal staging in lung cancer. However, there have been few studies of Gallium scanning specifically in oat cell bronchial carcinoma.
We have studied 39 such patients. All patients underwent Gallium scanning as part of pretreatment staging. Gallium scan was positive for primary tumour in 38 patients (97%) and suggested mediastinal spread in 31 patients (79%). In 20 patients (all with positive pretreatment scan) Gallium scan was repeated after induction chemotherapy (6 complete responders (CR), 8 good partial responders (good PR), 3 modest partial responders (modest PR) and 3 non-responders). Following chemotherapy Gallium scan returned to normal in all 6 CRs and in 7 of 9 good PRs. In 2 of 3 modest PRs and in all 3 non-responders there was no improvement in scan appearances following chemotherapy. Thus Gallium scan changes following chemotherapy correlate well with response to chemotherapy as assessed by conventional measures (restaging radiology and bronchoscopy). In 5 patients Gallium scan has been repeated 3 monthly up to 1 year. In 3 patients the scan remains negative and these patients continue in remission. In 2 cases the scan indicated relapse confirmed clinically.

Gallium in taken up avidly by oat cell tumours. Gallium activity appears to mirror clinical disease activity and may prove useful in the evaluation of response to chemotherapy.

No. 642

IMAGING OF SOFT TISSUE TUMORS WITH TECNETIUM(99m) DIMPICAPTOSUCCINIC ACID, SECOND REPORT. H. Ohta, Tamatsu Hospital, Kobe, Japan; K. Endo, H. Sakahara, T. Nakashima, K. Torizuka, Kyoto University, Faculty of Medicine, Kyoto, Japan.

We have previously reported the usefulness of Tc(V)-99m dimercaptosuccinic acid (Tc(V)-DMS) in the diagnosis of soft tissue tumors. But the amount of the cases is not so large and no case is followed. This time, we examined 150 cases (64 malignant cases and 86 benign cases) and 15 cases were followed with Tc(V)-DMS. And in some cases, time course study was also performed.

Tc(V)-DMS was found to have a sensitivity of 94% for malignant tumors and a specificity of 70%. Therefore the highest Tl uptake and best TR to background time for Imaging malignant tumours (TRS) after I.V. injection of 2 mCi of Tl-201 was 80%. False-negative 4 cases occurred in clear cell histiocytoma, and failure to image could be due to the small size of tumors. False-positive cases were observed in some inflammatory lesions, operation scar, neurogenic tumors and hemangiomata. And whether the recurrence of the tumor is present or not was correctly diagnosed in 12 cases. 3 misdiagnosis cases were false positive uptake to the operation scar.

Usually we take scintigrams 120 min after i.v. administration, we could obtained good images as clear as those of 120 min and enough to make correct diagnosis.

Tc(V)-DMS scintigraphy is early and cheap examination and would be surely useful in the diagnosis and follow-up of the soft tissue tumors.

No. 643


The interpretation of images obtained using thymidine (TdR) labeled with C-11 will require a detailed knowledge of the biochemistry of TdR utilization. The first problem is that cells may utilize either endogenously synthesized or exogenously supplied TdR. We measured these two sources in a number of mammalian cell lines, tissues and tumors by incubating them in the presence of the TdR analog 3H-bromodeoxyuridine (BUDR). After extraction of the DNA the degree of substitution of the TdR by BUDR was determined on density gradients. All the cell lines and tissues tested utilized both TdR sources. With this similar TdR uptake in similar experimental conditions, the specific activity of intracellular TdR can be calculated.

Utilization of TdR is important since TdR released from the DNA of dead cells may be taken up and compete with labeled TdR. Previous investigators have estimated the rate of reutilization of TdR at up to 60%, by comparing the rate of loss of H-3-TdR to the TdR analog I-123-Iidoamidotriacetic acid (IOTA) (Myers et al., Cell Tiss. Kinetics 9:215, 1976). Our data indicates that IOTA is being deiodinated in vivo giving spurious reutilization rates. 6-3-3-IOTA has similar retention to C-14-TdR indicating that little reutilization is occurring. This will greatly simplify the modeling of TdR metabolism.

Finally, we have synthesized C-11-thymidine and using Re probes in coincidence have measured its uptake in exteriorized rat intestine. This uptake was compared with H-3- and C-14-methyl-labeled-TdR. As TdR was degraded there was preferential retention of the methyl carbon, probably in proteins. This previously unrecognized problem will need further study.

No. 644


As animal models of tumor, B-16 melanoma, Lewis lung cancer, Hepatoma Ah109A, Ehrlich ascites tumor and Yoshida sarcoma were used. And as an inflammation model the drug-induced abscesses was used. Serial images were obtained at 6, 12, and 24 hours following intravenous injection of 0.1 mcI of IMP. For biodistribution, mice were fed with...
B-16 melanoma and Lewis lung cancer were sacrificed periodically. The tumor and other organs were assayed for radioactivity. As a result, the tumor tissues of B-16 melanoma and Lewis lung cancer were clearly visualized at 12 hours after injection. On the other hand, the tumor tissues of other three models were not well visualized. And the turpentine oil-induced abscess also showed good visualization. The mean tumor to blood ratio of B-16 melanoma and that of Lewis lung cancer at 12 hours after injection were 9.8 and 13.0 respectively.

In conclusion, our data suggest that 1-123-IMP may not be a specific agent for the diagnosis of malignant melanoma, although 1-123-IMP is useful to localize the metastatic as well as primary lesion of melanoma.

No. 646
Tc-99m ANTIMONY SULFIDE COLLOID (SbSC) LYMPHOSCINTIGRAPHY OF THE PROSTATE BY DIRECT TRANSRECTAL INJECTION. L.S. Zuckier, M. Finkelstein, P. Stone, S.Z. Freed, R. Bard, M.D. Blaufox and L.M. Freeman. Montefiore Hospital Medical Center / Albert Einstein College of Medicine, Bronx N.Y.

Bilateral pelvic lymphadenectomy, utilized in the staging and treatment of carcinoma of the prostate, is an extensive procedure with significant morbidity. Unilateral dissection would significantly reduce this morbidity if clinically justified. Lymphatic drainage of the prostate gland was studied to delineate drainage routes after direct prostate lobe injections.

8 patients with aspiration-biopsy proven or clinically suspected prostate carcinoma were studied. Tc-99m SbSC (0.25 mCi) was administered directly into the prostate by Franzen needle via a transrectal approach. Injection was directed into an involved lobe in all 8 subjects. A contralateral injection was additionally performed in 1 patient at a subsequent date. Anger-camera imaging with a LEAP collimator was performed at 1 and 4 hours in anteroposterior, anterior, posterior and lateral projections. In 1 patient injection was unsuccessful (having entered the intraprostatic venous plexus). Drainage in 4 studies was confined to the ipsilateral chain of lymph nodes, in 3 studies was bilateral and in 1 patient only contralateral nodes were imaged.

These studies with direct intraprostatic injection in patients with prostate carcinoma suggest that lymphatic drainage may be ipsilateral, contralateral or bilateral and cannot be predicted from the site of tumor. This should be considered in the determination of appropriate staging and treatment of patients with this condition.

Monday, 3:30-6:00 Exhibit Hall

PEDIATRICS

No. 647
SCINTIGRAPHY IN GASTROINTESTINAL BLEEDING IN THE PEDIATRIC POPULATION. T.R. Hall, J.M. Miller. (Children's Hospital of Los Angeles, Los Angeles, CA), J.R. Sty (Milwaukee Childrens Hospital, Milwaukee, WI)

Gastrointestinal (GI) bleeding in the pediatric population is a common problem in chronically ill patients. A total of 29 patients with GI bleeding were studied by scintigraphy using Technetium (Tc)-99m labeled red blood cells (RBC) or sulfur colloid at two major pediatric medical centers. The age range was from three weeks old to 20 years old with an equal sex distribution. Of the 19 patients studied with the labeled red cells using an in vitro labeling technique, evidence of GI bleeding was documented scintigraphically in 15 of the patients. Tc-99m labeled sulfur colloid scans in the remaining ten patients were positive for GI bleeding in six of the cases. A variety of bleeding abnormalities were detected by scintigraphy including stress and stomal ulcers, erosive gastritis, a duodenal hemangiomia, bleeding esophageal and duodenal varices and a case of retroperitoneal hemangiomia. Both Tc-99m labeled RBC and sulfur colloid are equally sensitive for the detection of active bleeding. However, Tc-99m labeled RBCs offer the advantage of detection of GI bleeding without competition from the liver and spleen and delayed imaging up to 18-24 hours following initiation of the study. We will illustrate the ease of performance and the value of this procedure in children, which makes this the method of choice for initial examination of older children with GI bleeding.

No. 648

Angular deformity of an extremity is known to occur following trauma or infection near the growth plate. It is hypothesized that this results from alteration of plate function. Bone-seeking tracers, which actively localize in the physiologic status of the plate and should be of assistance in assessing deformity. The two- or three-phase bone scintigrams of 16 patients with growth plate abnormalities were analyzed for patterns of physiologic uptake. Patients ranged in age from 4-15 years. Etiologies included fracture (7), surgery (4), infection (3), and other (2). In 11/16, there was a clinically significant angular deformity: varus (6), valgus (5). All 6 patients with varus deformity had physical activity in the involved bone which was appreciably greater in the lateral aspect of the plate than in the medial aspect. The reverse pattern was observed in 4/5 patients with valgus deformity, where medial plate activity exceeded lateral activity. In 5 patients with decreased activity that was symmetric across the plate, there was shortening of the extremity without angulation.

When growth plates are affected by trauma or infection, scintigraphy may be helpful in predicting the eventual outcome. Specific patterns of asymmetry were observed to correlate closely with varus and valgus deformity.

Monday, 3:30-6:00 Exhibit Hall

No. 649
THE USE OF GLUCAGON TO IMPROVE Tc-99m-PERTECHNETATE (TcP) ABDOMINAL SCINTIGRAPHY FOR ECTOPIC GASTRIC MUCOSA: CLINICAL EXPERIENCE. C.N. Stakianakis, A. Gentili, D.M. Buckner, and C.Oiticica. University of Miami School of Medicine, Miami, Florida.

Intravenous (iv) or intramuscular (im) injection of glucagon has an inhibitory effect on gastric wall motion and delays gastric emptying. TcP abdominal scintigraphy for the diagnosis of ectopic gastric mucosa is positive when focal activity appears outside the stomach but gastric content could either cover true abnormalities or produce false positive images. It has been shown that glucagon administration in dogs with experimental ectopic gastric mucosa improves the results of scintigraphy mainly by keeping in the stomach the gastric contents which were rich in TcP.

Glucagon was given iv or im to 21 patients immediately before injection of TcP. Comparing with 19 patients without glucagon an improvement of the reported focal or junal activity was found in 16/19 without and in 12/21 after

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glucagon). Although 2 mg were more effective than 1 mg of glucagon appearance of gastric contents in the jejunum was still evident in more than ½ of the patients about 40 min from the TcP injection. In 7 patients in whom 1 mg of glucagon (0.5 mg in infants) was injected before and an equal amount at 30 min after the TcP no duodenal or jejunal activity from gastric contents was observed.

We suggest the following protocol as the most effective in keeping the intestine empty of gastric contents: two injections (im or iv) of glucagon (0.5-1mg) one before and the second at 30 min after the injection of TcP.

Monday, 3:30-6:00 Exhibit Hall

PERIPHERAL VASCULAR

No. 650

Purpose of this study is to evaluate the difference of muscle blood flow (MBF) response to static and dynamic exercise (Ex) between active (ACT) and retired (RET) athletes by Xe-133 single dose multi-step method (SDMM) which has been developed and reported by us. MBF response of bilateral leg muscles (vastus lateralis [VLM], adductor magnus [AMM] and gastrocnemius [GCM]) are evaluated in 5 young rugby players (2 ACT and 3 RET) with single dose of Xe-133 (1-2 mCi/site) and following sequence of study: rest (R1)- static Ex (Ex1)- rest (R2)- dynamic Ex (Ex2)- rest (R3). Every 5 sec. data are aquired for 2.5 min. during R1, R2 and R3 using large field-of-view gamma camera interfaced to a computer. Squatting is used as Ex and continued for 1.5 min. for both Ex1 and Ex2. MBF in R1, Ex1, R2, Ex2 and R3 are calculated by SDMM. There is no significant difference between left and right leg MBF in all muscles both at rest and during Ex. Dynamic Ex (Ex2) induced higher MBF in all muscles than static Ex (Ex1). Although MBF after dynamic Ex (Ex2) returned to R1 level in AMM and GCM in both ACT and RET, however MBF in VLM, which is the most stressed muscle, at R2 is higher in RET than ACT (mean MBF: 22.8 v.s. 1.6 ml/min/100g, p<0.005). Although MBF after dynamic Ex remains high in VLM in both ACT and RET, MBF is higher in RET than ACT (mean MBF: 17.2 v.s. 12.5 ml/min/100g, p<0.1). These results indicate low MBF reserve in RET. In conclusion, patterns of MBF response on various Ex evaluated by SDMM is a good indicator of MBF reserve. Continuous training is likely to be important in maintaining MBF reserve on Ex.

No. 651
LEG MUSCLE PERFUSION STUDY USING Tl-201 SINGLE PHOTON EMISSION COMPUTED TOMOGRAPHY (SPECT). M.Oshima, T.Yano, N.Nishikimi, S.Sionoya, N.Akanabe and S.Sakuma, University of Nagoya Medical School, Nagoya, Japan.

The purpose of this study is to evaluate leg muscle perfusion with Tl-201 SPECT. Twenty-three patients with peripheral arterial disease underwent this examination. A cuff was applied above the knee bilaterally and was inflated to 50 mmHg above the brachial systolic pressure. During deflation of the cuff, 3 mCi of Tl-201 was injected intravenously. The lower leg SPECT imaging and whole body imaging were performed by rotating dual type digital gamma cameras(Toshiba GCA-70A) with on-line minicomputer. Transverse images of leg muscle were compared with clinical symptoms and arteriographic findings. For quantitative analysis, each slice counts of lower leg were normalized by whole body counts.

Results were as follows: 1) SPECT perfusion image of lower leg was obtained satisfactory, 2) SPECT image can be divided into anterior tibial muscle and posterior tibial muscle component, 3) Six out of 8 legs which showed obstrusive lesions with adequate collateralization demonstrated normal SPECT image, and 4) Ten out of 13 legs demonstrated abnormal defects correspond with the distribution of arteriograms. In conclusion, SPECT perfusion distribution with quantitative analysis was correlated with arteriographic findings and clinical symptoms.

No. 652

Numerous techniques have been used to study lower limb perfusion. Siegel derived an excellent predictive index of healing potential of ulcers. However, timing of reconstructive surgery and changes in perfusion have not been studied extensively. Reconstructive surgery was indicated for limb salvage and consisted of femoral-distal bypass. Tissue perfusion was studied with thallous chloride (55MgCl2), pre and post-op. Dynamic imaging of the initial phase (build up) and static imaging at equilibrium of calves, ankles and feet, and as a reference, myocardium and left upper arm, were performed. Five pts were studied, status and results for the affected limb are summarized in the table: age, sex, ankle-to-brachial index (ABI) and post-op ratios.

<table>
<thead>
<tr>
<th>Pt</th>
<th>age</th>
<th>sex</th>
<th>ABI</th>
<th>PVR calf</th>
<th>c/s/p</th>
<th>post/pre-op ratios</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>65 M</td>
<td></td>
<td>0.80</td>
<td>0.041</td>
<td>0.042</td>
<td>pre post calf foot</td>
</tr>
<tr>
<td>2</td>
<td>74 F</td>
<td></td>
<td>0.70</td>
<td>0.034</td>
<td>0.038</td>
<td>0.8 0.14 1.90</td>
</tr>
<tr>
<td>3</td>
<td>68 F</td>
<td></td>
<td>0.87</td>
<td>0.044</td>
<td>0.026</td>
<td>1.0 2.5 1.05</td>
</tr>
<tr>
<td>4</td>
<td>63 F</td>
<td></td>
<td>0.39</td>
<td>0.084</td>
<td>0.063</td>
<td>1.7 0.9 1.12</td>
</tr>
<tr>
<td>5</td>
<td>63 F</td>
<td></td>
<td>0.70</td>
<td>0.077</td>
<td>0.088</td>
<td>1.7 1.0 1.54</td>
</tr>
<tr>
<td>6</td>
<td>65 M</td>
<td></td>
<td>0.39</td>
<td>0.084</td>
<td>0.063</td>
<td>1.5 1.0 1.54</td>
</tr>
</tbody>
</table>

The build up curve was analyzed using a linear fit of the initial rise (lin) and an exponential fit (exp) of the first 10 minutes. Absolute count rate per pixel (c/s/p) is dose and cardiac output dependent, therefore, ratios are preferable. Myocardial uptake appeared to be a better reference than left arm. All pts were asymptomatic after surgery, showed increased perfusion of all affected limbs, and reached a plateau 3-4 minutes after injection. As expected, a dramatic improvement in flow parameters does not necessarily mean a better perfusion (pts 2,3).

No. 653
FOUR VS TWENTY-FOUR HOUR DELAYED INDIUM-111-PLATELET IMAGES FOR DETECTION OF LOWER EXTREMIT Y DEEP VENOUS THROMBOPHLEBITIS. J.E. Seabold, G.R. Conrad, D.A. Kimball, E.E. Frey, J.D. Coughlan. The University of Iowa, Iowa City, IA.

The purpose of this study was to determine if In-111-platelet scintigraphy (In-PS) performed 4 hours following injection of labeled cells would provide diagnostic information as to the presence of active deep vein thrombophlebitis in the lower extremities. Seventeen patients clinically suspected of thrombophlebitis underwent In-PS at 4 hours and 24 hours following injection of autologous labeled platelets as well as lower extremity contrast venography (CV). Eleven of the 17 (65%) patients were found to have one or more intraluminal filling defects 30 Cb indicative of active thrombophlebitis. Of these 11 patients, 8/11 (73%) had abnormal In-PS at 4 hours and 10/11 (91%) at 24 hours. All studies that were abnormal at 4 hrs remained positive at 24 hrs, but showed greater intensity and/or a greater number of abnormal sites. In-PS and CV were both negative in 4 cases. Two
In-111-oxine labelled platelet scintigraphy (LPS) is uniquely suitable for studying venous thrombosis because the half-life of the isotope and the life span of the injected platelets allow imaging for 5-7 days with a single injection of the labelled material. We and others have shown that LPS is a valuable technique for the surveillance of high risk patients. In this study we determined the accuracy of LPS and the optimum timing of imaging after platelet injection were determined in 23 symptomatic patients who underwent venography. Thirteen of these patients were receiving heparin at the time of injection and 10 were not. Sensitivity and specificity for the untreated group were 100% and 86%, and for the treated group were 91% and 83%. None of the patients receiving heparin had positive venograms, whereas 3 of 10 patients without heparin were positive. These results confirm our preliminary study in 10 patients. Sensitivity and specificity for the untreated group were 100% and 86%. The specificity in this latter group, however, was significantly lower in the treated group, 86%. We conclude from this preliminary analysis that LPS is useful in the diagnosis of deep vein thrombosis and that heparin adversely influences the sensitivity of this technique. In non heparinized patients sensitivity is better at 24 vs 4 hrs after injection of the platelet suspension.

In conclusion, LPS is a valuable technique in the surveillance of high risk thrombosis patients. In this study the accuracy of LPS and the optimum timing of imaging were determined. The sensitivity and specificity for the untreated group were 100% and 86% whereas for the treated group were 91% and 83%. These results confirm our preliminary study in 10 patients. Sensitivity and specificity for the untreated group were 100% and 86%. The specificity in this latter group, however, was significantly lower in the treated group, 86%. We conclude from this preliminary analysis that LPS is useful in the diagnosis of deep vein thrombosis and that heparin adversely influences the sensitivity of this technique. In non heparinized patients sensitivity is better at 24 vs 4 hrs after injection of the platelet suspension.
from compression of the internal pudendal artery on each side by the hypertrophic prostate.

Monday, 3:30-6:00

Exhibit Hall

PULMONARY

No. 658


The present study examines the role of polymorphonuclear leukocytes (PMNs) in hyperoxic lung injury using the nonsteroidal anti-inflammatory drug, ibuprofen. White New Zealand rabbits exposed to 100% O2 or air for 1 to 4 days were divided in two groups: the treatment group (I) was fed ibuprofen (75 mg/day) with drinking water whereas the control group (C) received water alone. At the end of exposure, all the animals were injected with 60-20 uCi of In-111 oxine labeled PMNs and digitized images were acquired at selected time intervals using a Siemens gamma camera interfaced to a VAX mini-computer. An influx of radioactive PMNs into the lungs was detected only in 72-hr and 96-hr oxygen exposed Group C animals, whereas Group I animals did not exhibit any accumulation of radioactivity into the lung. Quantitative assessment of PMN accumulation was performed both by region of interest studies of images and by counting the vital organs after sacrificing the animals. Although blood gas analysis of all 72-hr oxygen exposed animals did not show any abnormal values, the analysis of dry/wet weight ratios and histopathological examinations of the lungs indicated noncardiogenic edema formation. Post-mortem examination showed severe acidosis, gross cytoplasmic edema and partial destruction of lung endothelium were observed in both I and C groups after 96 hrs of O2 exposure. The present study clearly demonstrates that although ibuprofen cannot prevent hyperoxic lung injury, it inhibits the influx of PMNs into the injured lung, suggesting that PMNs are not directly involved in the injury process.

No. 659

CLINICAL PATTERNS OF RADIOAEROSOL PENETRATION. M. Collin, R.A. Holmes. Nuclear Medicine, University of Missouri and Harry S Truman Memorial Veterans Hospital, Columbia, MO.

Unlike the radioactive inert gases that readily diffuse throughout the aerated lung and measures regional ventilation radioaerosols, such as Tc-99m-DTPA, penetrates and evaluates the patency of the tracheobronchialalveolar Airways and are used clinically to detect endobronchial disease. We have studied more than 150 patients referred to exclude pulmonary embolism (PE) who received a Tc-99m-DTPA radioaerosol instead of radionuclide prior to a Tc-99m-MAA perfusion (Q) image. Nearly 15 percent of the patients had PE documented clinically or with radiologic studies. In practically all the patients where PE was demonstrated, a discordance between the Q and the normal radioaerosol images were seen, however, those with superimposed congestive heart failure, obstructive lung disease or senile emphysema made the interpretation more difficult due to altered patterns of radioaerosol penetration. More than half of the patients studied had some form of airway/parenchymal lung dysfunction that was frequently not appreciated by the referring physician. Patterns of central airway, retention and multifocal peripheral localization could be further characterized and differentiated into several conditions: a) emphysema (panlobar); b) bronchiectasis/cystic fibrosis; c), combination of a and b; d) smokers (small airway disease); e) acute asthma; and f) artificial airway applications. In conclusion, patterns of specific airway disease can be accurately detected with Tc-99m DTPA radioaerosol.

No. 660


Clearance of aerosolized Tc-99m-DTPA has been proposed as a measure of pulmonary epithelial permeability, but is affected by increased functional residual capacity (FRC). To examine this further, we studied the dose-response relationship of positive end-expiratory pressure (PEEP) and PEEP on clearance of aerosolized Tc-99m-DTPA (0.44 uCi). Lung activity was decay corrected, fit to an exponential, and expressed as % decrease per min (%/min). Sheep (n=30) were ventilated with 0, 2.5, 5, 10, 15 or 20 cm H2O PEEP while clearance was measured. PEEP by H2O washout was measured in 3 sheep while on 0, 2.5, 5, 10, 15 and 20 cm H2O PEEP ventilation. Data are shown as means±SEM; different than next lower step of PEEP (p<0.05):

<table>
<thead>
<tr>
<th>PEEP (cm H2O)</th>
<th>Clearance (%/min)</th>
<th>FRC (L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.39±0.05</td>
<td>0.76±0.19</td>
</tr>
<tr>
<td>2.5</td>
<td>0.40±0.03</td>
<td>1.26±0.12</td>
</tr>
<tr>
<td>5</td>
<td>1.14±0.19*</td>
<td>1.64±0.19</td>
</tr>
<tr>
<td>10</td>
<td>1.98±0.38</td>
<td>2.36±0.12</td>
</tr>
<tr>
<td>15</td>
<td>5.38±0.60</td>
<td>3.44±0.35</td>
</tr>
<tr>
<td>20</td>
<td>5.39±0.69</td>
<td>3.45±0.35</td>
</tr>
</tbody>
</table>

In 3 sheep ventilated with 20 cm H2O PEEP, clearance measured on 0 cm H2O PEEP was 0.55±0.07 %/min. Clearance shows a sigmoid relationship with both FRC and PEEP, having threshold and maximal effects. Increased clearance due to increased lung volume is reversible. Lung volume should be controlled in studies examining the pulmonary clearance of aerosolized Tc-99m-DTPA. (P01-HL32H18)

No. 661

PULMONARY Tc-99m DTPA CLEARANCE IN PATIENTS WITH RESPIRATORY FAILURE. M. Jacobs, S. Tennenberg, C. Huth, R. Branson, K. Adams. University of Cincinnati Medical Center, Cincinnati, Ohio.

The pulmonary clearance rate of inhaled radioaerosols is thought to be a measure of alveolar capillary permeability (ACP) with a rapid clearance rate associated with increased ACP. Abnormal pulmonary radioaerosol clearance rates (PRCR) have been described in cigarette smokers and various disease states associated with noncardiogenic pulmonary edema (NPE). Using a readily applicable technique for aerosol delivery we performed clearance studies using Tc-99m diethylenetriamine pentacarbamate on 27 patients with respiratory failure requiring mechanical ventilation. Our studies were successful regardless of ventilator type (volume-cycled, time-cycled or high-frequency pulse generator) or level of positive end-expiratory pressure used (up to 25 cm H2O). After blinded retrospective analysis PNE was judged present in 13 patients. One patient was eliminated from analysis due to an underlying lung disease (idiopathic pulmonary fibrosis) associated with abnormal PFR. Those patients with NPE had a mean PFR of 0.00 ± 0.01 while those without PNE had a significantly lower mean PFR of 1.8 ± 0.2 % per minute, p < 0.01. Twelve of 13 patients with NPE had PFR > 3.5 %/minute while all 13 patients without NPE had values < 3.5 % per minute (X̄ = 18.7, p < 0.01). We obtained bronchial secretion and measured the albumin content from 12 patients and found a significant positive correlation between the albumin content and PFR (r = 0.65, p < 0.01). We conclude that the PFR with a measure of acinar damage was successfully performed on mechanically ventilated patients. It may be useful in assessing the presence of NPE.
**Poster Sessions**

**No. 662**

RADIONUCLIDE EVALUATION OF LUNG INJURY IN PATIENTS WITH ADULT RESPIRATORY DISTRESS SYNDROME (ARDS). E.E. Kim, C.A. Pjura, P.A. Lowry, and G. Gutierrez. Univ. of Texas Medical School, Houston, TX.

ARDS, a form of acute severe respiratory failure following lung injury at the alveolar-capillary level, is characterized clinically by hypoxemia and decreased pulmonary compliance and radiographically by diffuse alveolar consolidation. Invariably, there is increased pulmonary-capillary endothelial permeability with leaking of fluid and protein into the pulmonary interstitium and airspaces.

We prospectively monitored this change in permeability in acute ARDS patients with ARDS utilizing two different techniques. The first method, utilizing Tc-99m aerosol, was employed with 10 patients. Each inhaled aerosol for 2 min., after which whole lung images were acquired at 30-sec. intervals for 10 min., utilizing a computer-equipped portable camera. Clearance rates were then determined for selected, peripheral areas of each lung and converted to mean percent decline per minute. The second method involved injecting 5 patients with 15 mCi of Tc-99m HSA after which images were obtained at 1-min. intervals for 45 min.. Ratios of right lung to heart activity were then plotted vs time and a slope index calculated by a linear least squares fit over the 15-45 min. data.

Changes in both indices over serial studies were well correlated with patient response as judged by clinical, radiographic and pulmonary function studies.

Consequently, we conclude that these radionuclide techniques are of potential value in the diagnosis and monitoring of ARDS patients and, potentially, in prognosis.

**No. 663**


The application of high resolution structural anatomy of CT to SPECT transaxial images gives the necessary landmarks to yield precise relationships of the vascular abnormalities to the lung and adjacent organs.

A computer program has been created to take the data acquired by SPECT and CT and to combine similar cross-sectional images into one composite image. The SPECT studies are obtained from a Siemens dual-headed ROTA camera using high resolution collimators. The data was acquired in 60 frames of 64 x 64 pixels at angular increments of 6 degrees. SPECT transaxial cross-sections were obtained with a C.D.A. (VAX 11/750) computer system. The CT cross-sections were obtained on a GE TC/T 9800 computer-equipped portable camera. The computer program converts both the SPECT and CT images of 256 x 256. Slight corrections for orientation and size are required for proper superimposition of corresponding transaxial cross-sections of SPECT and CT images. These images provided accurate relationships between the lung perfusion pattern to the adjacent organs. The definition of the boundaries provides a basis for quantifying the size and extent of perfusion changes. In this manner, the configuration and character of each perfusion defect can readily be defined and categorized. These composite images result in improved structural and physiological anatomy of lung vascular perfusion patterns.

**No. 664**


Lung uptake of iodobenzyl-propanediamine (HIPDM) has been reported, but the nature of this process has not yet been fully established. Thus, the mechanism of single-pass 125I-HIPDM accumulation has been studied in rat lung, isolated and perfused with an albumin Kreba-Ringer bicarbonate buffer. HIPDM lung accumulation was monitored by the tissue/medium ratio (T/M=cpm.g^-1 lung tissue/cpm.ml^-1 inflow).

As a function of time or concentration, HIPDM accumulation appeared to be a saturable process. During a 2 min perfusion, 97.5%/^-2.5 (n=8) extraction was observed with 2 mU HIPDM, but only 36%/-1.2 (n=3, p<0.001) was extracted when the concentration was 1mM. Cold (4°C) had little effect on pulmonary accumulation (87.5%/^-2.3, n=5, p<0.01), and the addition of ouabain or the use of sodium-free medium had no effect on pulmonary accumulation. The addition of 1 mU chlorpromazine, propranolol or imipramine significantly reduced the HIPDM accumulation to 42.5%/^-1.3, 51.3%/^-2.0 and 49.3%/^-0.7, respectively (n=4-6 each group, p<0.001). Thus, the pulmonary accumulation of HIPDM does not appear to be energy dependent, but is saturable and inhibited competitively by other basic amines that are known to bind by physico-chemical interactions to pulmonary endothelial cell membranes.

**Exhibit Hall**

**Monday, 3:30-5:00**

**No. 665**

AN ALTERNATIVE APPROACH TO ON-LINE MONITORING OF ELUTION PROFILES OF Rb-82 FOR RADIOASSAY/RADIATION DOSIMETRY. V. Dhawan* and G.P. Genarro*. *Memorial Sloan-Kettering Cancer Center, New York, NY, and +Squibb Institute for Medical Research, New Brunswick, NJ.

Generator-produced Rubidium-82 has been used with positron emission tomography (PET) to study blood-brain barrier permeability, myocardial imaging and renal perfusion. Static (dose calibrator) assays of Rb-82 bolus yield erroneous estimates of administered activity by ignoring the assymetric output of Sr-82/Rb-82 generators. Though on-line monitoring of elution profile improves accuracy for quantitative purposes, it requires an elution curve profile at any desired flow rate.

Using a compartmental model with liquid-chromatograph time theory, we derive a theoretical relationship between eluted activity vs time as a function of elution flow rate. Experimental elution curves were generated at various flow rates (25-75 mI/min) and eluted activity monitored with an appropriately positioned positron detector. Theoretical curves generated by the model were in excellent agreement with experimentally obtained curves. This proposed model will facilitate the design of Rb-82 infusion protocols for the abovementioned PET studies and also allow an accurate estimate of administered activity without the need for associated on-line monitoring equipment.

**The Journal of Nuclear Medicine**

No. 666

CA 19-9 is a clinically useful cancer marker for the carcinoma of pancreas and gastrointestinal tract. Recently the structure of Lewis, L is defined as a 2,3-diallylated monogalactoside, whose sugar sequence also occurs in the human Lewis (Le) blood-group system. This paper describes the relation of serum CA19-9 levels with Lewis blood-types in normal individuals and the presence of circulating antibodies to CA19-9 in some Lewis negative donors.

According to the presence or absence of Lewis antigens, 107 normal individuals were divided into 3 groups: Le(a+b), Le(a-b) and Le(a-). Serum CA19-9 levels were significantly different among groups they belong. There was more CA19-9 in the serum from normal Le(a+b-) individuals than Le(a+b+) individuals. However, CA19-9 was not detectable in the normal controls and most cancer patients, if not all, who belong the Le(a-b) blood-type. Such difference was not observed in other cancer markers such as CA 125 or CEA. Furthermore, autoantibodies directed towards CA19-9 were found in the serum from 10 (19%) of 53 Lewis negative donors, including normals and patients with benign or malignant diseases but not in Le(a+b-) or Le(a+b+) individuals. B lymphocytes from these cases will serve as a good source for the production of human monoclonal antibodies to CA19-9, which have many advantages for the radioimmunoimaging and therapy of cancer.

No. 667
FOUNDATION OF MATHEMATICAL PACKAGE FOR CONSTRUCTION OF LINEAR CURVE FOR IRMA (IMMUNO-RADIOOMETRIC ANALYSIS) Z. Kureishy, Dept. of Nuclear Medicine, Kuwait University, Kuwait.

A linear mathematical plot is derived which describes the Irma model and provides a means for plotting data in linear fashion without the use of cumbersome mathematical formulae or special graph paper.

The concept of data reduction in Irma is developed on several assumptions to simplify and explain the system. By using calculus a linear response is generated as illustrated below:

Decreasing function: \[ y = f(x), \text{if } f(x_2) < f(x_1) \]

Increasing function: \[ y = f(x), \text{if } f(x_2) > f(x_1) \]

A linear plot of dose concentration on the X-axis and semi-log plot of normalizing response on Y-axis gives a linear relationship, as indicated below, if \[ x = \text{linear dose} \]

\[ \text{B-Bkg} \quad (\text{S-Bkg}) - \text{Bo-Bkg} \quad \text{normalizing} \]

\[ \text{Bo-Bkg} \quad (\text{Bo-Bkg}) \]

where \( B = \text{count rate of known or unknown sample} \)

\( S = \text{maximum bound count of zero std} \)

\( Bkg = \text{count rate or non specific binding} \)

EASE of data acquisition and processing is obtained with the help of calculators and computers.

No. 668

The importance of biotin in man as well as the usefulness of the avidin-biotin complex tool has been recently emphasized. Relative investigations would be very much facilitated by a gamma-emitting tracer of the vitamin. We synthesized the \( N-[C-(4-OH-3-125I-phynyl)ethyl] \)

and the \( N-[C-(4-OH-3,5-di-125I-phynyl)ethyl] \) biotin amides (III) by coupling \( N\)-hydroxysuccinimidobiotin (I) to radioiodinated tyramine (II). Radioiodination of tyramine

\[ [\text{free amino group}] \]

was performed by a modified Chloramine T method, prior to the coupling in order to protect the biotinyl portion from the oxidative radioiodination conditions. By changing the tyramine amount it was possible to produce the mono- or the di-radioiodinated tyramine derivatives. The final products were separated from the reaction mixture by TLC (n-butanol: 2N NH.OH: ethanol, 3:1:1).

Rates in primary breast carcinoma were 10% (1/10), 33% (3/9), 25% (2/8) and 100% (1/1) of stage I, II, III, and IV. In patients with recurrent tumor, 9 of 13 (69%) cases had serum CA15-3 levels of over 30 U/ml and 7 cases showed more than 100 U/ml. One patient with stage III whose CA15-3 levels remained elevated after the operation developed bone metastasis and local recurrence. On the other hand, there was no positive case in 37 patients with no evidence of recurrence. In 74 patients with other malignant tumors, increased levels were found in 33%, 11%, 25%, 0%, 7%, 0% and 43% of sera from patients with gastric, esophageal, lung, uterine, cervix, and ovarian carcinomas respectively. Only 3 of 40 patients with benign diseases had elevated CA15-3 levels. In conclusion, the measurement of serum CA15-3 levels would be useful for the management of patients with breast carcinoma.

No. 669

CA15-3 is a new tumor marker measured by immunoradiometric assay using two monoclonal antibodies (115D8, DF3), which react with a circulating antigen expressed by human breast cancer cells. To evaluate the clinical usefulness of CA15-3, we measured serum CA15-3 concentrations in 60 normal subjects and 189 patients with various malignant tumors and benign diseases using a radiomunoaassay kit (CIS, France). Serum CA15-3 levels in normal subjects were 8.8±2.9 U/ml (mean±SD) and all of them were less than 15 U/ml. When the cutoff level was set at 30 U/ml, elevated CA15-3 levels were observed in 39% (15/38) patients with breast carcinoma. Positive rates in primary breast carcinoma were 10% (1/10), 33% (2/6), 25% (2/8) and 100% (1/1) of stage I, II, III, and IV. In patients with recurrent tumor, 9 of 13 (69%) cases had serum CA15-3 levels of over 30 U/ml and 7 cases showed more than 100 U/ml. One patient with stage III whose CA15-3 levels remained elevated after the operation developed bone metastasis and local recurrence. On the other hand, there was no positive case in 37 patients with no evidence of recurrence. In 74 patients with other malignant tumors, increased levels were found in 33%, 11%, 25%, 0%, 7%, 0% and 43% of sera from patients with gastric, esophageal, lung, uterine cervix, and ovarian carcinomas respectively. Only 3 of 40 patients with benign diseases had elevated CA15-3 levels. In conclusion, the measurement of serum CA15-3 levels would be useful for the management of patients with breast carcinomas.

No. 670
DEVELOPMENT OF A SENSITIVE ASSAY FOR BIOACTIVE PARATHYROID HORMONE. I. Yamamoto, N. Kitamura, J. Aoki and K. Torizuka. Kyoto University School of Medicine, Kyoto, Japan.

Most of assays to attempt to measure biologically active parathyroid hormone (PTH) by radiomunooassay are not sensitive enough to measure values in normal person. We developed relatively simple and sensitive assay for biologically active PTH, employing cyclic AMP measure-
ment, produced in cultured osteoblastic cells (MC3T3-E1), which possesses a number of receptors for PTH. First, bioactive PTH was extracted with isopropanol after loading 1 ml of plasma onto C18-silica cartridge (Sepak), lyophilized and stored at -20°C. Recoveries of PTH, assessed using 125I-labeled synthetic (3'Npyl)-human PTH (1-34) and 125I-labeled synthetic (3'Npyl)-human PTH (1-84) were more than 70% in this procedure. MC3T3-E1 cells were incubated in multi-well (96-well) dishes and cultured for a week and medium was changed to the medium which contained 1 mM isobutylmethylxanthine, 1 mM propranolol and materials for the test. MC3T3-E1 cells possess β-adrenergic receptor and also the effect of β-adrenergic stimulants was blocked by addition of 1 mM propranolol. After 10 min incubation at 37°C, reaction was stopped and cyclic AMP produced was measured by a radioimmunoassay. 5x10^{-11} M of bioactive PTH was detectable from 1 ml of plasma sample in this assay and thus we could measure bioactive PTH in all of sample from healthy volunteers. Samples from patients with hyperparathyroidism showed higher values than those from normal volunteers, while in patients with hypoparathyroidism, values for bioactive PTH showed lower than the detectable level. Thus, relatively simple and sensitive in vitro method, equivalent to nephrogenous cyclic AMP measurement in vivo, to evaluate bioactive PTH was demonstrated.

No. 671
CLINICAL EVALUATION OF MEASUREMENT OF SERUM VITAMIN D METABOLITES
Y. Yamamoto, N. Kitamura, J. Aoki, S. Dokoh and K. Torizuka
Kyoto University School of Medicine, Kyoto, Japan

1,25-dihydroxyvitamin D is a major steroid hormone, regulating calcium balance. However, clinical evaluation of the measurement of serum 1,25-dihydroxyvitamin D is hampered by its cumbersome purification procedure, in Kyoto University School of Medicine, Kyoto, Japan.

No. 673
Bi-212 LABELED MONOCLONAL ANTIBODIES FOR USE IN RADIOIMMUNOTHERAPY. W. L. Anderson-Berg*, M. Strand*, M. Brodie*, R. W. Atchert, and O. A. Gansow* The Johns Hopkins University School of Medicine, Baltimore, MD.

Optimal methods for labeling monoclonal antibodies (MAb) with the alpha particle emitting radionuclide Bi-212 have been developed. In previous studies Bi-206 labeled cyclic anhydride of DTPA (caDTPA) conjugated to MAb was unstable in vivo. We have therefore synthesized 1-(p-isothiocyanato-2-ethylbenzene)DTPA (SCN-Bz-DTPA); 1-(p-nitrobenzyl)-diethylenetriamine was reacted with Br(CH2)3COOH, reduced to the amine and reacted with thiophosgene to form a chelate which has improved thermodynamic stability for Bi labeling. Results showed that biologically labeled antibodies against a variety of tumor antigens were produced.

No. 674
IMMUNOREACTIVITY CHANGES IN T-101 MONOCLONAL ANTIBODY DUE TO VARIATIONS IN DTPA CONJUGATION. B. L. Bond, G. Araya, Section of Nuclear Medicine, University of Illinois School of Medicine at Chicago, IL.

Using MoAb T-101 as a model, we evaluated the effects of DTPA conjugation on MoAb immunoreactivity and in addition have established a set of favorable conditions for Indium-111 (In-111) labeling of DTPA-T-101. Briefly, concentrated antibody results in poor targeting and limits image resolution of many immunoscintigraphic agents. Exposure of the Ab binding site to the conjugation reaction is minimized with an immobilized antibody bound as a protecting group. The antigen covalently attached to CMB activated gel beads immunoabsorbs specific Abs and provides a heterogeneous reaction system as an affinity bound antibody-antigen gel polymer complex. Spherical packing of gel beads allows reaction design in the inefficient conjugation step with simple sequencing of washes and separations in columns giving characteristic separations. The gel polymer helix provides a stable, reproducible radioassay for 1,25-dihydroxyvitamin D and thus we could measure bioactive PTH in vivo, to evaluate bioactive PTH was demonstrated.

Monday, 3:30–6:00
EXHIBIT HALL

RADIOPHARMACEUTICALS: ANTIBODIES

No. 672
SOLID PHASE AFFINITY BOUND ANTIBODY CONJUGATION FOR SITE DIRECTED RADIOLABELING IN IMMUNOCONFORMATION. M. P. Bost, P0 Box 823, Jani, New Zealand.

Selective site directed antibody conjugation is of interest in preservation of binding site immunoreactivity with radiolabeling. Loss of specificity with labeling...
solution (8 mg/ml) in 0.1M bicarbonate buffer, pH 8.2, and solid cyclic DTPA anhydride (MoAb to DTPA ratio 1:1, 1:10, 1:20) were incubated for 60 minutes at 24 C. Conjugated products were separated on a Sephadex G-50 column and the protein fraction was then mixed with equal volumes of In-111 Acetate (1.0 mCi/mg) at a final pH of 5.5 for 30 minutes at room temperature. Radiochemical purity of each preparation was determined by ITLC Silia Gel chromatography.

Immunoactivity was measured by comparing the binding of DTPA conjugated MoAb and native MoAb to five serial dilutions of T-8402 lymphocyte cells*. Binding to DTPA MoAb was not significantly altered by preincubation with T-8402 at 0-6 hours in contrast to In-111 labeling efficiency was 30-35%. Ratios of 1:10 yielded 80% immunoreactivity with 90-95% labeling efficiency. Ratios of 1:20 also yielded 80% immunoreactivity with 90-95% labeling efficiency. Our results indicate that the MoAb can be conjugated with DTPA at a molar ratio of 1:20 without significantly altering the immunoreactivity. The final specific activity of In-111-DTPA-MoAb-T-101 averaged 1 uCi/ug protein with greater than 80% retained immunoreactivity. These results are ideal for an immunooscintigraphic system.

*Hybritech, Inc., San Diego, CA.

No. 675


The attachment of bifunctional chelators to murine monoclonal antibodies (MoAb) requires chemical modifications that may result in alteration of their biological behavior. The biochemical, immunological, and biological characteristics of In-111 labeled B6.2 and B72.3 were compared to the appropriate radiiodinated MoAb's following either reaction with the cyclic dihydricride of DTPA (cDTPA) (1-3 mg/ml of MoAb/10-fold molar excess of cDTPA) or periodate oxidation (10 mM) of the carbohydrate moieties of the MoAb's and reaction with a bis(1,6-hexanediamine)DTPA derivative (dDTPA). Reaction of MoAb's with cDTPA versus dDTPA gave differing forms of crosslinking and aggregation as measured on reducing and non-reducing SDS-PAGE as well as size-exclusion HPLC. Immunoreactivities of the radioliodinated MoAb's with either type of DTPA modification were comparable. Biodynamics of both antibodies with 1-125 unmodified MoAb's, In-111-cDTPA-MoAb's, and In-111-dDTPA-MoAb's were done in normal CD1 mice. At 1-6 hours both forms of labeled MoAb's distributed to the various organs and cleared from the blood at similar rates. However, at 24 hours significant differences were seen in blood clearance (In-111-cDTPA-MoAb > In-111-dDTPA-MoAb > 1-125-MoAb) and kidney (In-111-cDTPA-MoAb > In-111-dDTPA-MoAb > 1-125-MoAb). Thus, different chemical methods of attachment of bifunctional chelators may provide for a means of selection of the biological distribution to the non-target organs to suit the application.

No. 676

PREPARATION AND CHARACTERIZATION OF BIFUNCTIONAL ANTIBODIES WITH REACTIVITY TO CARCINOEMBRYONIC ANTIGEN AND INDIUM BENZYL EDTA. C.-H. Chang, C. N. Ahlem, B. Wolfert, S. M. Hochschwender, R. Jue, J. M. Frinkove, D. J. Carlo. Hybritech Incorporated, San Diego, California. We report herein on two convenient methods for preparation of bifunctional antibodies (BFA) through chemical combination of two monoclonal antibodies (MoAb) Fab' fragments of differing reactivity.

MoAb with reactivity to indium benzyl EDTA (IBE) and carcinoembryonic antigen (CEA) have been previously described. Purified MoAb were digested with peptin to produce Fab(‘) fragments. The reaction mixture was purified by gel filtration prior to reduction to Fab’. After reduction, Fab’ were purified by gel filtration and held for further processing. BFA were prepared through recombination of two Fab’ using protocols which re-generate the disulfide link or, alternatively, join the two fragments through a bi-maleimide bridge. Reformation of a disulfide linked BFA was achieved through dithionitrobenzoic acid (DTNB) activation of Fab’, purification and re-reaction with the second Fab’, in 95% yield. An alternative disulfide stabilized linkage system was developed using bi-maleimide methyl ether (BMME). Substituting BMME for DTNB in the aforementioned protocol, a recombinant Fab’ was obtained in 50% yield.

Synthetic BFA titers were similar to those of a biologically produced BFA with the same specificities. The BFA system was designed for two step radioisotope delivery to tumors, bearing CEA.

No. 677

DESIGN OF THERAPEUTIC COPPER-67 LABELED MONOCLONAL ANTIBOIDS. S.V. Deshpande, S. D. DeNardo, C.F. Meares, M. Pol, M.J. McCall, G.L. DeNardo. U.C. Davis Medical Center, Sacramento, CA 95817. DOE Grant #DE FG03-84ER60233.

The development of radiopharmaceuticals from monoclonal antibodies has led to the selection of several radiometals as choice nuclides for diagnostics and therapy. Investigators have found radiometal labeled MoAb reached higher tumor levels than their radiodinated counterparts. However, a parallel increase in hepatic uptake needs to be reduced before these agents can reach their clinical potential. Cu^+, an optimum therapeutic radionuclide has been chelated into a plasma stable form to MoAb (Lym 1) with TETA. However, various linkages of TETA to Lym 1 have been explored to obtain a blood and tumor stable compound which could be degraded and excreted rapidly if taken up in hematopoietic or RE cells. We have conjugated TETA to Lym 1 by two methods. (1) 2-Iminothiolane (2IT) was used to link Lym 1 to p-bromoacetamidobenzyl TETA (BAT) by formation of a thioether link. (2) By using disuccinimidyldi carbonate (DSC) to conjugate BAT to Lym 1. These conjugates were labeled with Cu^67 and had immunoreactivity of more than 70%. Mouse biodistributions were performed with Cu^67-p-nitrobenzyl TETA as a control. The 2IT conjugate has a biological half life of 1 day and shows less organ uptake (liver:3-5% I.D./g) while DSC conjugate showed a biological half life of 4-5 days and high organ uptake (liver:7-9% I.D./g). This may be due to cleavage of thioether link in case of 2IT conjugate. Further studies are needed to prove if this type of linkage design will enhance tumor to nontumor ratio in imaging and therapy.
have used, radiolabeled MoAb was made available with almost full retention of the immunoreactivity and in vivo stability. Transplanted tumors in nude mice were clearly visualized with In-111, Ga-67 and Tc-99m labeled MoAb as well as with 1-131 labeled ones at 24 and 48 hours after the administration. Tumor-to-blood ratios were higher than that obtained by radiiodinated MoAb in spite of higher nonspecific uptake in the liver and kidney. Tumor was also seen even at 6 hours after the injection of Tc-99m labeled intact MoAb without significant radioactivity in the thyroid. These results provided a good basis for the clinical utility of In-111, Ga-67 and Tc-99m labeled anti-tumor monoclonal antibodies for the radioimmunoimaging.

No. 679

RADIOLOCALIZATION OF COLON CARCINOMA XENOGRAFTS IN NUDE MICE WITH IN-111 LABELED B72.3 USING SCN-Bz-DTPA AS LIGAND. J. Esteban, D. Colcher, D. Simpson, O. Gansow, R. Atcher, J. Schlom. Laboratory of Tumor Immunology and Biology, National Cancer Institute, NIH, Bethesda, MD.

B72.3 is a murine monoclonal antibody (IgG1) that reacts with a glycoprotein present in 85% of colon carcinomas, but is virtually absent in normal adult tissues. It has properties that make it more suitable for radiolocalization studies. However, the current methodology uses conjugates that are unstable in vivo and lead In-111 resulting in accumulation in the liver. We have, therefore, used a new chelating ligand, 1-(p-isothiocyanatobenzyl)-dicyanomethinepentaaacetic acid (SCN-Bz-DTPA), and compared it with the current methodologies, mixed (MA) and cyclic anhydrides (CA) of DTPA. Biodistribution studies performed in athymic mice injected with the SCN-Bz-DTPA chelate when compared with the other chelates. SCN-Bz-DTPA chelate could have utility for radiolocalization studies in patients if the uptake of label by normal liver, which could obscure possible metastases, is minimal as in the model system.

No. 680


We have developed methods to label antibodies with copper-67, a potentially useful medical radioisotope, using N-benzyl porphyrin chelating agents N-benzyl-5,10,15,20-tetraakis(4-carboxyphenyl) porphine and N-4-nitrobenzyl-5-(4-carboxyphenyl)-10,15,20-tri(4-sulfophenyl) porphine. Formation of an activated copper-67 labeled porphyrin with either 1,3-(3-dimethylaminopropyl) carbodiimide hydrochloride and N-hydroxsuccinimide or 1,1'-carbonyldimidazolide was successful in coupling an average of 2 to 4 porphyrins per antibody molecule, depending on the coupling method. The coupling reactions were optimized as a function of preactivation time, coupling time, coupling pH, and reagent concentrations. Sodium dodecylsulfate polyacrylamide gel electrophoresis was used as an analytical method to determine coupling yields. After removal of non-conjugated porphyrin by gel filtration, the porphyrin-antibody conjugates can be rapidly labeled by copper-67 chloride in aqueous solution. Studies of antigen binding capacities post-conjugation are in progress. Thus conjugation of N-benzyl porphyrins to antibodies followed by radiometalation is a feasible protocol to radiolabel antibodies with copper-67. (Research supported by U.S. Department of Energy and Office of Health and Environmental Research and NIH Grant CA 25427.)

No. 681


In this study we report the pharmacokinetics of bi-functional antibody (BFA) mediated delivery of In-111 benzyl EDTA (IBE) to nude mice bearing carcinoembryonic antigen (CEA) colon tumors (T). Disulfide-linked and disulfide stabilized BFA (F(ab')2) molecules were synthesized from mononuclear antibodies (Mab) with reactivity to CEA and IBE. BFA doses (14 μg) were injected 4, 24, 48, 72 and 96h before IBE and animals were sacrificed at 1, 2, 4 and 24h post administration. Maximum T IBE concentration was found at 1-2h post administration and 48-72h post Mab administration. IBE accumulation in T was greatest with stabilized BFA. T to blood (B) and muscle (M) ratios demonstrated the disulfide stabilized BFA was superior (T/B = 21.0, T/M = 88.5) to disulfide BFA at 24h. The radiation dose which remained at the T was found to be greatest for disulfide stabilized BFA 24h post IBE injection. The described BFA delivery system is the first antibody mediated delivery system which permits rapid localization of a radioisotope in tumor subsequent to antibody accumulation, with imaging being theoretically possible within 4h.

No. 682


For the application of radioimmunoimaging, Ga-67 labeled antibody have been prepared by using deferoxamine(DFO) as a bifunctional chelating agent. In the present study, we have used hCG as a model antigen, monoclonal antibody to hCG as a model antibody and three coupling reagents to the attachment of DFO to antibody; glutaraldehyde, N-succinimidyl 3-(2-pyridyldithio)propionate (SPDP) and succinimidyl 6-maleimidohexanoate (EMCS), introducing Schiff's base, disulphide bond and chloethere bond, respectively. The immunoreactivity of obtained radiolabels was determined with the solid-phase radioimmunoassay.

The coupling reagents greatly affected the in vitro properties and in vivo distribution of antibody as well as the immunoreactivity, radiochemical purity and in vivo stability were satisfactory. Different from the homocoupling reagent; glutaraldehyde, the formation of polymerized antibody was not detectable in case of heterocoupling reagents; EMCS or SPDP. The radiolabel with disulphide bond showed the fastest clearance from the circulation. However, the liver to blood and spleen to blood ratios of the radioactivity were the lowest when labeled antibody with thioether bond was injected, in spite of showing the similar blood clearance to antibody with Schiff's base. The radiolabel with thioether bond appeared most feasible for the in vivo use due to its low uptake in the liver and the in vivo stability. These coupling methods would be added to the antibody labeling with a positron emitter of Ga-68.
PREPARATION AND BIODISTRIBUTION OF POLYCHELATE-RADIOLABELLED MONOCLONAL ANTIBODIES. P. Shreve and R.L. Wahl. University of Michigan Medical Center, Ann Arbor, MI.

Chelate molecules covalently linked to monoclonal antibodies (MoAbs) provide a means of labeling antibodies with radioactive metals. Attempts to achieve high levels of specific activity by linking several chelates directly to the antibody at multiple sites may result in a loss of antibody immunoreactivity. We investigated the use of a separate polymeric chelate molecule linked to the antibody at a single site as an alternative means of labeling.

Deferoxamine, a siderophore which forms stable complexes with Ga-67 was linked to a polycarboxylate polymer (polyacrylic or polyglutamic) bearing a free thiol moiety. The resulting polymeric chelate molecule was then covalently linked to antibody at a single site by a heterobifunctional coupling agent. 5G6.4, a murine IgG2ak MoAb was labeled with Ga-67 using a small polychelate (8 chelates, 6K daltons) and a large polychelate (18 chelates, 13.5K daltons). Labeling was also conducted with In-111 DTPA and I-125.

Biodistribution in rats showed rapid hepatic and renal uptake of the MoAbs labeled with the large polychelate. MoAbs labeled with the small polychelate had organ distributions more comparable with that of In-111 DTPA. Hepatic and renal uptakes of the labeled antibodies was consistently lower than any of the metal chelate labeled antibodies. We conclude that small polymeric chelate molecules can be used to label MoAbs. This method of labeling may be useful in achieving increased levels of specific activity for imaging and therapeutic applications of MoAbs labeled with metallic radionuclides.


To develop new agents that selectively react with the -SH group(s) of the Fab' monomer of the anti-melanoma monoclonal antibody (MAA-MoAb)-763 and with In-111, excess Deferoxamine (DF) was reacted with succimidyl-4-(p-maleimidophenyl)butyrate (SMPB) or N-succinimidyl-3-(2-pyridydithio)propionate (SPDP) in 50 M Pi, pH 8.0, 50% acetonitrile at room temperature for 10 min., and then incubated at 37°C for 1 hr. with freshly prepared MAA-MoAb-763-Fab', pH 8.0. Remaining -SH groups were blocked with N-ethylmaleimide. The Fab'-bifunctional chelate conjugate was isolated by using Sephadex G-50 column chromatography, labeled with In-111, and then repurified on Sephadex G-50. Binding of the Ab to melanoma cells (Human Colo-38) and control cells (lymphoma) in tissue culture was evaluated and compared with Fab'-DTPA binding. While labeling of Fab' with DTPA resulted in complete loss of immunoreactivity, almost full immunoreactivity (>95%) was obtained with In-111-(DF-SMPB-Fab' and In-111-DF-SPDP-Fab' (n=3 per sample). Binding of the control MAA-MoAb-763-Fab' was found to be 100% and the control lymphoid cell line was less than 3%. These findings indicate that the use of bifunctional chelating agents that bind to the Ab at non-critical sites results in significantly improved immunoreactivity.


Development of a purification method for Fab fragments is important because the immunoreactivity of the fragment is very sensitive to chemical modifications. We have developed a simple and fast purification method using a High-Performance Hydroxyapatite (HPHT) chromatography equipped with a 0.8x1cm hydroxyapatite column. This report describes our evaluation of the HPHT chromatographic purification of Fab fragment of monoclonal antibody 96.5 (anti-melanoma p97). HPHT chromatography separated unmodified Fab, I-125-Fab (specific activity 1.3 mCi/mg) or Fab-DTPA (0.6 DTPA/Fab) into two peaks with retention times of 6 and 16 min respectively. The column was eluted with 0.12M phosphate buffer (pH 6.8) at a flow rate of 1 ml/min. The immunoreactivity of each peak from the I-125-Fab purification was determined by a direct cell binding assay (CBA) using FDM 32 skin melanoma cells. For peak 2, 85% of the activity bound to cells whereas for peak 1, 28% was capable of binding to cells. As assessed at 50% inhibition of tracer binding in a competitive CBA, peak 2 from the Fab-DTPA purification was 9 times more potent than peak 1 and also two times that of the unpurified (pre HPHT) Fab-DTPA. Peak 2 from Fab-DTPA and peak 2 from the purification of unmodified Fab had equal potencies. We conclude that HPHT chromatography can be utilized to purify conjugated or unmodified Fab into the higher immunoreactive fraction which has a potential advantage in tumor targeting.

RADIOPHARMACEUTICALS: GENERAL

No. 686

UPTAKE OF C-14-LABELED ALICYCIC α-AMINO ACIDS IN TRANSPLANTED PHEOCHROMOCYTOMAS. S.L. Byrd and J.E. Crook, Medical and Health Sciences Division, Oak Ridge Associated Universities, Oak Ridge, TN.

This study was directed at finding a suitable scanning agent for physiologic studies of pheochromocytomas using positron emission tomography (PET). The biodistributions of C-14-carboxyl-labeled 1-aminocyclopentaneacrylic acid (ACPC) and two of its analogs, 1-aminocyclobutaneacrylic acid (ACBC) and 1-aminocyclohexanecarboxylic acid (ACAC), were studied in male New England Deaconess Hospital (NEDH) rats bearing NRC-259 transplanted pheochromocytomas. Tissue uptake was studied at 30 min post-injection, which has been shown to be compatible with the short half life of C-14. The tissue distribution was reasonably uniform with a few exceptions. Uptake in the tumor was relatively high (1.82 percent per gram for ACBC, 1.36 for ACPC, and 1.64 for ACAC). With all three compounds the tumor-to-tissue ratio was above 2:1 for all tissues except the pancreas. The blood had less than 5% of the injected dose remaining at sacrifice and had the lowest tissue concentration of the twelve tissues studied. All three compounds have been labeled with 131I. However, only ACBC and ACPC have been used successfully at our institution for clinical imaging studies of other types of tumors. Based on a comparison of the results of this study with the uptake of these compounds in other tumors which have been scanned successfully using PET, it is felt that they show promise as scanning agents for pheochromocytomas in humans. (This research was supported by contract number DE-AC05-76OR0033 between the U.S. Department of Energy and Oak Ridge Associated Universities.)
The W-178/Ta-178 generator reported by Neirinckx has a number of unique virtues, including short-lived (9.3 min) low dose daughter, long-lived (22 days) relatively easily produced parent [Ta-181 (p,4n) W-178], high yield and compatibility with the multiwire gamma camera. However, the reported eluting solution of HCl and 0.1 hydrogen peroxide the breakthrough rises rapidly after elution of 25 to 35 column volumes, limiting the number of patient studies and requiring very careful breakthrough monitoring. Accordingly, we attempted to improve the generator’s performance by testing changes in eluting solution. With HCl concentration lowered to 0.03N, the onset of breakthrough did not occur until more than 200 column volumes were eluted, and was very gradual. The eluted activity had a sharp profile, with 98% eluted in .7 column volume. A yield of 30% was achieved at 20°C. A significant inverse relationship was seen between yield and temperature with yield rising to 60% at 5°C with no effect on column chromatography (elution profile), or breakthrough performance. Several units have been used in clinical studies for periods in excess of 30 days, with highly stable performance, Ta-178 yield of up to 120 mCi and breakthrough consistently below 0.002% of loaded W-178 activity. Thus, with these modifications the W-178/Ta-178 generator is a very practical, low cost clinical system, which provides high doses of Ta-178 for first pass radionuclide angiography with many potential benefits.

No. 688

GADOLINIUM-LAbeLED PHARMACEUTICALS AS POTENTIAL MRI CONTRAST AGENTS FOR THE LIVER AND BILIARY TRACT. A. Najafi, E. C. Amparo, N. Hutchison, R. F. Johnson Jr., University of Texas Medical Branch, Galveston, TX.

Three gadolinium-labeled compounds, potential MRI contrast agents for liver and biliary tract, were studied: 1) Gd-DTSTDA, 2) Gd-DTPA-Liposomes, and 3) Gd-DTPA dihexadecylamide. In each case, “Carrier Added” Gd with specific activity of 1.0 uCi/mg was used. Each labeled compound was injected into a rabbit and gamma camera scintiphotos were obtained. The rabbit was imaged in a 0.6T MRI system before and after injection. Pulse sequences were chosen that would yield TI-weighted images, allowing calculation of T1 relaxation times. Gd-DTSTDA proved unsatisfactory due to in vivo instability; this was confirmed in our rat biodistribution study. Gd-DTPA-Liposomes showed good uptake in the microcirculation system of the liver and spleen. Gd-DTPA dihexadecylamide showed very good uptake in the hepatocytes with subsequent excretion into the biliary tract. This compound showed very little uptake in the kidneys. Both Gd-DTPA-Liposomes and Gd-DTPA dihexadecylamide produced significant shortening of the T1 relaxation times of the liver and observable increase in intensity on the TI-weighted images. Gd-DTPA-Liposomes and Gd-DTPA dihexadecylamide show promise as potential MRI contrast agents for liver and biliary tract imaging.

No. 689

THE EFFECT OF SERUM CONCENTRATION ON THE LABELING EFFICIENCY OF INDIUM-111 CHLorATES. K. Ramberg, R. Connolly, R. Hanson, W. Baur, A. Callow and P. Kahn. Tufts-New England Medical Center, Northeastern University, Boston, MA.

The purpose of this study was to determine the effect of serum concentration on the labeling efficiencies of In-111-oxyine (In-ox), In-111-tropolone (In-trop), and In-111-mercaptopyrindine-n-oxide (In-merc). Bovine endothelialial cells in monolayer were used as the cell model. The cells were grown to confluence in 24 well plates with media (DME) and 10% fetal bovine serum. The media with serum was removed and the cells rinsed once with serum-free DME. DME with 0, 2.5, 5 or 10% calf serum was added to the cells. The cells were then incubated at room temperature for 30 minutes with In-ox, In-trop, or In-merc. The media was removed and the cells harvested with trypsin and assayed for radioactivity.

Results are shown below:

<table>
<thead>
<tr>
<th>Serum</th>
<th>In-ox</th>
<th>In-trop</th>
<th>In-merc</th>
</tr>
</thead>
<tbody>
<tr>
<td>0%</td>
<td>61.7 ± 0.72</td>
<td>41.0 ± 1.14</td>
<td>66.6 ± 0.87</td>
</tr>
<tr>
<td>2.5%</td>
<td>34.2 ± 0.68</td>
<td>4.9 ± 0.41</td>
<td>6.2 ± 0.24</td>
</tr>
<tr>
<td>5.0%</td>
<td>25.5 ± 0.58</td>
<td>3.3 ± 0.25</td>
<td>4.7 ± 0.14</td>
</tr>
<tr>
<td>10%</td>
<td>14.4 ± 0.70</td>
<td>2.0 ± 0.11</td>
<td>2.5 ± 0.12</td>
</tr>
</tbody>
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In this model the addition of serum significantly decreased the labeling efficiency of all three chelates with In-ox the least affected.

No. 690


Glucose-insulin treatment is known to delay overall cardiac free fatty acid (FFA) oxidation. In this study we compared the effect of this metabolic intervention on the relative oxidation of IP and PA in isolated LADNERK-Prefused rat hearts. In total 6 hearts were perfused with an oxygenated Krebs-Henseleit buffer (11 mCi glucose, 0.1 IE/ml short acting bovine insulin) at a flow rate of 10 ml/min. An IP/PA mixture, complexed to 2.5% bovine serum albumin, was injected into the aortic inflow. The production rates of (C-14)CO2 and (I-123) hydrophilic metabolites (primarily (l-123)benzoic acid) were determined in serial samples of the effluents over 15 min. (C-14)CO2 production reached a rapid peak at 3-4 mln p.i. and then declined exponentially. In contrast, (I-123) hydrophobic metabolites showed a similar initial clearance up to 5 min r.i.p., however, a second rise at a plateau-phase was observed until about 8 min p.i. Final slopes of both curves were similar. Since IP is known to be converted to phenylazal-C-1 and G-fragment carboxylates, these data suggest re-utilization of IP metabolites either for FFA-re-synthesis, and/or more probably in triglyceride synthesis due to glucose-insulin mediated increased availability of alpha-glycerol-phosphate. Metabolic intervention thus may have differential effects on cardiac turnover of aliphatic and aromatic FFA. In addition, the data suggest a stringent standardization of dietary state in clinical applications of IP.

ORNL is operated by the U.S. Department of Energy under contract DE-AC05-840R21400 with Martin Marietta Energy Systems, Inc.

No. 691


Bleomycin (BLM) has undergone extensive investigation both as a cancer chemotherapeutic agent and as a carrier for radionuclides for imaging. In this study we investigated the preparation, chromatographic evaluation and biodistribution in mice of ruthenium (Ru-103, Ru-97)-BLM and compared it with Co-57-BLM and Cu-67-BLM. Ru-103-BLM was obtained in high labeling yields (>60%) using the following conditions: 1.8 mg BLM, 8-20 mmol SnCl2, pH 6-8, 3 hr reaction. Purification by CM-25 Sephadex column (silica gel) using 10% (w/v) ammonium formate/methanol (1:1) gave good separations with RF values of 0.73, 0.68, 0.60, and 0.25, corresponding to various labeled BLM species. HPLC analysis of Co-57-BLM and Cu-67-BLM using

Tumour affinity of radiolanthanides prompted investigation of Sm-153 uptake in melanoma. (SAMURAM-153) (T4 46.7h, 103 keV Y) was prepared from enriched Sm-152 in the AAEC reactor. Sm-153 chloride, Sm-153 citrate, Sm-153 DTPA, Sm-153 HIDA, Sm-153 PIP (pyridoxal isonicotinyl hydrazone) and Sm-153 PBH (pyridoxal benzoyl hydrazone) were used. All the tumour uptake at 1, 5, 10, 24 and 48 h in both melanotic (AMEL) and amelanotic (AMEL3) B16 melanomas of C57 black mice was compared with that of Ga-67 citrate and Se-75 methionine given IV to 5 animals for each time period. The tumour uptake was higher than that of the other agents, which were used as controls, and was higher than that of Ga-67 citrate at all time periods.

To continue at 70°C for 3 or 24 hours; and then non-radioactive I-127/NaI was added to the above mixture at 24h. For analysis at each passaging assured comparability of the degree of melanogesis and absence of necrosis.

No. 695

RADIOIODOINATION OF 3-QUINUCLIDINYL BENZILATE USING NO-CARRIER-ADDED CONCENTRATION OF I-125/NaI. K.S. Lee, R.E. Gibson, W.C. Eckelman and R.C. Reba. The George Washington University Medical Center, Washington, DC.

3-Quinuclidinyl benzilate (QNB) is a potent muscarinic antagonist which binds to muscarinic acetylcholine receptors. A radioiodine labeled analogue of QNB is one of the ideal ligands - it can bind to these receptors specifically and may be useful for clinical diagnosis.

A simple method was developed to radioiodinate QNB using milligram or microgram amounts of QNB and thallium trifluoroacetate in trifluoroacetic acid followed by the addition of I-125/NaI, aluminum chloride, and I-127/NaI. Three reaction steps were involved: QNB was reacted with thallium trifluoroacetate at 60°C for 24 hours, then radioactive I-125/NaI and aluminum chloride were added to the reaction mixture and the reaction was allowed to continue at 70°C for 3 or 24 hours; and then non-radioactive I-127/NaI was added to the above mixture at 70°C for another hour. The optimal mole ratio of QNB:aluminum chloride:thallium trifluoroacetate was 2:2:1. The radiochemical yield of [3-125I]QNB (116%) for milligram amounts of QNB and 2±0.5% for microgram amounts of QNB and specific activity (8.4±2.7 Ci/m mole) were determined.

No. 696

N-ISOPROPYL p-[1-123I]-IDOAMPHETAMINE: A NO-CARRIER-ADDED SYNTHESIS VIA ORGANOBORANES. G.W. Kabalka, R.S. Varma, and Y. Gal. The University of Tennessee, Knoxville, TN.

N-isopropyl p-[1-123I]-idoamphetamine (I-123 IMP) has proven to be a valuable agent for cerebral blood flow measurements. I-123 IMP has also been utilized to evaluate pulmonary endothelial metabolism and enterohepatic absorption. The material is generally prepared via an iodine exchange reaction which can lead to difficult isolation problems when no-carrier-added sodium iodide is utilized. Organoboranes have proven to be useful intermediates for isotope incorporation [Kabalka, Act. Chem. Res., 17, 215 (1984)]. The borane reagents are unique because they can be prepared containing a variety of physiologically active functional groups. Thus it is often possible to prepare a radio-labeled agent, such as a fatty acid, via a sequence in which the radiolotope is incorporated in the final step. This minimizes synthesis time and maximizes yields. We have developed a synthesis of I-123 IMP via the reaction of the corresponding boronic acid with I-123 sodium iodide as supplied by Medi-Physics, Inc.
No. 696
A TRIGLYCERIDE ESTER OF P-IODOPENTANEOIC ACID AS A POTENTIAL LIVER IMAGING AGENT. S. Schwender, J. Weichert, M. Longino, M. Gross, and R. Counsell. The University of Michigan and VA Hospital, Ann Arbor, MI.

A triglyceride analog, glycerol-2-palmitoyl-1,3-di-15-(p-iodophenyl)pentadecanone (DPPG) was synthesized and radiolabeled for evaluation as a potential functional hepatic scintigraphic agent. This compound was administered in a TWEEN saline vehicle to female rats. At 5 min the liver showed accumulation of radioactivity of 7.0±4.0%dose/g (mean±sem, n=4), corresponding to 52±1.5%dose/organ. The hepatic activity gradually decreased until at 1 h 2.5±4%dose/g remained. DPPG is hydrolyzed to the free acid within 5 min as shown by gel electrophoresis (37±5.1% in the albumin fraction) and lipid extraction of the liver (55.8±3.4% remaining as the parent compound). Gamma camera scans were obtained on control rats (C) as well as rats pretreated with ethinyl estradiol (E), streptozotocin (S), and heparin (H). Animals were scanned up to 90 min post-injection. Following this TC-99m sulphur colloid was injected and an image acquired for comparison of liver uptake. C showed peak uptake at 15 min with clearance of the radioactivity from the liver apparent by 90 min. S, E, and H all showed more activity in the blood in comparison to C. C showed peak accumulation at 15 min with clearance of the radioactivity from the liver apparent by 90 min. S, E, and H all showed more activity in the blood in comparison to C. Activity was normalized to the measured uptake in the liver at 30 min.

No. 697
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Weichert, M. Longino, M. Gross, and R. Counsell. The

A potential liver imaging agent. S. Schwendner, J. Pretreated with ethinyl estradiol (E), streptozotocin (S), and heparin (H). Animals were scanned up to 90 min post-injection. Following this, TC-99m sulphur colloid was injected and an image acquired for comparison of liver uptake. C showed peak uptake at 15 min with clearance of the radioactivity from the liver apparent by 90 min. S, E, and H all showed more activity in the blood in comparison to C. Activity was normalized to the measured uptake in the liver at 30 min.

No. 698

High-purity iodine-123 has attracted considerable attention as the ideal radionuclide label for a variety of diagnostic agents including the brain-localizing L-iodoamphetamine (IMP) and HIPDM. The chemical nature of iodine has a significant effect on many radioiodination reactions, for example when using I-123 from different sources. In this study, HPLC methods have been developed for the isolation and characterization of many common inorganic as well as organic forms of iodine. Of the various solvent mixtures and reverse-phase columns (C8, C18, C18), evaluated, RP8 Lichrosorb columns and an eluting solution (pH 7) containing 0.05 M phosphate, 0.002 M NaH2PO4, and 10% acetonitrile provided the best separations. A procedure was also developed for determining the carrier iodine content of radiiodine solutions by monitoring UV absorption at 225 nm. The curve was linear for 0.01-10 μg iodide. Using well-characterized standards, HPLC retention factors were established for I(2,3), I(2,4), I(2,5), CH3I, and CH4I. A number of unidentified species were also separated using the above system. BLIP-produced (p,5n) I-123 consistently provided >95% I123 and almost no iodate. The iodination of IMP (using an exchange method) was more sensitive to iodate impurity, whereas the iodination of HIPDM was not. Labeling conditions and mechanisms can be better optimized from a knowledge of the composition of radiiodine solutions. The HPLC technique developed in this study allows a rapid separation of various iodine species with excellent resolution and appears superior to the routinely used TLC and paper chromatographic methods. (Research supported under U.S. Department of Energy Contract No. DE-AC02-76CH00016.)

No. 699

Benzodiazepines are known to bind to a specific binding site in brain. We have prepared and evaluated two radiiodinated benzodiazepines.

I-125 labeled 5-[2-(fluorophenyl)-2,3-dihydro-7-iodo-1-methyl-1H-1,4-benzodiazepine (I) and 5-[2-(fluorophenyl)-1,3-dihydro-7-iodo-1-methyl-2H-1,4-benzodiazepine-2-one (II) were prepared from the direct exchange of Na-125 with I and II in glacial acetic acid in the presence of CuSO4. In vivo distribution of I-125-I and I-125-II was determined in rats at 5 min and 2 hr after I.V. injection. The specific activity (SA) was varied from 0.4 Ci/mmol to 300 Ci/mmol. Both compounds were rapidly taken up by the brain: 1.5% dose/g of I and 6.8% dose/g of II at 5 min. The activity then cleared from the brain with time. Brain to blood ratios were >3 for I at 5 min to 2 hr and >2 for II at 5-10 min, decreasing to 0.8 at 30-60 min. No appreciable activity was found in the thyroid. A major fraction of both compounds appeared to be excreted through the hepatobiliary system. Similar brain uptake was observed for I-125-I with SA of 0.4 Ci/mmol and 300 Ci/mmol. High brain uptake and brain to blood ratio obtained with I-125-I indicated that radiiodinated compound I may be useful for brain imaging.

Monday, 3:30-6:00 Exhibit Hall
RADIOPHARMACEUTICAL: POSITRONS
No. 700
SYNTHESIS OF CI-I CARBOXYL-LABELLED DOPA. M.J. Adam, J.R. Grierson, T.J. Roth and J.D. Pate. UBC/TRIUMF Program on Positron Emission Tomography, University of British Columbia, Vancouver, Canada V6T 2A3.
C-11 labelled dopa has been prepared via the Strecker method in order to study the decarboxylation of dopa in patients suffering from movement disorders. The Strecker synthesis has previously been used to prepare a wide variety of amino acids labelled with C-11 [L.C. Washburn et al., Radio pharmaceuticals 11; Proc. of 2nd Int. Symp. Radiopharm., Seattle, WA, pp 767-777 (1979)] but was never applied to the synthesis of C-11 dopa. The only reported synthesis of C-11 dopa is via the carbonation of an lithio-derivitative of the precursor [J.M. Bolster et al., J.A.A.R. 34, 1650 (1983)].

The bisulphate addition complex of 3,4-dimethoxy-phenylacetylene is heated in a sealed bomb at 195°C with sodium carbonate, ammonium chloride and potassium cyanide for 5 min. The bomb was cooled, 1 mL of NaOH (6.25 M) added and the bomb heated again to 195°C for 5 min. The bomb was cooled, the contents were neutralized with 1 mL of H2PO4 (6.25 M), diluted with 20 mL H2O and passed through C-18 Sep Paks. The C-11 dimethoxydopa was eluted from the Sep Paks with 1 mL MeOH/H2O and the solution evaporated to dryness. HI was added and the mixture heated to 155°C for 5 min. The HI was evaporated and two portions of H2O (5 mL each) were added and successively evaporated. The residue was dissolved in phosphate buffer and filtered to give C-11 dopa in 60% radiochemical yield (decay corrected to EOB) in an overall synthesis time of ~1 h. The final product was >95% radiochemically and chemically pure.

**No. 701**


In a continuing effort to produce positron-emitting radioligands with the appropriate characteristics for PET studies of dopamine receptors, we have synthesized N-[3-[18F]fluoropropyl]spiroperidol (FPSP) and evaluated its specific distribution and metabolism in the baboon. Following i.v. administration, FPSP localized in those brain regions (striatum) known to contain high concentrations of dopamine receptors. Striatal accumulation of radioactivity was stereospecific, i.e., it was blocked by pretreatment with (+)-butaclamol but not by (-)-butaclamol. The absolute striatal uptake ([% dose per cm^2] was intermediate between that of [3H]-spiroperidol and [18F]-N-methyl spiroperidol. The peripheral metabolism of FPSP followed the same time course as other [18F]-labeled butyrophenones studied. Because 3-[18F]fluoropropanolic acid, a possible radiolabel of FPSP, would be converted rapidly in vivo to [18F]O, particular attention was paid to determine the effect, if any, of this metabolite on the uptake of FPSP by dopamine receptors in vivo. Whereas mouse studies indicated a significant accumulation of radioactivity, the brain radioactivity was >75% unchanged FPSP at 1 h after injection. PET baboon studies demonstrated that peripheral metabolism had little if any effect on the specific activity of brain distribution. The ratio of striatum to cerebellum radioactivities at 3 h after injection was 5.9, which is close to the corresponding ratio of 6.1 found for [18F]-N-methylspiroperidol. Research supported by DOE, OHER and NIH Grant NS-15380.

**No. 702**

**PURIFICATION OF REACTOR-PRODUCED FLUORINE-18 FLUORIDE USING HIGH PRESSURE ION CHROMATOGRAPHY.** J.M. Bennett, M.A. Channing, and R.D. Finn. National Institutes of Health, Nuclear Medicine Department, Bethesda, MD.

Reactor-produced 18F labeled fluoride is an important alternative for facilities which do not have access to a particle accelerator. Fluorine-18 can be prepared via a two-step nuclear reaction:

\[
{\text{L}}_{\text{n}}(\text{n},\alpha){\text{H}}_2 \quad \text{and} \quad {\text{O}}_{\text{n}}(\text{n},\alpha){\text{F}}_2
\]

In our experiments quartz tubes containing 0.4 g of 95.56% enriched 18LiCO have been irradiated for 2 hours at a thermal flux of 1.3 x 10^{14} \text{n cm}^{-2} \text{sec}^{-1} at the National Bureau of Standards Nuclear Reactor. Typically, 80% of fluorine-18 is produced concurrently with 40 \text{mCi} of 18\text{Li}. A method has been developed utilizing high performance ion chromatography (HPIC) to not only separate, but isolate and purify the fluorine-18 species as its tetramethylammonium salt. Potential sources of cationic radionuclidic contaminants have been identified, quantified, and monitored by analytical HPIC, while radionuclidic impurities have been determined using gamma spectroscopy and scintillation counting.

The reactivity of the final reagent fluoride was determined by monitoring its incorporation as fluorine-18 labeled 2-fluoro-2-deoxy-D-glucose upon reaction with methyl 4,6-O-benzylidene-2,3-cyclic sulfato-D-mannopyranoside.

**No. 703**


We have previously reported the synthesis and evaluation of Br-75 labelled SCH 23390 analog as a selective radioligand for the study of CNS dopamine D1 receptors (Eur. J. Pharmacol. 108:327, 1985). The time course of distribution of this drug in the primate brain was found by PET to be rapid which suggested to us that C-11 (t1/2 = 20 min) would be the ideal label for this radioligand. Here we report the preparation of C-11-SCH 23390 and its biodistribution in the mouse.

C-11-SCH 23390 was prepared by the reaction of its des-methyl analog in IMF with C-11-CH3I. Ten minute reaction at 40°C resulted into 60%-80% radiochemical yield based on C-11-CH3I. HPLC purification gave a product which was found by mass spectrometry to have identical fragmentation pattern as the authentic sample. Administration of C-11-SCH 23390 into several sets of mice and analysis of its whole body distribution showed that the critical organs are the liver, kidney, and the G.I. tract. The distribution of the drug in the mouse brain showed that striatal uptake to cerebellum ratio of 23 h postinjection. Moreover, the binding in the striatum was found to be saturable. In conclusion, these results show that C-11-SCH 23390 should be the radioligand of choice for PET studies of CNS dopamine D1 receptors.

**No. 704**

**THE SYNTHESIS OF NO-CARRIER-ADDED a-[11C]METHYLL-TRYPTOPHAN:** M. Dikic and T. Chaly, Brain Imaging Centre, Department of Neurology and Neurosurgery, Montreal Neurological Institute, McGill University, Montreal, Quebec, Canada.

The metabolic pathway of a-methyl-L-tryptophan (a-MTyr) and its influence on tryptophan metabolism was studied by Sourkes et al (Neuropharm. 11 (1972) 197) who found that a-MTyr follows the metabolic pathway of tryptophan. We report here the synthesis of a-[11C]MTyr, a potential tracer for the measurement of in vivo synthesis and turnover of the neurotransmitter serotonin. The starting material (I) prepared by reacting tryptophan methyl ester with a mixture of benzaldehyde and triethylamine at about -10°C. The resultant shift base (I) (1 mmol) was reacted with CH3Li (1 mmol) in THF. [18F]CH3I dissolved in THF was added to the reaction mixture kept in a dry ice-acetone bath. The mixture was then warmed, filtered, and the solvent evaporated under reduced pressure. The protecting group was removed by hydrolysis with 2M HCl for 3 min at 115°C (bath). After hydrolysis, the solution was extracted with ethyl ether. The aqueous layer...
No. 705
SYNTHESIS AND EVALUATION OF SOME [C-11]-4-ARYL PIPERAZINIUM SALTS AS MYOCARDIAL IMAGING AGENTS. D.R. Elmaleh, S. Padmanabhan, G.J. Boudreaux, H. Kizuka, E. Livni, M.A. Hassan, J. Cooney, R.N. Hanson and H.W. Straus, Massachusetts General Hospital, Boston, MA.

The purpose of this work was to synthesize and evaluate a series of [C-11]-substituted phenyl piperazinium salts as myocardial imaging agents. Three analogs were synthesized, [C-11]-1-methyl 1-(2-hydroxyethyl)-4-phenyl piperazinium iodide (IIa); [C-11]-1-methyl-1-(2-hydroxyethyl) -4-(2-methylphenyl)piperazinium iodide (IIb) and [C-11]-1-methyl-1-(2-hydroxyethyl)-4-(4-iodophenyl)piperazinium iodide (IIc). The compounds were prepared by the reaction of [C-11]-methyl iodide and the precursor secondary amines. Their radiochemical purity (>99%) was ascertained by HPLC. Biodistribution studies were performed at various time intervals (5,30,60 minutes) following intravenous administration of the compounds IIa-IIc. Two and three dimensional images were obtained in dogs following the i.v. injection of (IIa) (3-5 microliters).

In rats the concentration of (IIa-IIc) in the heart varied from 3 to 4 at 5 minutes. For IIc, the concentration in the heart (dose/gram) remained essentially the same between 5 and 30 minutes (3.44 and 3.25 respectively). Ratios (% dose/gram) of target to non-target tissue (blood) were high in rats. Imaging studies of the dog clearly demonstrated activity retention in the myocardium for over 30 minutes. IIc and (IIa-125) piperazinium salt were compared for their biodistribution in rats.

These results suggest that some of these agents could be useful as tracers for myocardial imaging studies.

No. 706

Corticosteroids exert a variety of physiological, biochemical and behavioral effects, modulate homeostatic mechanisms and, in high doses, exhibit major anti-inflammatory, anti-neoplastic and anti-edema potency. Because corticosteroid ligands bind specifically to cortisol and subcoronal receptors, undertook the synthesis of high specific activity F-18-labeled steroids to study regional brain uptake and disposition. DFP was synthesized in 2-26 radiochemical yield (100 min EOB) from [1-13C]tranylcypromine and NCA precursor in dry dimethylformamide (200 uL). The fraction containing C-11 was isolated, peptide and deamination by MAO and parahydroxylation. As part of the structure-activity relationship studies, we have prepared the N-[C-11]-methyl analog of a potent MAO inhibitor trans-2-phenylcyclopropylamine (tranylcypromine) and have studied its tissue distribution in rats. C-11-tranylcypromine (C-11-TC) was prepared from tranylcypromine and C-11-labeled methyl iodide in DNP, followed by purification on HPLC. Uptake of C-11-TC in the brain was 1.25, 0.99 and 0.94 of injected dose per gram at 5, 30 and 60 minutes, respectively, while that of C-11-NMCP was 2.70, 2.67 and 2.67, respectively. Brain-to-blood ratios of C-11-TC were approximately one-third that of C-11-NMCP. The results of the preliminary biodistribution study suggests that C-11-NMCP is superior to C-11-TC as a brain blood flow agent. C-11-TC, however, would be a potential MAO indicator in the brain.

No. 707
BIO-DISTRIBUTION OF [11C]TRANYLCYPROMINE IN RATS: A POTENTIAL BLOOD FLOW AGENT AND MAO INDICATOR IN THE BRAIN. S. Padmanabhan, H. Kizuka and D.R. Elmaleh, Massachusetts General Hospital, Department of Radiology, Boston, MA 02114.

We have recently synthesized and evaluated a number of radiolabeled 3,4-dimethylphenethylamine analogs (phenetidines) as potential brain blood flow agents. In particular, N-[C-11]-methylchlophenetidine (C-11-NMCP) was found to exhibit favorable properties for PET studies; high brain retention and prolonged retention of radioactivity. A major advantage of using p-halo substituted phenetidine analogs is the high level of unchanged compounds in the brain and blood, due to blockage of some metabolic pathways including deamination by MAO and parahydroxylation. As part of the structure-activity relationship studies, we have prepared the N-[C-11]-methyl analog of a potent MAO inhibitor trans-2-phenylcyclopropylamine (tranylcypromine) and have studied its tissue distribution in rats. C-11-tranylcypromine (C-11-TC) was prepared from tranylcypromine and C-11-labeled methyl iodide in DNP, followed by purification on HPLC. Uptake of C-11-TC in the brain was 1.25, 0.99 and 0.94 of injected dose per gram at 5, 30 and 60 minutes, respectively, while that of C-11-NMCP was 2.70, 2.67 and 2.67, respectively. Brain-to-blood ratios of C-11-TC were approximately one-third that of C-11-NMCP. The results of the prelimin ary biodistribution study suggests that C-11-NMCP is superior to C-11-TC as a brain blood flow agent. C-11-TC, however, would be a potential MAO indicator in the brain.
L-Tyrosine plays an important role in the formation of catecholamines and melanin. L-Tyrosine labeled with N-13 may prove useful for in vivo studies of syndromes associated with aberrant aromatic amino acid metabolism. We synthesized L-[N-13] tyrosine from N-13 ammonia by coupling the glutamate dehydrogenase and glutamate oxaloacetate transaminase reactions, with p-hydroxyphenylpyruvate as the amino acceptor, utilizing enzymes immobilized on CNBr activated Sepharose. After incubation, the reaction mixture contained 5% tyrosine, 39% glutamate and 42% N-13 Tyrosine was separated from unreacted N-13 ammonia and glutamate on a Porapak Q column. A yield of 20 mCi of N-13 tyrosine (radiochemical purity >97%) was produced from 400 mCi N-13 ammonia 25 min EOB.

Organ uptake of N-13 tyrosine after retro-ocular injection in tumor-bearing mice was determined. Most of the activity was in liver and pancreas with additional activity in intestines, stomach and tumor. Tumor uptake from N-13 tyrosine was 5.0% at 60 minutes compared to 1.5% from N-13 ammonia, 2.7% from N-13 glutamate and 9.0% from N-13 valine. A rabbit bearing a VX2 tumor on each hind leg was also imaged. Activity was observed in the liver, pancreas, intestines, stomach, kidneys and tumor. Tissue distribution confirmed the results in mice except that the VX2 tumor did not take up as much N-13 activity as the mouse tumor possibly due to extensive necrosis.

Our studies demonstrate that N-13 tyrosine can be synthesized and has potential as a tumor localizing agent for studying in vivo metabolism.

No. 710


Previous work of this laboratory had defined the conditions under which Tc-IV could be reduced to a 'pure' Tc-IV and how one could avoid interfering photoaquations of that reduced technetium species. The method of choice in the preparation of lipophilic Tc-complexes is ligand exchange of the hexahalotechnetate in non-aqueous media. We have prepared a large variety of complexes, whose properties can be tailored to suit the desired lipophilicities, such as complexes having octanol/water partition coefficients ranging from 20 to 500+. Bidentate ligands yield 2 types of complexes: TcL2X and TcL3*, where L is the bidentate and X is a monodentate ligand. Tridentate ligands give TcL2 complexes, either charged or neutral. The complexes obtained were characterized by chromatography and electrophoresis, and could be easily purified by CHCl3/H2O partition. Yields of 90% or better have been obtained when using a suitable base to trap the HX produced on ligand exchange. Stability of the complexes under various solvolytic and aequous conditions have been studied. As an example, the Tc(ox)2Cl2 (where ox = 8-hydroxyquinolinol) and Tc(ox)2Cl2* have been obtained in 92% yields when...
using acetonitrile as the reaction solvent. Such complexes exhibited a stability of better than 95% over a 24 hr. period, when redissolved in an aqueous medium containing 5% ethanol.

**No. 713**


The preparation of Tc-99m dianimodithiol (Tc-99m-N$_2$S$_2$) complexes via the p-methoxybenzyl (MBz) protected thiol ligand (1) obviates several problems associated with direct use of the unprotected ligand. The protected thiol reacts with thionyl chloride oxidation and are more easily purified and handled. They also permit the synthesis of symmetrical and unsymmetrical N,N'-disubstituted N$_2$S$_2$ ligands which cannot be prepared directly from the macrocyclic disulfide, the usual precursor. Furthermore, they provide a means for attaching functional groups which do not tolerate typical disulfide reduction conditions.

In a typical reaction, thiol deprotection is carried out in situ by treating 1 with trifluoroacetic acid at 70°C for 10-30 minutes. The reaction mixture is then neutralized with phosphate buffer and filtered. Addition of Tc-99m pertechnetate and stannous chloride yields the expected Tc-99m N$_2$S$_2$ complex in >98% yield as determined by TLC and HPLC. Use of anisole as the reducing agent. Due to the nature of the reaction mixture in the human heart (Holman, et al). Past syntheses of transition metal TBI complexes in combination with a macrocyclic disulfide, the unipositive cationic complex 99mTc(TBI)$_6^{+}$ (TBI = tertiary butyl isonitrile) has proved to be an interesting molecule in preparing 99mTc complexes capable to cross the BBB. In the present study new polyamidinodithiol ligands of 99mTc were prepared and evaluated in mice comparatively to BAT safety. The compounds studied were of the following types:

- **HS-CRR CH$_2$NR'=(-CH)$_2$-NR' CH$_2$ CRR-SH (A)**
- **HS-CRR CH$_2$NR=CH$_2$-CH$_2$-CH$_2$-CH$_2$-CRR-SH (B)**

No. 714

**METAL ISONITRILE COMPOUNDS FOR THE CONVENIENT PREPARATION OF HEXAXIS (ISONITRILE) Tc(I) COMPLEXES.** A. Carpenter, Jr., L. Maheu, K. Linder, T. Tulip, J. Thompson*, M. Doshi, M. Mathew, M. Patz and V. Subramanyam*; E.I. DuPont de Nemours, NEN Medical Products, N. Billerica, MA and *Central Research and Development, Wilmington, DE.

The unipositive cationic complex 99mTc(TBI)$_6^{+}$ (TBI = tertiary butyl isonitrile) has been reported by Jones et al. to be a good candidate for the preparation of 99mTc-isonitrile complexes because of its high solubility in organic solvents. Optimal radiochemical yields were obtained from complexes of Cu(TBI)$_2$, Ag(TBI)$_2$, and Cu(TBI)$_2$. Little or no 99mTc(TBI)$_6^{+}$ was obtained when using other metal complexes as the source of isonitrile (e.g. Mn, Fe, Cu). Best yields of 99mTc-isonitrile were generally achieved at elevated temperatures (~100°C) with a stannous or sulfur compound as the reducing agent. Although many of the transition metal TBI complexes were found to be convenient stable, non-volatile sources of TBI, the best overall results were obtained with the bis-isonitrile, the most stable configuration. We undertook the preparation and evaluation of several transition metal TBI complexes in combination with a variety of reductants for making 99mTc(TBI)$_6^{+}$. Optimal radiochemical yields were obtained from complexes of Cu(TBI)$_2$, Ag(TBI)$_2$, and Cu(TBI)$_2$. Little or no 99mTc(TBI)$_6^{+}$ was obtained when using other metal complexes as the source of isonitrile. Best yields of 99mTc-isonitrile were generally achieved at elevated temperatures (~100°C) with a stannous or sulfur compound as the reducing agent. Although many of the transition metal TBI complexes were found to be convenient stable, non-volatile sources of TBI, the best overall results were obtained with the bis-isonitrile. The reaction of Tc-99m pertechnetate with each ligand in the presence of stannous ion produces two complexes, which were isolated by normal phase HPLC and reconstituted with saline for injection. Biodistributions at 5 min after injection showed that complexes IA, IIA and IIIA had the highest uptake of tracer in the brain. Biodistributions of these three complexes at times up to 2 hr showed that retention of complex IIIA was nearly twice that of IA and IIA after 30 min. These studies suggest that perturbation of the aminoethyl moiety produces significant differences in the biodistribution in mice. In particular, the addition of a methyl group to the 4-position of the piperidine ring increases the retention of tracer in the brain.


**No. 717**

**VALIDATION OF Tc-99m-d, 1-HEXAMETHYL PROPYLENE AMINE OXIME (Tc-99m-d, 1-HMPAO) AS A REGIONAL CEREBRAL BLOOD FLOW FLOW**

Tc-99m-d,1-hexamethylpropylene amine oxime (Tc-99m-d,1-HMPAO) was validated as a regional cerebral blood flow (rCBF) agent by comparing its cerebral uptake and retention to Sn-113 microspheres in rabbit brain.

Two groups of rabbits (4 per group) were studied. Sixteen discrete cerebral tissue samples were dissected from each animal. The samples included cortical grey matter, white matter, midbrain, diencepha­lon, pons, medulla, and spinal cord. The first group of rabbits sacrificed 5 min. post injection (p.i.), gave a Tc-99m-d,1-HMPAO/Sn-113m microsphere (Tc/Sn) ratio of 1.082 ± 0.300 (N = 60) over a range of rCBF values (28 - 134 ml/min/100g). The second group sacrificed one hour p.i. gave a Tc/Sn ratio of 1.024 ± 0.169 (N = 64) over an rCBF range of (24 - 202 ml/min/100g).

Linear regression analysis of the Tc/Sn ratio vs. rCBF for early and delay studies gave slopes of -0.0063 ± 0.0015 and -0.0015 ± 0.0005 respectively. This excellent correlation indicates that Tc-99m-d,1-HMPAO distribution reflects cerebral blood flow and should be readily amenable to study human cerebral blood flow disorders.

No. 718

EVALUATION OF ISCHEMIC DAMAGE OF GASTROCNEMIUS MUSCLES OF RICE BY Tc-99m PYROPHOSPHATE: A POSSIBLE MODEL FOR MYOCARDIAL ISCHEMIC INJURY. P. V. Kulwani, M. Bennett, R. W. Perry. The University of Texas Health Science Center at Dallas, Dallas, TX.

Among various models of myocardial infarction and ischemic damage, dog models with permanent or temporary ligation of coronary arteries are used extensively. However, studies with these models are involved, extensive, and expensive. Facilitated, percutaneous, or delayed surgery may be readily employed in these models of types of studies. Thus we are exploring the possibility of utilizing small animal models, viz., etc.

In this study one hind leg of the animal was tied with a suture string for various time intervals from 15 min to 5 days; then the tie was released. Tc-99m PPI (an indicator of muscle injury) took on a rapid initial uptake pattern. The serum and blood samples were also taken for counting. In a separate group of animals CX and JLM enzyme measurements were obtained to verify the muscular damage by the suture tying process. The ratio of radioactivity in unit area of damaged muscle to that in control muscle was calculated for each group of animals (8 in each group). The muscle sections were observed with a regular microscope for gross histology. Muscular damage was not apparent by gross histology or by enzyme measurements at early time intervals. The uptake of Tc-PPI in tied muscle was noticeable in animals tied only for 15 min and reperfused for 24 hrs.

The results parallel those reported for uptake of Tc-PPI in myocardial infarcts in dogs. Thus, our study shows that Tc-99m PPI distribution reflects cerebral blood flow and should be readily amenable to study human cerebral blood flow disorders.

No. 719

NEW Tc-99 COMPLEXES BASED ON N-LIGANDS. HJ. Kung, Y-Z. Guo, C-C. Yu, R.H. Mach, S.M.N. Egan, and M. Blau. Department of Nuclear Medicine, SUNY at Buffalo, NY.

In developing new Tc-99m labeled brain imaging agents, several lipid-soluble and neutral Tc-99 complexes based on the N₂S₂ ligand were prepared to determine the chemical structure and radiolabeling stability. The complexes can be prepared by reducing Tc-99m or Tc-99m pertechnetate with Sn(II) glucoheptonate or sodium dithionite in the presence of a ligand. The complexes were extracted with chloroform and purified further by silica gel column chromatography and reversed-phase HPLC. The structure of the complexes was determined by IR, NMR, elemental analysis and x-ray crystallography.

Crystallization. The structure of the complexes were determined by IR, NMR, elemental analysis and x-ray crystallography.
Poster Sessions

Proceedings of the 33rd Annual Meeting

No. 722


With the aim of optimizing the brain (B) uptake and retention of analogues of Tc-99m for SPECT, the ready availability of freeze-dried kits of dl-WPAO, and the minimal clearance, the Tc-99m- SQ 30217 is particularly advantageous with leukocytes, since tinned glucocaptonate is a superior tinning agent for high-yield Tc-99m labeling of RBC, leukocytes, and platelets. Results from these studies demonstrate that stannous glucocaptonate is a superior tinning agent for high-yield Tc-99m labeling of RBC, leukocytes, and platelets.

(Research supported under U.S. Department of Energy Contract No. DE-AC02-76CH00016.)

Monday, 3:30-6:00 Exhibit Hall

RENAI

No. 724

EVALUATION OF ACUTE TUBULAR NECROSIS BY FACTORIAL ANALYSIS OF RENAL PERFUSION IN KIDNEY TRANSPLANTS. J. Decourt, M. E. Meran, M. Koylo, L. Lippens, C. S. Marcus, Division of Nuclear Medicine/Harbor-UCLA Medical Center, Torrance, Ca.

The classical complications of allotransplant renal transplants are acute tubular necrosis (ATN), rejection and drug toxicity. We report on quantitation of ATN by performing factor analysis to the flow (FAP) component of Tc-99m DTPA renography. We studied 13 patients within 24 hrs. post cadaveric transplantation, assuming that they represented a relatively pure form of ATN. The control group was 9 patients with normal renography studied 2 months or more after transplantation. 20 mCi were injected intravenously and images acquired in anterior projection at 1 sec/frame. We limited the 4 factors FAP to the first 50 sec. after appearance of the bolus in the abdominal aorta. The area analyzed was transplant and corresponding iliac artery (IA). This provided 4 images and corresponding curves: background, IA, and 2 kidney images. The corresponding kidney curves were: one with a bell shape (K1), and the other with an ascending slope only (K2). K1 corresponds to parenchymal function in ATN* while the flow is well preserved. It demonstrates that quantitative information on clinical entities like ATN can be derived from the flow segment of the DTPA renogram.

*Italics

No. 725

COMPARISON OF TRIAMIDE MERCAPTIDE (N3S) COMPLEXES AS POTENTIAL RENAL TUBULAR FUNCTION AGENTS. D. Eshimi, A. Taylor, A. R. Fitzhsberg and S. Kastin, University of Utah Health Sciences Center, Salt Lake City, UT.

Tc-99m Mercaptoacetylglycylglycylglycline (Tc-99m MAG3), a triamide mercaptide (N3S) ligand, has been shown to have biological properties similar to I-131 o-iodohippuric acid (OIH). Substitutions were made at the terminal amino acid to determine the effect this would have on the biological behavior of the complex. Ten new N3S complexes were screened in mice with the most promising ones being Tc-99m mercaptoacetylglycylglycline-R (Tc-99m MAG2-R), where R was: Ala, Asn and Glu (both complexes).
These complexes were further evaluated in rats utilizing constant infusion clearances, extraction efficiencies and plasma binding. The results show:

<table>
<thead>
<tr>
<th>Compound</th>
<th>Plasma Extraction (%)</th>
<th>Binding Efficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tc-99m MAG3</td>
<td>85%</td>
<td>85%</td>
</tr>
<tr>
<td>Tc-99m MAG2-Ala</td>
<td>78%</td>
<td>85%</td>
</tr>
<tr>
<td>Tc-99m MAG2-Gln-A</td>
<td>96%</td>
<td>66%</td>
</tr>
<tr>
<td>Tc-99m MAG2-Gln-B</td>
<td>52%</td>
<td>56%</td>
</tr>
</tbody>
</table>

HPLC analysis of urine showed no metabolism for any of the complexes.

In summary, these four triamide mercaptide complexes all compared favorably to simultaneously administered 131I OIH in normal rodents and represent a new ligand class for Tc-99m which may provide a variety of complexes for the evaluation of renal tubular function.

No. 726

QUANTITATIVE ASSESSMENT OF THE DIURESIS RENOGRAF
K. Klettner, N. Nürnberger, R. Dudczak
1st Med. Dept. and Dept. of Urology, Univ. of Vienna

Recently there have been numerous critical reports concerning the ability of diuresis renography (DRG) to distinguish between nonobstructive and obstructive urinary tract dilatation. So far, mainly qualitative criteria were used for the interpretation of data, and this is why we tried to quantify the DRG. Forty patients with urinary tract dilatation were studied by DRG as well as by the invasive pyeloureterometry (PUM-Whitaker test). The DRG (0.5 mg frusemide/kgBW) was performed immediately following standard renography (15uCi 113mIn/0.9% NaCl) in hydrated patients (10 ml/kgBW). Upper urinary tract volume was estimated from i.v. urography in all patients and in some patients directly measured using the nephrostomy. Assuming an approximately sigmoidal shape for the renal curve of the frusemide application, the maximal elimination rate (Emax) of the tracer was determined. This value, closely related to the maximal urinary flow rate after frusemide, is calculated using the slope in the turning point of the curve. For grouping the pressure-flow values from the PUM, the scheme proposed by Whitaker was used.

Considering the Emax values alone, 33 patients could be attached to the same group as by the PUM. The remaining 7 patients were classified to adjacent groups by the different methods. In no case a complete mismatch (obstr. vs. nonobstr.) was obtained. A further improvement was gained in patients with considerable urinary tract dilatation (up to 250 ml) by normalizing the Emax values using the measured urinary tract volume. Using this quantification, the DRG seems to be suitable to save the invasive PUM in cases of extremely reduced renal function.

No. 727

THREE-PHASE EVALUATION OF SCINTIGRAPHIC FINDINGS IN TESTICULAR TORSION

To further evaluate the spectrum of findings in testicular torsion, Tc-99m pertechnetate flow studies and scintigrams of 16 surgically proven cases were reviewed. Three phases of each study were assessed: spermatocord flow (SCF) in the early dynamic phase, hemiscrotal flow (HSF) in the late dynamic phase, and hemiscrotal static (HSS) activity. All examinations were performed in a clinical setting of the acute hemiscrotum.

Five patients had viable testicles following detorsion and eight required orchectomy for non-viability. Three patients had torsion of the testicular appendages. Decreased flow to the involved hemiscrotum (decreased HSF) was present in only 1 of 13 patients with torsion of the spermatic cord. SCF was symmetric in all but one case, where it was increased to the side of a non-viable testicle. HSS activity was assymmetric (decreased) In all cases of viable torsion. In the non-viable group, HSS activity was symmetric in 2 cases, but increased in 6/8. Five of these six patients demonstrated a "halo sign" on the HSS images. Flow parameters were normal in all 3 cases of testicular appendage torsion. HSS images showed normal, decreased, or increased uptake, respectively.

We conclude that the finding of decreased flow by dynamic scintigraphy has low sensitivity and is therefore not a reliable marker of testicular torsion. Increased HSF and HSS activity and the "halo sign" are predictors of non-viability. Findings in torsion of the testicular appendages may be variable.

No. 728

RENAI FUNCTIONAL CHANGES AFTER CONVERTING ENZYME (CE) INHIBITION OR NITROPRUSSIDE (NP) IN HYPERTENSIVE RATS
H.B. Lee and M.D. Blaufax. Albert Einstein College of Medicine, Bronx, NY

Converting enzyme inhibition may enhance Nuclear Medicine diagnosis of Renovascular Hypertension (RVH). However, its effect on differernt models of RVH needs further study. RVH was induced in rats by clamping the renal artery (RA) and measuring GFR and RPF pre and post for NP. (The groups studied were: 1) 2K 1RA clamped for 1 week; 2) 2K 2RA clamped for 1 week; 3) 2K 2RA clamped for 1 week; 4) 1K 1RA clamped for 1 week; 5) SHR no RA clamped; 6) 2K 1RA clamped for 1 week; Group 6 was studied using NP to the lower mean arterial pressure (MAP) to a similar degree as CE.

% CHANGE AFTER ANTIHYPERTENSIVE DRUG

<table>
<thead>
<tr>
<th>GROUP</th>
<th>NP</th>
<th>RA</th>
<th>RA</th>
<th>RA</th>
<th>BP</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>-14.7*</td>
<td>-11.4*</td>
<td>0</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>-14.7*</td>
<td>-11.4*</td>
<td>0</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>-14.7*</td>
<td>-11.4*</td>
<td>0</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>-14.7*</td>
<td>-11.4*</td>
<td>0</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>-14.7*</td>
<td>-11.4*</td>
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<tr>
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<td>-14.7*</td>
<td>-11.4*</td>
<td>0</td>
<td>10</td>
<td></td>
</tr>
</tbody>
</table>

*p<0.05 N=unclamped RA C=cclamped RA Changes in renal function with CE were qualitatively similar in all the models with clamped kidneys. In SHR rats CP changes in RPF changes were related to vasodilatation. The effect on the unclamped kidney of rats with RVH was similar. NP changed the BP with little change in renal function. These data support a potential role for CE in enhancing the diagnosis of RVH.

No. 729

DYNAMICS OF RUBIDIUM-82 IN THE KIDNEYS: MEASUREMENT OF EXTRACTION FRACTION AND FLOW
N.A. Mullan, R. Eka, S. Marani and K.L. Gould. University of Texas Health Science Center, Houston, TX.

Rubidium-82, a potassium analog and generator produced positron emitter, has been investigated in a preliminary study as a tracer for measuring renal plasma flow. Seven acute dogs were studied with beta probes to understand the dynamics of Rubidium-82 in the kidneys. Four dogs had arterial, venous and ureter catheters placed to measure the extraction and excretion of Rb-82 in the kidneys. Tota arterial injections were also carried out to obtain the washout rate constants. Three dogs were studied for renal plasma blood flow by comparing Rubidium-82 obtained flows with microspheres obtained flows. Seven acute dogs with Rb-82 were carried out in two dogs and one patient. First pass extraction fraction for Rb-82 ranges from 80-95% with an average of 89%. Majority of the excretion of Rubidium is to the venous side rather than the ureter with the rate of washout being flow dependent. Flow measurements with Rubidium and microspheres correlated well with the average control
flow of 5.0 ml/min/gm measured by microspheres and 4.5 ml/min/gm of flow measured by Rb-82. Reduction in renal flow was observed by both techniques when arterial flow was reduced by constricting the renal artery. PET studies of the dogs were obtained every two seconds for the evaluation of the dynamics of the renal artery input function and renal uptake. Kidneys of a patient were also imaged with Rb-82 and demonstrate the feasibility of using this technique in man. Due to its short half-life and high extraction in the kidneys, the potential use of Rubidium-82 for renal plasma flow measurements with PET needs to be further investigated.

No. 732

RENAI BLOOD FLOW IN RENOVASCULAR HYPERTENSION ASSESSED BY PosITRON TOMOGRAPHY WITH RB-82: EFFECT OF CAPTOPRIL. M. Tamaki, C.A. Habito, R.M. Alpert, M. Harli-Kovach, J.A. Correia, M.A. Nederman, S. Dragoteke, H.W. Strauss. Massachusetts General Hospital, Boston, MA. Serial measurements of renal perfusion were recorded with positron emission tomography (PET) and Rubidium-82 (Rb-82) in a canine model of renovascular hypertension. Rb-82 calculated perfusion was compared to that determined by left atrial injection of microspheres. Renal perfusion images and microsphere injections were recorded in each of 7 dogs at: (a) control, (b) during renal artery stenosis and (c) stenosis with intravenous injection of captopril (1.2mg/kg). The tissue concentration of Rb-82 (Ci) in each PET transverse section of the kidney was determined and arterial blood activity of Rb-82 (Ca) measured by well counting during the equilibrium scan. Ci/Ca was correlated with microsphere renal blood flow according to a steady state single compartment model (t=0.90). Mean blood pressure was 115±15 (mean±sd) at control, significantly increased to 130±10 and went down to 98±15 after captopril infusion. Rb-82 determined flow and microsphere (g) flow in each step were:

<table>
<thead>
<tr>
<th></th>
<th>Stenotic Kidney</th>
<th>Contralateral Kidney</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>3.12±1.36</td>
<td>3.03±1.07</td>
</tr>
<tr>
<td>Captopril</td>
<td>0.99±0.65*</td>
<td>1.09±0.25*</td>
</tr>
</tbody>
</table>

These data indicate that captopril infusion resulted in a significant increase in flow to the contralateral kidney while flow to the stenosed kidney slightly (p=NS) decreased. These changes were associated with a decrease in blood pressure.

No. 730


The etiological diagnosis of renal allograft dysfunction although very important has not yet been resolved. Determination of the perfusion index (IP) improves the accuracy of DTPA studies, but not to optimum.

FA was performed on 87 DTPA studies of 35 RT patients, by the now standard routine using a 64 x 64 matrix, aquisition of 1 frame/1 sec for 40 sec and 1 frame 20 sec for 17 min. A diagnosis was established within 24 hrs of each DTPA study mostly by biopsy and in some cases by surgery or other modalities. The global, cortical and medullary PI was calculated by ROI drawing, as described earlier.

The FA was restricted to a square containing the kidney and blood vessels supplying it. In the first min an arterial and a parenchymal factor are found. In the second group of images (2-20 min p.i.) factors representing parenchymal washout, accumulation in the collecting system and bladder become evident. The weight of these factors, their curves and pictorial outlines are obtained without the need of empirical ROI drawing. In addition, unsuspected findings such as peri-graft inflammation, infarcts, intrarenal venous congestion and coronary obstruction were detected.

This method seems to provide new information not available otherwise. Its value in diagnosing rejection vs. immunosuppressive-induced nephropathy is still under investigation.

No. 731

TOTAL AND SPLIT RENAI FUNCTION IN PATIENTS WITH RENO-VASCULAR HYPERTENSION. A. Singh, G. Reams, K.W. Logan, R.A. Holmes, J. Bauer. University of Missouri and Harry S. Truman Memorial Hospital, Columbia, MO.

Quantitative split renal function studies were performed in 8 patients with renovascular hypertension on therapy with angiotension converting enzyme inhibitors (ACEI). Effective renal plasma (ERPF) was measured using I-131 hippuran and a 44 minute plasma sample. Glomerular filtration rate (GFR) was measured from the renal uptake (2-3 min post-injection) of Tc-99m DTPA. All individuals had their total ERPF estimated by p-anichinopurpurate (Cpah) and total GFR estimated by inulin (Cinulin) clearance techniques. The results are shown below.

<table>
<thead>
<tr>
<th></th>
<th>Total Function (ml/min/1.73m²)</th>
<th>Split Function (ml/min/1.73m²)</th>
<th>Ipsilental Contralateral P</th>
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</thead>
<tbody>
<tr>
<td>DTPA</td>
<td>674±10</td>
<td>31±7</td>
<td>3644 NS</td>
</tr>
<tr>
<td>Cinulin</td>
<td>741±3</td>
<td>164±33</td>
<td>212±20 &lt;0.05</td>
</tr>
<tr>
<td>Cpah</td>
<td>312±56</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Conclusions: 1) Total GFR by DTPA closely parallels the GFR by inulin clearance. 2) Total ERPF by Hippruman was higher than the total ERPF by Cpah. 3) Split function measuring ERPF may be more valuable than GFR measurements in patients with renovascular hypertension.

No. 732.2

SYNTHESIS AND EVALUATION OF RADIOLIOINATED 2-DEOXY-2-IODOVINO ALTROSE DERIVATIVES AS POTENTIAL BRAIN IMAGING AGENTS. M. M. Goodman, M. F. Knapp, Jr., and A. P. Callahan, Nuclear Medicine Group, Oak Ridge National Laboratory, Oak Ridge, Tennessee 37031

Single photon tomography of the brain using iodine-123-labeled glucose analogues may enable the in vivo study of transport and utilization of glucose in patients with pathological disorders. This study was undertaken to design and evaluate 2-deoxy-2-(E)-ido- vinyl-D-altrose derivatives as agents for monitoring glucose metabolism in the brain. The synthetic approach involved the scission of an anhydro sugar with a Grignard reagent. The starting material methyl 4,6-O-benzylidene-2-deoxy-2-ethyl-8-D-altropyranoside (II) was prepared by treating methyl 2,3-anhydro-4,6-O-benzylidene-8-D-altropyranoside (I) with ethynylmagnesium chloride. Hydrostannylation of (I) with (n-Bu)₂SnH gave the key intermediate, methyl 4,6-O-benzylidene-8-D-altropyranoside (III). I25I labeling of (III) followed by hydrolysis (40% CH₃SO3H) gave 3-deoxy-5-(E)-ido- vinyl-D-altrose (V) whereas hydrolysis (20% CF₃COOH) followed by treatment with pyridine-C₆H₅ gave methyl 2-deoxy-2-(E)-ido- vinyl-D-altrose (VII). 125I-labeled (V) and (VII) were evaluated in rats. Iodovinyl (VII) showed good brain uptake and a normal blood pool but poor brain uptake and no blood pool with the iododeoxy analogue (V).
Studies with DMIPP, the 3,3-dimethyl analogue of 15-(p-iiodophenyl)pentadecanolic acid (IPP), have shown the inhibitory effect of 3-dimethyl-substitution on \(\beta\)-oxidation. DMIPP shows high heart uptake in fasted rats and prolonged myocardial retention \(T_{1/2}\) IPP, 5-10 min; \(T_{1/2}\) DMIPP, 5-7 h). Lipid analyses of heart extracts show high levels of free fatty acid and slow conversion to triglycerides. A fatty acid CoA synthetase-CoA oxidase system demonstrates significant oxidation of straight-chain fatty acids (IPP, etc.), but no oxidation of DMIPP and the 3-monomethyl analogue (BNIPP). The prolonged myocardial retention of DMIPP thus appears to result from inhibition of \(\beta\)-oxidation. Studies in patients with \([1-123]DMIPP\) also demonstrate this unique "trapping" and high heart: blood ratios with excellent SPECT images. These results suggest that \([1-123]DMIPP\) may be useful for the evaluation of aberrations in regional fatty acid uptake that may occur in chronic hypertension and cardiomyopathies.

ORNL is operated by the U.S. Department of Energy under contract DE-AC05-840R21400 with Martin Marietta Energy Systems, Inc.

No. 732.4
SYNTHESIS AND HIGH MYOCARDIAL SPECIFICITY OF A NEW OLEIC ACID TYPE RADIOIODINATED TELLURIUM FATTY ACID. P.C. Srivastava, F.F. Knapp, Jr., and A.P. Callahan, Nuclear Medicine Group, Oak Ridge National Laboratory (ORNL), Oak Ridge, TN 37831, and M. Varma and G.W. Kabalka, Chemistry Dept., University of Tennessee, Knoxville, TN 37996-1600

A new tellurium fatty acid, \(9(10)-[\text{I}^{125}]\)iodo-5-tellur-9-hexadecenoic acid \(([\text{I}^{125}]\)); with a double bond between C-9 and C-10 similar to oleic acid and iodine stabilized at C-9(10), has been prepared and evaluated in rats. The boronic acid intermediate, \(\text{H}_2\text{C}-\text{CH}_2\text{C}-(\text{B}-(\text{OH})_2)-(\text{CH}_2)_2-\text{I}\) \((2)\) was prepared as a series of chemical manipulations. \(\text{Na}[\text{I}^{125}]-\text{chloramine-T iodination of } (2)\) gave a 4,5 mixture of \(\text{H}_2\text{C}-(\text{CH}_2)_3-\text{CH}-(\text{I}^{125})-(\text{CH}_2)_2-\text{I}\) which after condensation with \(\text{Na}-\text{Te}-(\text{CH}_2)_2\text{COO}-\text{H}_2\) followed by hydrolysis of the ethyl ester yielded \(\text{H}_2\text{C}-(\text{CH}_2)_3-\text{CH}-(\text{I}^{125})-(\text{CH}_2)_2-\text{COOH}\) \(([\text{I}^{125}]\)). The \([\text{I}^{125}]\) shows prolonged and high myocardial uptake (mean % dose/gm of 5 rats) and is a candidate for further evaluation with \(\text{I}^{123}\).

<table>
<thead>
<tr>
<th>(T_{1/2}) min</th>
<th>Heart</th>
<th>Blood</th>
<th>Liver</th>
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</thead>
<tbody>
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<td>14.23</td>
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<tr>
<td>30</td>
<td>5.76</td>
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<td>0.57</td>
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<tr>
<td>60</td>
<td>6.52</td>
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<td>9.24</td>
<td>0.50</td>
<td>28.78</td>
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ORNL research supported by the Office of Health and Environmental Research, U.S. Department of Energy, under contract DE-AC05-840R21400 with Martin Marietta Energy Systems, Inc.

No. 732.8
A RADIOIODINATED HALOPERIDOL ANALOGUE: CONVENIENT PREPARATION OF AN ATTRACTIVE BRAIN IMAGING AGENT. P.C. Srivastava and F.F. Knapp, Jr., Nuclear Medicine Group, Oak Ridge National Laboratory, Oak Ridge, TN 37831

\(^{[78]}\text{Br}\)Bromoperidol shows high brain uptake in rats (S. M. Morrell and G. L. Stocklin, J. Med. Chem., 28, 1319, 1985) and meperidines show interesting CNS properties suggesting the design and evaluation of similar \(\text{I}^{123}\)-analagues for brain imaging studies by SPECT. For preliminary studies the radiolinated haloperidol analogue, \(1-(\text{E}-[\text{I}^{123}]\)iodo-1-penten-5-yl)-4-(4-chlorophenyl)-4-hydroxypiperidine \((1)\) has been prepared (250 mCi/mmol, 70% yield) by condensing \(\text{E}-\text{I-borono-5-iodo-1-pentene with 4-(4-chlorophenyl)-4-hydroxypiperidine followed by } \text{Na}[\text{I}^{123}]-\text{chloramine-T iodination}\) of the borono intermediate, \(\text{I}^{125}-(1)\) shows good brain uptake (% dose/gm; range of 5 rats) and high brain: blood ratios (10, 5 min). The data suggest that similar \(\text{I}^{123}\)-labeled agents may be attractive for evaluation as potential brain imaging agents.

Studies with DMIPP, the 3,3-dimethyl analogue of 15-(p-iiodophenyl)pentadecanolic acid (IPP), have shown the inhibitory effect of 3-dimethyl-substitution on \(\beta\)-oxidation. DMIPP shows high heart uptake in fasted rats and prolonged myocardial retention \(T_{1/2}\) IPP, 5-10 min; \(T_{1/2}\) DMIPP, 5-7 h). Lipid analyses of heart extracts show high levels of free fatty acid and slow conversion to triglycerides. A fatty acid CoA synthetase-CoA oxidase system demonstrates significant oxidation of straight-chain fatty acids (IPP, etc.), but no oxidation of DMIPP and the 3-monomethyl analogue (BNIPP). The prolonged myocardial retention of DMIPP thus appears to result from inhibition of \(\beta\)-oxidation. Studies in patients with \([1-123]DMIPP\) also demonstrate this unique "trapping" and high heart: blood ratios with excellent SPECT images. These results suggest that \([1-123]DMIPP\) may be useful for the evaluation of aberrations in regional fatty acid uptake that may occur in chronic hypertension and cardiomyopathies.

ORNL is operated by the U.S. Department of Energy under contract DE-AC05-840R21400 with Martin Marietta Energy Systems, Inc.

No. 732.6

A new tellurium fatty acid, \(9(10)-[\text{I}^{125}]\)iodo-5-tellur-9-hexadecenoic acid \(([\text{I}^{125}]\)); with a double bond between C-9 and C-10 similar to oleic acid and iodine stabilized at C-9(10), has been prepared and evaluated in rats. The boronic acid intermediate, \(\text{H}_2\text{C}-\text{CH}_2\text{C}-(\text{B}-(\text{OH})_2)-(\text{CH}_2)_2-\text{I}\) \((2)\) was prepared as a series of chemical manipulations. \(\text{Na}[\text{I}^{125}]-\text{chloramine-T iodination of } (2)\) gave a 4,5 mixture of \(\text{H}_2\text{C}-(\text{CH}_2)_3-\text{CH}-(\text{I}^{125})-(\text{CH}_2)_2-\text{I}\) which after condensation with \(\text{Na}-\text{Te}-(\text{CH}_2)_2\text{COO}-\text{H}_2\) followed by hydrolysis of the ethyl ester yielded \(\text{H}_2\text{C}-(\text{CH}_2)_3-\text{CH}-(\text{I}^{125})-(\text{CH}_2)_2-\text{COOH}\) \(([\text{I}^{125}]\)). The \([\text{I}^{125}]\) shows prolonged and high myocardial uptake (mean % dose/gm of 5 rats) and is a candidate for further evaluation with \(\text{I}^{123}\).

<table>
<thead>
<tr>
<th>(T_{1/2}) min</th>
<th>Brain</th>
<th>Blood</th>
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<tr>
<td>30</td>
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<td>0.41</td>
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</tr>
<tr>
<td>60</td>
<td>0.38</td>
<td>0.70</td>
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Jass, JR, 881
Jaworski, S, 950
Jajoll, F, 982
Jaktenc, A, 994
BONE/Joint

No. 820

TECHNETIUM-99m MDP 4-H AND 24-H WHOLE BODY RETENTION MEASUREMENTS IN SKELETAL DISEASE. F.P. Castronovo, K.A. McKusick and H.W. Strauss. Massachusetts General Hospital, Boston, MA.

A simple technique for determining the whole body retention of Tc-99m labeled methylene diprophosphonate (MDP) has been utilized for the 4-h and 24-h time periods. Twenty eight adult patients (22 prostate cancer patients, osteoporosis) were administered 20 mCi (740 MBq) Tc-99m MDP and thereafter a qualitative scintigram was performed as well as whole body retention measurements at 4-h and 24-h. The prostate cancer patients all had positive bone scintigrams, and of this group, 7 were in relapse and 15 in remission on chemotherapy. All the osteoporotic patients had active disease.

Mean percent whole body retention values were significantly greater at 4h and 24h for the cancer patients in relapse relative to both the prostate cancer patients in remission and the osteoporotics: 4-h/24-h: 74.3/60.2, 57.5/33.5, and 48.0/30.3, respectively. The whole body retention values for relapse exhibited a significantly longer half time period. Again the cancer patients in relapse exhibited a significantly longer half time relative to those in remission and the osteoporotics (70.4 hr vs. 25.7 hr and 29.2 hr, respectively).

An additional index of skeletal pathology was developed by combining the 4-h/24-h values to calculate the $T_{1/2}$ for this time period. Again the cancer patients in relapse had significantly longer half times compared to both the prostate cancer patients in remission and the osteoporotics (70.4 hr vs. 25.7 hr and 29.2 hr, respectively).

The combination of 4-h and 24-h whole body retention values with the associated $T_{1/2}$ b has potential for further and classifying patients during the course of their skeletal disease.

No. 821

DEGRADATION BONE IMAGE QUALITY FROM TC-99M GENERATOR ELUATE CONTAMINANT(S). J.J. Coupal and W.J. Shih. Veterans Administration and University of Kentucky Medical Centers, Lexington, KY.

Beginning mid-November 1985, a rash of Tc-99m-oxidronate (Tc-99m-HMDP) bone images showing diffuse liver (and sometimes gallbladder) radioactivity was experienced throughout the United States. In 12 (including ours) of 13 complaints to radiopharmaceutical manufacturer B, the Tc-99m was derived from a generator of manufacturer A to label Sn-HMDP kits from manufacturer B. Since we encountered degraded images sporadically and unpredictably, we attempted to resolve the problem. In all cases, aluminum ion in generator eluate was less than 1 ug/ml. Miniaturized chromatography of affected Tc-99m-HMDP radiopharmaceuticals revealed 2.31% - 6.86% hydrolyzed reduced Tc-99m ("colloid") (normal <1.5%) and 3.06% - 10.02% free pertechnetate (normal <1%). However, since neither thyroid nor stomach was seen on total body or spot films, at least some of the measured free pertechnetate was a radiopharmaceutical species that migrates chromatographically like pertechnetate. Since findings suggest presence of unknown oxidant(s) in the generator eluate, we prospectively employed two saline eluates containing less than 5 ppm dissolved oxygen (LD0 saline) from manufacturer C to dilute pertechnetate eluate to 5.0 ml to make Tc-99m-HMDP. That has led to absence of liver and/or gallbladder radioactivity from most Tc-99m-HMDP preparations. Until the putative contaminant(s) can be identified and eliminated, we suggest employing LD0 saline routinely to prepare Tc-99m-HMDP bone agent.

No. 822


The value of DPA bone mineral density (BMD) for diagnosis of diseases such as osteoporosis and evaluation of treatment is necessary for the repeated measurements made during the evaluation of therapy. A large nuclear medicine department must therefore establish an effective quality control programme to maintain precision since repeat measurements, or even data acquisition and sequential analysis of the same study, may be performed by different technologists.

Bone mineral density in g/cm² was determined for the 2nd to 4th vertebrae using a commercially available DPA scanner (Lunar Radiation Corp) employing a Gd-153 1Ci source. All new technologists are initially required to analyze the same set of 10 studies. These 10 studies represent 5 different patient studies which are duplicated and ordered for analysis randomly. Analysis of the technologist with a correlation coefficient less than 0.98 for the duplicate pairs must re-analyse the data and repeat this until the desired intra-technologist precision is achieved. These data are then used to determine the inter-technologist precision, and new technologists are accepted only when comparison to each established technologist exceeds a correlation coefficient of 0.96. In order to determine that this quality control programme was successful, we scanned 20 patients twice, each repeat within a 2 hour period. Between the two scans, the patient walked around and was then reposisioned. Data collection and analysis were performed by the technologist on duty and no attempt was made to restrict one patient to the same technologist each time. Analysis of these data gave a correlation coefficient of 0.96 with a 95% confidence interval of 0.09g/cm². It should be stressed that repeat measurements for evaluation of reproducibility must be performed within a short period as possible. This is particularly true in patients scanned twice with an average interval of 12 and 8.6 year half-lives respectively. Spectra from...
the most recent source indicates that there are no short-lived contaminants with half-lives of about 30 days. The observed background count rates range from 3 to 20 cps in the 40-keV and 200-keV windows. We assumed a uniform density of the thickness of the overlying soft tissue thickness. Improper correction for "true" background produced a 50% decrease in the measured crossover fraction at a soft-tissue thickness of 25 cm.

The usual gadolinium sources used for bone mineral determinations contain high energy and long-lived contaminants and improper correction of their background radiation can produce large errors in the determinations of the count correction factors used in the analysis of bone mineral data.

CARDIOVASCULAR

No. 824
MEASUREMENT OF LEFT VENTRICULAR DIASTOLIC FUNCTION: EFFECT OF CYCLE-LENGTH WINDOWING C.C. Chen, J.E. Juni University of Michigan Medical Center, Ann Arbor, MI.

Variations in cardiac cycle length during ECG-gated blood pool studies cause errors in measurement of left ventricular diastolic function. This study evaluated the effects of different cycle-length windows on the measurement of peak filling rate (PFR) and time to PFR during forward gated blood pool studies. Additional errors contributed by malpositioning the center of cycle-length windows were studied. To model normal variations in cycle length, simulated time-activity curves with cycle lengths varied in a Gaussian distribution were used to create 25 sets of 300 cycles. With the variation of one standard deviation (SD) set at 20% of the mean cycle length (MCL), forward gating had the following results. With cycle-length windows centered around the MCL, rms error in PFR using a 5% window was 0.2% compared to 0.7% with a 20% window (P<0.001). 5% and 20% windows were more accurate than using no windowing which had rms error of 3.6% (P<0.001). 50% and 40% windows had 1.79% and 1.81% rms errors, respectively. Using a 5% window, setting the window center at 94% MCL versus 106% MCL produced rms errors of 4.7% versus 1.7% (P<0.001). 20% windows centered at 94% MCL and 106% MCL produced 4.5% and 1.6% rms errors, respectively (P<0.001). Similar results were obtained when cycle lengths were varied with one SD set at 10% MCL, as found in normal hearts. (1) Windowing significantly improved the accuracy of forward ECG-gated blood pool studies. (2) When the windows are centered at the true mean cycle length, the narrower the window widths the more accurate are the measurements; narrowing windows less than 20% MCL did little to increase accuracy. (3) Malpositioning the center of the window produced additional errors in measurement of PFR. Overestimating the MCL produced more accurate measurements than underestimating the MCL.

No. 825

This work-in-progress was undertaken to support our previously suggested new hypothesis concerning the dynamic features of discrete sub-aortic stenosis (DSS). 19 Patients suffering from DSS, diagnosed by echocardiography, heart catheterization and angiocardiography (Group A) were further evaluated by ECG-gated Tl-201 myocardial scintigraphy. The results were compared with 20 patients suffering from idiopathic hypertrophic sub-aortic stenosis (IHSS) (Group B) and 28 normal controls. The latter combination of "perfusion/wall motion" mismatch has already been suggested by us as a new specific diagnostic sign for IHSS and was demonstrated in 100% Group A and B patients and none in Group C. The recent DSS similar to IHSS produced by this work-in-progress, serves as additional proof in support of our previously expressed hypothesis that most of the cases of DSS involve dynamic features similar to those of hypertrophic obstructive cardiomyopathy. Accordingly, ECG-gated Tl-201 study seems to provide an additional sensitive method for the early diagnosis and evaluation of DSS patients, in a similar way to that of IHSS patients. The value of this method for the post surgical follow-up of DSS patients is now prospectively investigated.

No. 826

In heart failure, the function of cardiac sympathetic nerve endings is grossly disturbed. To assess the potential of sympathetic neuronal imaging for early detection of myocardial failure, scintigrams were acquired at 0.5, 2, 4, and 13 hours after intravenous administration of I-131 MIBG to ll normal dogs, 3 autotransplanted (denervated) dogs, 3 dogs with left (L) ventricular (LV) failure and 4 dogs with compensated LV hypertrophy (LHV) due to surgical arteriovenous shunt. Nine dogs were sacrificed at 4 1/4 hours for determinations of I-131 MIBG and norepinephrine (NE) content in L atrium, LV septum, LV free wall, liver, and spleen. There was a good correlation between I-131 MIBG and NE tissue content (r = 0.74, p<0.001). The best scintigraphic discriminator between the subsets was the 0.5 - 2 hour LV efflux rate (LVER) in % per hr:

<table>
<thead>
<tr>
<th>Normal(NL)</th>
<th>Denervated</th>
<th>LV failure</th>
<th>LHV</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVER&lt;35%</td>
<td>&gt;35%</td>
<td>&gt;35%</td>
<td>&lt;35%</td>
</tr>
</tbody>
</table>

Thus, the I-131 MIBG myocardial retention characteristics of LV failure dogs are similar to denervated dogs, whereas LVH dogs behave like NLs. Qualitatively, spiculated sequestration of I-131 MIBG was preserved in LV failure dogs, correctly reflecting the fact that sympathetic neuronal dysfunction in cardiac failure is not a generalized phenomenon. 1-123 MIBG scintigraphy should be explored as a means of early detection of myocardial failure in patients.

No. 827

Ischemia is a potent inhibitor of cardiac FFA utilization and degradation. IP SPECT has now been used in conjunction with sub-maximal exercise (SME) in 15 patients (pts) with CAD as follows: SME (6 min), IP injection and SPECT (I) followed by SME and SPECT (II) to increase regional differences of IP turnover. In 14/15 patients, segments with reduced IP uptake were observed after (I). Filling-in of these defects in (II) was observed in 11/15 pts. Infarctions showed clear uptake defects in both images (4 pts). Five pts without CAD (controls) showed homogeneous uptake and radioactivity release of 40-50%. Circumferential profiles showed inhomogeneous IP metabolic release in all 15 CAD pts. In one case, where a filling-in of the defect was clearly observed after the second SME with IP, Tl-201 imaging and ventriculography at the same...
level of SME did not define the extent of exercise-induced ischemia. IP-SPECT and repeated SME may be a useful tool for the definition of stress-induced early ischemic changes in CAD.

ORNL is operated by the U.S. Department of Energy under contract DE-AC05-84OR21400 with Martin Marietta Energy Systems, Inc.

No. 828

High dose doxorubicin (D) therapy has been reported to cause severe, irreversible and frequently fatal complications in patients with heart failure (CHF). To assess the efficacy of serial resting radionuclide angiography (RNA) with technetium-99m-pertechnetate using first pass or multiplated techniques for monitoring cardiotoxicity, we analyzed left ventricular ejection fraction (LVEF) and CHF incidence, severity and reversibility in 17 patients (pts) who had serial studies (1 RNA) and high dose (450 mg/m²) D. CHF developed in 34% (19 pts) of this group, and was mild in IS (7%), moderate in 17.1%, and severe in 5 (2%) pts. Of 17 pts with abnormal baseline LVEF (< 50%), CHF developed in 3 pts (18%). Despite identical baseline LVEF in both groups (62 ± 9%), pts developing CHF had a greater decline in LVEF (28 ± 14%) vs pts without CHF (14 ± 10%, P < 0.001) and received more D (624 ± 155 vs 545 ± 45 mg/m², P < 0.002). Routine treatment of CHF improved CHF in 30/34 pts (88%), including all 3 pts with abnormal baseline LVEF and CHF. No CHF death occurred in pts managed by RNA guidelines. Thus, in pts with normal or abnormal baseline LVEF monitored with serial resting RNA who receive high dose D: (1) CHF is associated with greater decline in LVEF and with higher total dosage; (2) the incidence, severity and reversibility of CHF are favorable. Serial resting RNA can be effectively utilized with appropriate guidelines to monitor high dose D therapy with either normal or abnormal baseline ventricular function.

No. 829

Current infarct seeking methods have conceptual limitations: Overestimation by TI-201 by imaging of residual ischemia, late imaging possibilities of Te-99m PYP, which also may accumulate in only partially necrotic tissue. To assess myocardial infarct size and location we applied In-111 labelled monoclonal antimyosin Fab (mAM) and Tc-99m PYP in 12 pts with recent myocardial infarction. Infarct size (IS) was estimated semiquantitatively from planar 3 views scans for both compounds and compared to TI-201 perfusion images in the same pts. mAM was injected within 18 hrs (as early as 8 hrs post M1 in 2 pts). PYP between 24 and 72 hrs. Target to non-target ratios for mAM were: infarct/control myocardium = 2.5 ± 1.3, infarct/liver, 5.4 ± 5.2. Location of mAM and PYP-defined infarcts was concordant in all 12 pts following successful reperfusion. 15 cases, IS correlated significantly (r=0.72, p < 0.01) but mAM-IS was systematically smaller than PYP-IS. TI-201 was equivocal in 2 smaller posterior MI's, picked up by both other tracers. IS by mAM and PYP both correlated with CK-maximum enzyme release (r=0.64, p < 0.01). In 2 pts following successful reperfusion IS was significantly smaller than area-of-risk out-lined by TI-201. We conclude that infarct imaging with Fab mAM provides reliable information regarding infarct size and location with the advantage of being more confined to the "true" area of necrosis. However, TI-201 as an additional reference tracer may facilitate assessment of the precise area-of-risk. Thus, this technique might contribute to the assessment of reversibly compromised myocardium.

No. 830
SERIAL RADIONUCLEIC ASSESSMENT OF SPECIFIC HEMODYNAMIC CONSEQUENCES OF SURGICALLY INDUCED LEFT TO RIGHT SHUNTS IN MATURING MINISWINE. R. Stratbucker, R. Kelly, K. Kilzer, E. Robertson, M. Calhufe, and L. Simonon; University of Nebraska Medical Center, Omaha, NE.

Comprehensive, non-invasive definition of the hemodynamic status of left to right (L/R) cardiac shunts in an animal model during maturation may yield useful criteria in the clinical management and/or intervention in affected children. Serial Nuclear Medicine (NM) measurements, i.e., pulmonary to systemic flow ratio (Qp:Qs), left & right ventricular ejection fractions (EF's), stroke counts (SC's), and ventricular time activity curves with slope parameters (SP's), were performed. An average of 5 studies each were done on 26 anesthetised miniswine. Animals were followed from infancy to full maturity at 9 months. Eight had surgically created neonatal L/R shunts and the balance were sham operated controls. One in three had parallel invasive studies. The NM measurement of Qp:Qs (gamma variate analysis) tracked the invasive measurement (Qs, saturation analysis) with a correlation coefficient of 0.75. Qp:Qs's ranged from 1.27 to 3.02 with a mean of 2.5 and remained surprisingly constant. Control Qp:Qs's averaged 1.11 (SEM 0.031). Heart rate dropped more for shunts (38%) than controls (20%) during the maturation period. RVEF nearly doubled in shunts (.35 to .57) but changed little in controls. LVEF changed little in either case. These findings may assist in assessment of the physiologic status of recirculating lesions in the young.

CDA
No. 831
HUMAN FACTORS ENGINEERING IN A NETWORKED NUCLEAR MEDICINE FACILITY. R. Brown GE, Feldt DA, Juni JE; University of Michigan Medical Center, University Hospital Ann Arbor, MI.

Implementation of Picture Archiving Computer Systems are hindered by a lack of perceived value by physicians and technologists. We are implementing a distributed system which is unique in providing 1) "instant" quality control during scan acquisition; 2) automatic flow of images to reading areas and image archives; 3) rapid personnel management and electronic communication.

Scans are acquired at 15 workstations on several floors all feeding into the networked system. Without leaving the patient, the technologist can electronically forward images to the scan reading room where a physician can determine the scan’s quality and request additional views if needed. Physicians and technologists are automatically located by the system for real-time communications. Images acquired during the day are automatically forwarded to high-resolution workstations for interpretation. Images are automatically archived onto magnetic disk (short-term) and/or optical disk (long-term). This allows rapid access to all images acquired from any camera at any time.

This network supports clinical image processing, distributing clinical patient reports through the hospital information network, receiving lab reports, maintenance of all clinical protocols, maintaining service logs on all equipment, word processing as well electronic mail and message services.
The usefulness of dynamic renal studies with Tc-99m DTPA for measurements of glomerular filtration (GFR) is limited by underlying spatially inhomogeneous nonrenal activity, or 'background'. A new method is proposed to correct for the major inhomogeneities while grouping pixels to minimize statistical fluctuations. Successive 'annuli' one pixel wide are constructed inwards and outwards from the renal ROI boundary, and divided into 3 sectors for the liver (or spleen), the lower lateral renal boundary, and the lower medial boundary. In each sector, the outer annular arcs establish a background count density and a radial count density gradient, for biguadratic interpolation across the inner arcs. This method was compared in 10 consecutive studies to the older technique. This new method provides an accurate starting point for improved measurements of glomerular function from radionuclide renal studies.
We studied rat MTC tissue culture incubated for 24 hours in either 1 (RIE-1), and mouse colon cancer (MC-26) cells in 0.5, 1 Pixel. Then ROIs were placed over the two areas using two different filters (Ramp-Hanning, Butterworth), and three different cut-off frequencies (0.25, 0.5, 1 Pixel). Then ROIs were placed over the two areas with different radionuclide concentrations. The mean ROI values were transformed, and compared to corresponding logarithms for the radionuclide concentrations. We were able to demonstrate a high correlation between the transformed mean ROI values, and the radionuclide concentrations (r=0.9929). Furthermore, scatter correction was applied to the cross sections using the double energy method of Jaszczak et al. Scatter correction did not improve the correlation coefficient (r=0.9831) or reduce the standard deviation, but reduced the offset error. The non-scatter corrected SPECT cross sections are reliable for determining low and high radionuclide concentrations. The Butterworth filter with a cut-off frequency of 0.5 gave best results.

DOISMETRY

No. 837

EVALUATION OF EXTERNAL MONITORING VS. URINE ASSAY FOR DETERMINING POST-THERAPY 1-131 RETENTION. J.A. Ponto, L.L.B. Ponto, and J.A. Bricker. University of Iowa, Iowa City, IA.

External exposure-rate monitoring with energy-compensated (comp) and uncompensated (uncomp) probe detectors was compared with the traditional urine assay method for the determination of 1-131 body retention following thyroid cancer treatment. Preliminary theoretical calculations and modified isoresonance measurements indicated that exposure-rate monitoring should be performed at a minimum distance of 105 cm from the midpoint of the patient's torso. Body retention in each of 17 patients with thyroid cancer treated with 66-208 mCi 1-131 was periodically determined using the urine assay method until body retention fell below 30 mCi (total number of determinations = 25). Determination of body retention using external monitoring with both comp and uncomp probes was performed by comparing exposure-rates at the time of administration and at the time of subsequent urine assay. Linear regressions between body retention determined from urine assay and from comp and uncomp probe measurements were: urine = 0.77 + 0.961 comp (r² = 0.812) and urine = 4.73 + 0.672 uncomp (r² = 0.747). Predictive distributions fit to this data indicate that body retention determined by external monitoring with comp and uncomp probes must be less than 20 mCi and 16 mCi, respectively, to be 95% confident that body retention determined by urine assay is less than 30 mCi. Advantages of external monitoring methods include simplicity and low exposure to hospital personnel. A comp probe is preferred because its uniformity in response to primary and scattered photons provides greater accuracy.

ENDOCRINE

No. 838

IN VITRO UPTAKE OF 1-131 MIBG BY MEDULLARY CELL CARCINOMA OF THE THYROID. G.J. Poston, E. James, H.D. Fawcett, C.M. Townsend, J.C. Thompson, M.L. Musynowitc, University of Texas Medical Branch, Galveston, TX.

Controversy exists as to whether or not medullary thyroid cancer (MTC) takes up 1-131 metaiodobenzylguanidine (MIBG). We studied rat MTC (6-23), rat pheochromocytoma (PC-12), rat small bowel (RIE-1), and mouse colon cancer (MC-26) cells in tissue culture incubated for 24 hours in either 1 microcurie of 1-131 MIBG or 1 microcurie of 1-131 NaI. After determination of culture medium and washing of cells, retained radioactivity of the cells was measured. Results are expressed as mean counts per million cells ± S.D. n=6 for each group.

GASTROENTEROLOGY

No. 839

ASSESSMENT OF LIVER PRESERVATION BY 31P NMR: EFFECT OF ISONIAZID, ANOXIA AND REPERFUSION. Richard Lee, ME Cloone, A Lanir, P Kasulis. Department of Radiology, New England Deaconess Hospital, and Harvard Medical School, Boston.

Human liver transplantation is a major advance in medical science, but its application is hampered by limited preservation techniques for the donor liver. We hypothesized that donor livers could be preserved longer if the liver energy charge could be maintained. ATP decay, inorganic phosphate appearance and phosphate chemical shift in mouse livers were studied by 31P NMR spectroscopy. Cold flush followed by cold preservation in Collins solution resulted in slower ATP decay than preservation in Krebs-Henseleit buffer or saline. ATP decay was much slower at cold temperatures (factor of 1.81 ± 0.06 for every 10°C). Injection of chlorpromazine into the mouse liver drastically decreased ATP decay rate and inorganic phosphate appearance.

In perfusion experiments with oxygenated Krebs-Henseleit buffer, ATP/Pi remained constant for 3 hr at 37°C and for more than 6 hr at 20°C. During ischemia produced by reduced perfusate flow, ATP rapidly fell to undetectable levels with concomitant rises in inorganic phosphate and sugar phosphate. Intracellular pH fell continuously during ischemia (10-60 min at 20°C). With reperfusion, ATP concentration was higher than baseline within 5-7 min and then fell back to baseline; pH was rapidly restored. After warm ischemia for 10-30 min, the ATP level recovered only partially. During anoxia at 37°C, ATP/Pi decreased slowly but constantly to complete decay at 60 min and only partially returned with restoration of oxygen. Reoxygenation resulted in massive liver enzyme release and broadening of the 31P spectra, suggesting free radical formation.

No. 840

INDIUM III LABELLED LEUKOCYTES IN THE DETECTION OF TUBERCULOUS ENTERITIS. KE Pettigrew, A Houlder, M Garb, AE Simjee, Dept. of Medicine, University of Natal and dwentia, New England Deaconess Hospital, and Harvard Medical School, Boston.

INTRODUCTION: Indium III labelled leukocyte scanning is now an established technique for the detection of sepsis and has been used in the imaging of inflammatory bowel disease. We know of no reported series in which the technique has been applied to tuberculous enteritis (TE). PATIENTS: 5 Patients in whom a diagnosis of TE was made and confirmed by histology were studied. 4 of the 5 patients were on anti-TB treatment for periods up to 1 month before investigation. METHOD: The extent of the disease was determined by a combination of upper and lower GI endoscopy and radiology. Scanning: this was performed within 2 weeks of the diagnosis. Leukocytes were labelled in saline with Indium III oxide and abdominal scans were performed at 4 hrs and 24 hrs. Results were assessed by a radiologist unaware of the endoscopic or radiological assessment.
The Journal of Nuclear Medicine  

No. 841  
RADIONUCLIDE GASTRIC EMPTYING STUDY IN PATIENTS WITH ANOREXIA NERVOSA, BULIMIA, OR ANOREXIA NERVOSA/BULIMIA. W.J. Shih, L. Humphries, P.A. Domstad, F.X. Castellanos, F.H. DeLand. University of Kentucky and Veterans Administration Medical Centers, Lexington, KY.

To evaluate gastric emptying in patients with anorexia nervosa (Abulimia (B)), or AN/B, 48 patients (46 females, 2 males) with upper G-I symptoms ingested 150 uCi Tc-99m triethelene tetraamine polystyrene resin in cereal and were imaged in the supine position. Data were accumulated at 5 min intervals to obtain the gastric emptying time (GET). In four patients GET was normal (40–85 min), in 19 rapid GET, and in 24 was prolonged GET. Twenty-four of 25 with prolonged GET were given 10 mg metoclopromide (MP) IV, with good response in 18 and no response in 6. Among 19 with AN, 10 had prolonged GET, 8 had rapid GET, and 2 were normal GET. Therefore, this radionuclide study enables (1) objective measurement of gastric emptying to separate those patients with rapid or normal GET from those with prolonged GET, avoiding possible side effects from MP medication, (2) prediction of the effectiveness of MP therapy in patients with prolonged GET.

No. 842  

Previous studies in experimental animals suggested that the radiopharmaceutical Ru-97-iminodiacetic acid might be useful as an alternative to I-131 Rose Bengal when delayed hepatobiliary studies are needed. The advantages of Ru-97 are based on a relatively long half life (T 1/2 = 2.9 d), a convenient primary gamma photon (216 KeV), and similar biological behavior as Tc-99m. The findings suggest that surface charge is a significant factor in the labeling of RBCs with Tc.

No. 843  
HEMATOLOGY

No. 844  
IMMUNOLOGY

No. 845  

Vascular clearance patterns, HAMA formation, and scintigraphic biodistribution imaging were used to measure patient response to radioimmunotherapy. Eight of 14 patients developed HAMA prior to or during treatment with 4 injections of 25–60 mCi of I-131(anti-CEA) NP-2. Only 2 patients were skin test positive. The appearance of circulating plasma protein aggregates indicating complexes between HAMA and radioantibody was revealed by gel filtration chromatography. This was associated with spleen visualization on scintigraphy. NP-2 did not combine with circulating CEA, demonstrating negligible contribution to the formation of the immune complexes detected. Progressive shortening of blood clearance rates of radioantibody paralleled rising HAMA titers as measured by enzyme immunoassay. A shift of circulating antibody-associated radioiodine to free iodine followed the formation of complexes with HAMA, suggesting splenic dehalogenation of radioantibody. Higher HAMA titers accelerated the conversion of circulating radioactivity to mostly free iodine within a few hours after injection. In patients without HAMA, the circulating

works-in-progress.

The Journal of Nuclear Medicine
radioactivity was entirely associated with antibody up to 8 days after injection, during which time the spleen was not visualized by scintigraphy. Evaluation of splenic uptake on diagnostic studies combined with peripheral immune complex assay can be used as an assessment of immune complex formation and injected antibody integrity. (Supported in part by NIH grant 39841).

**INSTRUMENTATION**

No. 845


A SPECT system for imaging In-111 labeled anti-cardiac myosin Fab fragments and other In-111 agents was investigated. The all-digital system consisted of dual heads, rotating gantry, body contouring, medium energy collimation (10.3 mm FWHM at 10.2 cm), and acquisition photopeaks (PF) at 172 + 247 keV (15% window) and in the Compton scatter (CS) region, 120 keV (25% window). System performance was evaluated with a 22.2 cm diameter phantom containing line sources (LS) or a 6 cm diameter spheroid. Line spread functions (LSF) were calculated from a 1 pixel slice of the LS (radius of rotation=17.5 cm). LSF showed:

<table>
<thead>
<tr>
<th>Energy (keV)</th>
<th>FWHM/Air (cm)</th>
<th>FWHM/Water (cm)</th>
<th>FWHM/LSF (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>120</td>
<td>26.0</td>
<td>27.6</td>
<td>55.1</td>
</tr>
<tr>
<td>172</td>
<td>18.3</td>
<td>19.2</td>
<td>36.3</td>
</tr>
<tr>
<td>247</td>
<td>18.0</td>
<td>18.5</td>
<td>35.4</td>
</tr>
</tbody>
</table>

Slices of LS in air and water, with attenuation correction (AC), were compared and showed a 5% scatter contribution. For a cold ball in a hot background the CS component was evaluated from SPECT image profiles. Scatter contributed 5% of the counts. If AC was ignored, this decreased to 2%, indicating that AC is necessary. We conclude that scatter is a major component of In-111 images and that In-111 activity quantitation with SPECT will require both attenuation and scatter corrections. The latter seems readily obtainable from data collected simultaneously through a Compton window.

No. 846

A FAST GAMMA RAY DETECTION SYSTEM FOR IN-VIVO MEASUREMENT OF BODY CARBON. J.J. Kehayas, K.J. Ellis, and S.H. Cohn, Medical Research Center, Brookhaven National Laboratory, Upton, NY.*

A miniature 14 MeV neutron generator is used for in-vivo carbon oxygen and hydrogen measurements for the determination and monitoring of body fat. The neutron generator is pulsed at a rate of 10 kHz and delivers 10^3 neutrons/pulse. A target-current feedback system regulates the source of the accelerator to assure constant neutron output.

Carbon is measured by detecting the 4.44 MeV γ-rays from inelastic scattering. The short half-life of the 4.44 MeV state of carbon requires detection of the γ-rays during the 7us neutron pulse. Generators with low pulsed rates were found inappropriate for carbon measurements because of their low duty-cycle (high neutron output during pulse).

The detection system consists of NaI(Tl) detectors and fast electronics for handling the high event rate during the neutron pulse. Fast ADCs with a constant conversion time of 1.5 μs are used for counting. A buffer based micro-multichannel analyzer designed for maximum data throughput is used for data acquisition.

A microcomputer controls the micro-multichannel analyzer and stores the data. This independent fast data acquisition system is operating at counting rates of 100 KHz per detector and can be easily interfaced with a mainframe computer.

*Work supported by DOE No. DE-AC-02-76CH00016.

No. 847

INSTALLATION OF A HIDAC POSITRON CAMERA. S. Kuijik1, G. Bennett2, Y-N Tang1, D. Townsend2, M. Deffries2, F. Meconic2, A. Jaevons4, A. Brill1, A. Donahue2, Brookhaven National Laboratory, Upton, NY; 1Nabob General Hospital, Geneva, Switzerland; 2VUB, Brussels, Belgium; 3CERN, Geneva, Switzerland.

A positron camera based on the High Density Avalanche Chamber (HIDAC) detector has been installed in the Med. Dept. of BNL. Each detector has a sensitive area of 31 cm x 31 cm, an intrinsic spatial resolution of 2.3mm, (3.5mm in reconstructed images), and a detection efficiency of 12% for 511 keV photons. The positron camera consists of a pair of HIDAC detectors operated in coincidence with a 20 nsec resolving time. A similar pair of detectors has been undergoing clinical evaluation in Geneva for the past eighteen months. The detectors were mounted on the same gantry as that used for the UNICON, a dual-headed Anger camera at BNL. The HIDAC detectors are mounted orthogonally to the UNICON heads, in order to conduct simultaneous PET and SPECT studies with the system.

The detectors are interfaced through CAMAC to a PDP 11/34 which is linked over DECNET to a host VAX 11/780. A typical study is performed in step-and-shoot mode with 20 angular positions of the detectors and the data stored in list mode.

To date, the system has been used for a number of phantom studies, and system performance factors have been established. Clinical trials have begun and are expected to last for a period of 8-10 months.

Work supported by Swiss National Science Foundation, NFWO (Belgium) and U.S. Department of Energy.

**NEUROLOGY**

No. 848

DOPPLER-SONOGRAPHY (DS) & IMP SPECT IN PATIENTS WITH ISCHEMIC CEREBROVASCULAR DISEASES. D.Deisenhammer, K. Heil, P.Migl, Ch.Luft. Wagner-Jauregg-KH, Linz, AUSTRIA.

The purpose of this study was to investigate the influence of neck vessels pathology proved by DS on IMP accumulation measured with SPECT. In DC hemodynamic relevant stenosis was assumed when flow reversal, oscillating flow or amplitude attenuation of more than 50% was observed in ophthalmic collaterals. SPECT System: 30 min post i.v. inj. of 5mCi IMP a dual head rota camera (25 cm diameter of rotation, LEAP-collimators) acquired 64 projections in 50 min with a linear sampling distance of 3mm. After the weighted subtraction of scatter using multiple energy windows the projections are smoothed with a variable filter to suppress noise prior to reconstruction. Bellini’s method is used to correct for attenuation, axial slices are reconstructed after Shepp,Logan. 12mm resolution was found in the 2mm thick final tomograms. Semi quantitative CBF was estimated by taking the ratio of local tracer uptake to the mean uptake of the contralateral grey matter.

Values are defined as abnormal when exceeding more than 2 standard deviation from the mean. 60 patients with reversible or irreversible ischemic disease have been examined (mean age 45 y, 25 males). Decreased IMP-uptake was observed in all cases with infarction, in 1/3 of those larger than the infarcted region defined by TCI. In all patients without infarction IMP distribution was normal when DS was normal; whereas in all cases with abnormal DS IMP revealed abnormal regions on the same side, even when excellent compensatory circulation was seen in angiography.
No. 849

STUDY OF METABOLIC AND HAEMODYNAMIC ASPECTS OF HUNTINGTON'S DISEASE BY POSITRON EMISSION TOMOGRAPHY.

PET was used to provide regional measurements in 7 HD subjects, with minimal caudate atrophy, for oxygen metabolism (rCMRO2), oxygen extraction fraction (rOEF), blood volume (rCBV), blood flow (rCBF), pH (rCPH) and glucose metabolism (rCMRGlc). In addition regional rate constants for the transport and phosphorylation of F-18 labelled deoxyglucose (FDG) were measured. Results were compared with similar data from a control group of 5 older normal patients, rCMRO2, rCMRGlc, and rCBF in the caudate nucleus exhibited a coupled depression. Transverse profiles taken through the caudate showed tissue uptake were analyzed with the caudate/cortex ratio for an area of interest of the control group indexed for each parameter was 20% while in the HD group the indices were 40-50%. Metabolic and haemodynamic measurements in the cortex of the HD patients were not significantly different from those of the control group. The caudate/putamen region showed a 13% reduction in rCMRGlc while rCMRO2 and rCBF were reduced by more than 20%. The FDG rate constants are similar for the HD and control groups except for k21 expressing FDG backflow, in the caudate/putamen. The ratio of k2 in the cortex to k2 in the caudate/putamen is a factor of two smaller in HD patients than in controls.


No. 850

EVALUATION OF Tc-99m HM-PAO AS A CEREBRAL BLOOD FLOW TRACER USING QUANTITATIVE MULTIPLE-RADIONUCLIDE AUTOGRAPHY. J. L. Lear, K. Mido, D. Navarro, and T. Martinez. Stanford University and V. A. Medical Center, Palo Alto, CA

Tc-99m hexamethylpropyleneamine oxime (HM-PAO) has been proposed as a potential tracer for cerebral blood flow (CBF) based upon observations of high cerebral uptake after intravenous administration. The purpose of this investigation was to evaluate the local cerebral distribution of HM-PAO as compared to that of a reference CBF tracer, C-14 iodoantipyrine (IAP).

Mixtures of 15-20 mCi of HM-PAO and 60-70 µCi of IAP were administered by intravenous infusion to a series of awake and anesthetized rats. Arterial samples were obtained during the infusion and the rats were killed by KCl injection after approximately 45 seconds. Autoradiographs of brain sections were first made from 18 hour exposures and therefore primarily represented HM-PAO. The sections were removed from the film for 2 days to allow the Tc-99m to decay, and second exposures of 7 days duration were made which represented IAP. The images were analyzed using a digital autoradiographic scanner and the slight amount of C-14 exposure in the first set of images was subtracted. CBF values for both tracers were computed using a standard diffusible tracer model, and CBF images were generated and compared on a pixel by pixel basis. We found that the distribution of HM-PAO was different between the awake and anesthetized rats, with a more heterogeneous pattern occurring in the awake animals. This caused both over- and underestimation of CBF by HM-PAO compared to IAP, which was most likely secondary to violation of the assumption of well-mixed tissue compartments in the diffusable tracer model with HM-PAO. These differences occurred over very small areas and would not be detectable with the resolution of SPECT in human studies.

No. 851


The purpose of this study was to determine whether areas of low density on CT or high signal intensity on MRI scans represent changes of the BBB in patients with Alzheimer type (1), multi-infarct (2), depressive dementia (1) or stroke (1). These patients had PET scans as a measure of BBB permeability to Ga-68 EDTA. Serial images were obtained 6.5 cm above the O.M. Line, and arterialized venous blood was used to quantify the plasma input function. The multiple time/graphic analysis method of Patlak, et al. (J Cereb Blood Flow Metab 1983; 3:1-7) was used to determine the unidirectional transport constant, k2, for the blood to brain transport of Ga-68 EDTA. This was done by finding the linear least squares slope of the Ci(t)/Cp(t) versus \( \int C_p(t)dt/C_p(t) \) curve. Time t was assumed to be the start time of the scan. Vascular volume, Vv, was estimated by the intercept of the least squares line. Each pixel was treated as a separate ROI to generate k2 and Vv maps. Results showed average k2 and Vv values in all patients of 0.000286 and 0.0249, respectively, both within the reported normal range (Ianotti et al. Acta Neurol Scand 1985; T2(1):104). The k2 maps showed no distinguishing features for any disorder tested, and the Vv maps were nearly uniform, indicating no focal areas of increased intravascular volume. This study showed no differences between the BBB transfer constant or intra-vascular volume for various clinical types of dementia and normal brain.

No. 852


Persistent depression following stroke has been shown to correlate with lesions in the left hemisphere. Animal studies have shown right sided ischemic lesions to decrease biogenic amines in the ipsilateral cortex to a greater degree than left sided lesions (Science, 205:707-710,1976). We carried out C-11-methylspiperone PET scans in 11 subjects with varying strokes and depression. Five had left-sided and six had right-sided strokes. Early images indicated that there was a reduction in blood flow ipsilateral to the lesion in all studies, regardless of side. To estimate the degree of binding remaining in a stroke-involved hemisphere, we defined the ratio of the S2 binding in the cortex to the cerebellum late in the scan in both the affected and unaffected hemisphere. The cortex/cerebellar ratios in the late scans were higher in the ipsilateral cortex in right-sided lesions compared to left lesions (p<0.05). These results support the observation that right and left sided ischemic lesions have different effects on endogenous biogenic amines and their receptors. The ipsilateral increase in receptor binding in the right sided lesions may suggest an asymmetry in compensatory receptor up-regulation mechanisms in the two hemispheres following stroke. An additional 4 patients are being studied with a focus on unilateral cortical strokes and kinetic modelling.

No. 853


The Journal of Nuclear Medicine
A goal of positron emission tomography is the measurement of the rate of secretion of neurotransmitters by their effect on the kinetics of injected radioligands. High affinity ligands such as C11-3-N-methylspiperone (NMSP) may bind so tightly that the much lower affinity of endogenously secreted dopamine may not affect the rate of binding of the tracer. Cocaine, a potent dopamine uptake inhibitor, was administered intravenously in order to increase synaptic dopamine concentrations; subjective effects were observed almost instantly. Three subjects received cocaine (C, 10 mg, or 30 mg, or 40 mg after NMSP injection. Since we have previously observed a linear relationship of the caudate/cerebellum over time, we used this measure of the rate of binding to the receptor to monitor possible competition of NMSP with cocaine. We observed a change in the slope (SL) of the caudate/cerebellum (CA/CB) vs time of only -0.003, -0.009 and -0.0074/min. which was within the 95% tolerance limits of 23 normal subjects (-0.0553 to 0.0473/min.) for SL. A fourth subject received a control NMSP PET followed the next day by a 2nd scan in which the same cocaine IV dose was given 4 min. prior to NMSP. The change in slope was only 2% which is within our observed reproducibility (5-10%). All subjects had physiological evidence of a substantial response to the cocaine. Our preliminary data suggest that endogenous dopamine release does not have a significant effect on NMSP binding in normal PET scan conditions. Studies with amphetamine are in progress.

Proceedings of the 33rd Annual Meeting

D. Danashvar, A. Wilson, H. Ravert, R.F. Dannals. The Johns Hopkins Medical Institutions, Baltimore, MD.

ONCOLOGY

No. 854
PRELIMINARY STUDIES OF IN-111-Labeled ZCE 025 MONOCLONAL ANTIBODY (MoAb) IMMUNOSCINTIGRAPHY IN METASTATIC COLORECTAL CARCINOMA. H. Abdel-Mab, C.S. Higano, A.N. Schwartz, M.D. Cerqueira, VA Medical Center and University of Washington, Seattle, WA, and M.W. Unger, Hybritech, Inc., San Diego, CA.

We have performed an investigation to determine the utility of Indium-111-labeled (In-111) ant carcinoembryonic antigen (CEA) monoclonal antibody (MoAb) scanning in the detection of metastatic colorectal carcinomas (Co). 6 patients (pts) with confirmed metastases (mets) and 2 pts with suspected mets based on rising serum levels were studied. Each received 5.5 mCi of In-111 labeled MoAb ZCE 025 (anti-CEA murine MoAb of the IgG, class produced by Hybritech, Inc.). The MoAb was infused over 2 hours at doses of 2.5 mg (2 pts), 10 mg (4 pts) and 20 mg (2 pts). Total body scans with region of interest analysis were performed at 3 and 6 days post-infusion. 11 tumor masses were demonstrated by surgery and conventional diagnostic x-ray methods in 6 pts. 2 pts were free of tumor. ZCE 025 MoAb visualized 12 of these 15 tumor masses (80% detectability rate). With respect to tumor sites, MoAb visualized 8/8 lymph node mets, 2/2 lung mets greater than lcm in diameter, and 2/2 local recurrence. All lesions were seen at day 3, but more easily seen at day 6. MoAb visualized 2 sites of recent surgery, not shown to harbor recurrence by CT and needle biopsy.

The high detectability of mets from colorectal carcinomas with In-111-labeled ZCE 025 MoAb demonstrates the potential of this antibody as a diagnostic agent as well as a therapeutic agent.

PERIPHERAL VASCULAR

No. 855
VENOUS DOPPLER DIRECTED INTERPRETATION OF TC 99m RBC-cathARTOGRAPHY. Frank M. Grund, Robert P. Miller, Rex B. Shafer. V.A. Medical Center, Minneapolis, MN.

A simple method to optimize Tc-99m DTPA radioaerosol (RA) contribution to Tc-99m MAA (MAA) lung perfusion (Q) images. C.K. Kim, E.J. Fine, K.J. Chun, and L.M. Freeman. Montefiore Medical Center, Bronx, NY.

Ventilation (V) imaging with RA is convenient and cost effective. In our institution, patients (pts) inhale nebulized Tc-99m DTPA (30 mCi in 3 ml saline and 9L/ min) for approx. 3-5 min. before the Q scan. The amount of RA deposited in the lungs varies widely depending on pts' pulmonary status and effort. Inhalation of 2-3 mCi of RA may obscure Q (3 mCi MAA) findings. We have developed a simple way of monitoring V studies to minimize excessive physiological information from Tc-99m RBC venograms and venous doppler analysis allowed accurate assessment of proximal deep venous thrombosis.

In these early results, we plan to continue this research to determine the predictive accuracy of each test individually and when used concomitantly.

PULMONARY

No. 856
A SIMPLE METHOD TO OPTIMIZE Tc-99m DTPA RADIOAEROSOL (RA)'s CONTRIBUTION TO Tc-99m MAA (MAA) LUNG PERFUSION (Q) IMAG- ES. C.K. Kim, E.J. Fine, K.J. Chun, and L.M. Freeman. Montefiore Medical Center, Bronx, NY.

Accurate non-invasive tests are required by clinicians to diagnose deep venous thrombosis. We propose to improve the accuracy of Tc 99m RBC venograms by examining venous blood flow with doppler ultrasound. Tc 99m RBC venograms are not widely used because of the difficulties presented in interpretation. Doppler ultrasound allows physiologic assessment of the venous blood flow and may help resolve indeterminate RBC venograms. We studied 12 patients after contrast venography was performed because of symptoms and signs of deep venous thrombosis. Tc 99m RBC venography was performed using an in vivo labeling technique with the injection of 30 mc TC 99m permethane (in a forearm vein 15 minutes after the injection of stannous pyrophosphate. The nuclear medicine physician responsible for interpretation of the RBC venogram performed venous doppler exams using a 5.3 MHz ultrasound stethoscope. Thus far, 6 patients with negative contrast venograms and 4 patients found to have proximal deep venous disease were correctly diagnosed with these non-invasive studies. As expected, this approach did not diagnose small calf vein thrombi in 2 patients. Knowledge of the anatomical and physiological information from Tc 99m RBC venograms and venous doppler analysis allowed accurate assessment of proximal deep venous thrombosis.

In these early results, we plan to continue this research to determine the predictive accuracy of each test individually and when used concomitantly.

PULMONARY

No. 857
SINGLE PHOTON EMISSION COMPUTED TOMOGRAPHY VERSUS PLANAR IMAGING IN PULMONARY PERFUSION DEFECTS. A. Palla, S.S. Tuneh, R.J. English, S.Z. Goldhaber, B.L. Holman. Harvard Medical School, Boston, MA.

To assess the role of emission tomography (SPECT) in the evaluation of pulmonary embolism (PE), we compare planar
(P) and SPECT imaging after the injection of Tc-99m MAA (3mCi) in 19 patients. Pulmonary angiography (PA) was done in all patients except 6 with normal perfusion scan. All images were acquired on a large field of view gamma-camera (GE 400/470). 64 projections encompassing 360°, 64x64 matrix and 20°/projection were used. Segmental and non-segmental defects were determined on each modality independently, and then assigned as high (HP), moderate (MP), low (LP), indeterminate (IP), or nil (NP) probability of PE. The defects in each modality were outlined as follows:

<table>
<thead>
<tr>
<th>SEG DEFINITION</th>
<th>HP</th>
<th>MP</th>
<th>LP</th>
<th>IP</th>
<th>NP</th>
</tr>
</thead>
<tbody>
<tr>
<td>SEG DEF P</td>
<td>37</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>SEG DEF SPECT</td>
<td>92</td>
<td>11</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>NON SEG DEF P</td>
<td>19</td>
<td>2</td>
<td>3</td>
<td>17</td>
<td>0</td>
</tr>
<tr>
<td>SPECT</td>
<td>14</td>
<td>0</td>
<td>18</td>
<td>6</td>
<td></td>
</tr>
</tbody>
</table>

Comparison between our impression and PA was as follows:

- SPECT showed segmental defects in all patients with positive PA, while PA failed to show segmental defects in 2.
- SPECT and PA showed 15 and 5 segmental defects, respectively, in 4 with negative PA. In conclusion, SPECT detected all segmental perfusion defects.

No. 858


The lung is responsible for the active uptake of biogenic amines such as serotonin and norepinephrine. MIBG is taken up by adrenomedullary cells by an energy-requiring, sodium-dependent active process. To determine if MIBG might be useful for evaluation of pulmonary endothelial cell function, the mechanism of single-pass labeling of MIBG accumulation was studied in rat lungs, isolated and perfused with an albumin Krebs-Ringer bicarbonate buffer. 131-I-MIBG lung accumulation was measured by the percent lung extraction per gram of lung tissue after 2 minutes of perfusion with 131-I-MIBG under the experimental conditions below:

<table>
<thead>
<tr>
<th>EXPERIMENTAL CONDITIONS</th>
<th>N</th>
<th>Extraction% ±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control 0.01μM MIBG (37° celsius)</td>
<td>8</td>
<td>19.72±2.34</td>
</tr>
<tr>
<td>+ Serotonin (0.7μM)</td>
<td>5</td>
<td>15.25±2.29*</td>
</tr>
<tr>
<td>+ Imipramine (10μM)</td>
<td>5</td>
<td>5.87±0.82*</td>
</tr>
<tr>
<td>+4° celsius</td>
<td>5</td>
<td>2.95±0.64*</td>
</tr>
<tr>
<td>+ ouabain (0.5μM)</td>
<td>7</td>
<td>7.93±1.21*</td>
</tr>
<tr>
<td>2.0μM MIBG</td>
<td>5</td>
<td>7.31±1.29*</td>
</tr>
</tbody>
</table>

*p<0.001, 4 p<0.01

The addition of 0.5μM norepinephrine to the medium containing 131-I-MIBG (0.1 to 0.5μM) also demonstrated significant (24%, p<0.05) inhibition of MIBG lung extraction. Thus, the pulmonary accumulation of MIBG appears to be energy-requiring and sodium-dependent, with characteristics very similar to norepinephrine uptake. Studies of MIBG lung extraction may be useful for clinical investigations of lung endothelial cell function.

RADIOPHARMACEUTICAL CHEMISTRY

No. 859


Ellipticine (1) an intravenous anesthetic used widely in Europe, has been implicated in the death of patients due to marked lowering of plasma cortisol. Recent studies have shown that ellipticine is a selective inhibitor of two adenocortical cytochrome P450 enzymes, P450-2c11 and P450-11. The goal of this work was to synthesize and evaluate radioiodinated ellipticine and structurally related imidazole as possible rapid imaging agents for the adrenal cortex.

Starting with 4-iodocetophenone compounds 2-6 were synthesized in 5-6 steps by literature methods. Exchange labeling with NaI-125 was achieved in high yield by a solid-state method using ammonium sulfate as promoter. The in vivo affinities of 2-4 for the whole adrenal were determined in rats following intravenous injection: only compound 4 showed significant adrenal localization at 5 and 30 min. Further evaluation of 4 showed peak adrenal uptake at 0.5-2.0h with complete washout at 24h. Maximum adrenal-to-kidney (20) and adrenal-to-blood (42) concentration ratios occurred at 0.5 h. Similar results were obtained in dogs. Compounds 5 and 6 have been synthesized and are under evaluation in hopes that they will show high adrenal affinity as well as rapid hepatic clearance.

No. 861


Although radiolabeled meta-iodobenzylguanidine (MIBG) has been used to image peripheral organs and tumors based on its affinity for adrenergic neurons, application of MIBG to mapping central catecholamine stores is limited by its failure to pass the blood-brain barrier (BBB). We report here the synthesis of derivatives of MIBG that have lower pKa's and higher lipophilicities than MIBG.
Proceedings of the 33rd Annual Meeting

Works-in-Progress

itself. The goal was to have these derivatives serve as protracer forms that would enter the brain following i.v. injection and be quickly hydrolyzed to the parent tracer MIBG. I-125-MIBG in free base form was acylated with the appropriate anhydride, acid chloride or ester to give 1-6. Tracers 2 and 4 exhibited 10-20 fold higher concentrations in the rat brain than MIBG 1-30 min after i.v. injection. In contrast to 4, compound 2 showed virtually no washout from the brain over the first 30 min suggesting hydrolytic stability in phosphate (pH 7.1) buffered ethanol is k_» 2. Tracers 3 and 5, though highly lipophilic, gave low brain uptakes due likely to enhanced blood binding. These initial experiments show that a protracer form of MIBG can penetrate the BBB and that in certain cases (ie., 2) intra-brain hydrolysis may occur.

**RENALELECTROLYTE/HYPERTENSION**

**No. 862**


Eleven patients with adrenocortical failure were studied to assess the respective value of the measurements of PRA and PV during substitutive therapy. Seven patients suffered from primary adrenocortical failure and 4 had undergone bilateral adrenalectomies for Cushing's disease. Patients were studied whilst receiving cortisone and/or hydrocortisone. Two patients had 2 measurements and another was evaluated on 5 occasions. Plasma volume was measured using 11115 labelled albumin and PRA was determined by radiimmunoassay of angiotensin I generated. Results of PRA (ng/ml/h), PV (% of normal) and blood pressure (BP, mm Hg) are summarized below.

<table>
<thead>
<tr>
<th>PAT.</th>
<th>BP</th>
<th>PRA</th>
<th>PV</th>
<th>PAT.</th>
<th>BP</th>
<th>PRA</th>
<th>PV</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>130/80</td>
<td>11</td>
<td>67</td>
<td>2</td>
<td>130/80</td>
<td>10</td>
<td>78</td>
</tr>
<tr>
<td>2</td>
<td>130/80</td>
<td>9.5</td>
<td>66</td>
<td>3</td>
<td>130/80</td>
<td>70</td>
<td>66</td>
</tr>
<tr>
<td>3</td>
<td>130/80</td>
<td>6.8</td>
<td>70</td>
<td>4</td>
<td>130/80</td>
<td>17.8</td>
<td>70</td>
</tr>
<tr>
<td>4</td>
<td>130/80</td>
<td>6.8</td>
<td>70</td>
<td>5</td>
<td>130/80</td>
<td>7.4</td>
<td>98</td>
</tr>
<tr>
<td>5</td>
<td>130/80</td>
<td>7.1</td>
<td>87</td>
<td>6</td>
<td>130/80</td>
<td>6.6</td>
<td>88</td>
</tr>
</tbody>
</table>

In 12 of the 16 measurements, PV was inversely correlated with PRA; 2 patients had a low PRA despite a low PV and 1 patient had a high PRA with a high PV. The reason for this discrepancy could be the fact that renin release depends on multiple factors. Despite these discordant measurements, a statistically significant inverse relationship was found between PRA and PV (r=-0.5, p<0.01). Our results suggest that PRA in patients with adrenocortical failure is most often related to plasma volume. Further studies are needed to precise the specific value of each test in the follow-up of these patients.
Categorical Seminars

SATURDAY

CARDIOVASCULAR NUCLEAR MEDICINE 1986
(sponsored by the SNM Cardiovascular Council)

8:00-3:30 Room 40

Educational Objective:
To highlight controversies and new areas of development in cardiovascular nuclear medicine

TOPICS:
1. New Tc-99m perfusion tracers
2. Dipyradamole stress imaging
3. Prognosis in coronary artery disease
4. Exercise left ventricular functions
5. Imaging artifacts
6. T1-201 washout
7. T1-201 SPECT
8. Artificial intelligence
9. Thrombolysis
10. Infarct-avid scintigraphy

Summary: This year's categorical course in cardiovascular nuclear medicine is divided into six topics, each of which includes several speakers presenting either opposing viewpoints or complementary subjects. The orientation is heavily clinical, and the course is designed for clinicians practicing advanced nuclear cardiology. Topics to be discussed include:

1) Imaging artifacts and the need for quality control in equilibrium radionuclide angiography and myocardial perfusion imaging with thallium-201.
2) The differentiation of myocardial ischemia from myocardial infarction and assessment of myocardial viability. The utilization of radionuclide techniques for assessment of thrombolytic effect will be included.
3) The potential clinical utility of positron emission tomography. The emphasis will be on the potential problems associated with implementing a PET laboratory in a non-research hospital setting.
4) New advances in myocardial perfusion imaging, such as radiopharmaceuticals labeled with technetium-99m and alternatives to dynamic exercise, specifically pharmacologic stress intervention.
5) New developments in computer techniques applicable to nuclear cardiology. The pitfalls associated with assessment of thallium-201 washout from planar studies will be addressed. Single photon emission computed tomography and quantification of thallium-201 will be updated. Lastly, the potential role of artificial intelligence and smart expert systems for image interpretation will be addressed.
6) The role of exercise radionuclide angiography in establishing prognosis in coronary artery disease. The clinician's perspective in decision making also will be included.

Chairmen: Harvey J. Berger, M.D., Centocor, Inc., Malvern, PA; Elias H. Botvinick, M.D., University of California, San Francisco, CA

8:00 Introductions. Harvey J. Berger, M.D., Centocor, Inc., Malvern, PA

Infarct vs Ischemia: How Can They be Differentiated?

8:05 Evaluation of Coronary Thrombolysis with Myocardial Perfusion Imaging and Radionuclide Angiography. Daniel S. Berman, M.D., Cedars-Sinai Medical Center, Los Angeles, CA

8:30 Infarct-Avid Scintigraphy—New and Old Tracers. Harvey J. Berger, M.D., Centocor, Inc., Malvern, PA

What is the Role of PET Imaging in Clinical Cardiology?

8:55 Panel Discussion/Debate

Protagonists: Lance Gould, M.D., University of Texas, Houston, TX; Ed Geltman, M.D., Washington University, St. Louis, MO; Heinrich Schelbert, M.D., University of California, Los Angeles, CA

Moderators: Elias H. Botvinick, M.D., University of California, San Francisco, CA; Daniel S. Berman, M.D., Cedars-Sinai Medical Center, Los Angeles, CA

9:45 Break

Imaging Artifacts and Quality Control: How Do They Affect Clinical Interpretation?

10:00 Thallium-201 Perfusion Imaging. Michael Dae, M.D., University of California, San Francisco, CA

10:25 Equilibrium Radionuclide Angiography. E. Gordon DePuey, M.D., Emory University Hospital, Atlanta, GA

Efficacy of Cardiovascular Nuclear Medicine Procedures

10:55 Systematic Approach to Decision-Making in Patients with Coronary Artery Disease: A Clinician's Appraisal. Bernard Siegal, M.D., Hahnemann University, Philadelphia, PA

11:40 Use of Exercise Radionuclide Angiography to Define Prognosis in Coronary Artery Disease. Robert H. Jones, M.D., Duke University, Durham, NC

12:00 Lunch

New Approaches to Myocardial Perfusion Imaging

1:15 Technetium-99m Tracers: Thallium Replacements? B. Leonard Holman, M.D., Brigham and Women's Hospital, Boston, MA

1:40 Dipyridamole Pharmacologic Stress: When Should It Be Used Instead of Exercise? Jeffrey Leppo, M.D., University of Massachusetts, Worcester, MA

2:05 Pitfalls in Washout Analysis of Exercise Thallium-201 Scintigrams. Denny Watson, Ph.D., University of Virginia, Charlottesville, VA

2:30 Quantification of Thallium-201 Images: How Important are Evaluation of Washout and Use of Tomography? Jamshid Maddahi, M.D., Cedars-Sinai Medical Center, Los Angeles, CA

3:05 Artificial Intelligence: Can Cardiac Images Be Interpreted by Computers? Ernest V. Garcia, Ph.D., Emory University School of Medicine, Atlanta, GA
Educational objective:
To educate constituents regarding state of the art and promising developments which may impact their clinical practice through 1990.

Summary: The purpose of the course is to inform the practitioners of nuclear medicine of many new and exciting developments which will impact the clinical practice of nuclear medicine over the next five years. New developments in radiopharmaceuticals, brain imaging with single photon agents, positron tomography and its impact on the clinical practice of nuclear medicine, monoclonal antibodies including diagnostic and therapeutic implications, cardiac imaging including newer radiopharmaceuticals and quantitative tomographic techniques, new modes of therapy using non-sealed sources, the impact of nuclear magnetic resonance, computers including important characteristics for individual departments ranging from the one camera practice to a multimodality large department and newer and evolving forms of instrumentation will all be discussed by leading experts in the field. Emphasis will be placed on the clinical importance to the field of nuclear medicine.

By the completion of the course, attendees will have had exposure to state of the art and emerging technologies and be made aware of new advances which would impact their clinical practices within the next few years.

Moderators: Alan D. Waxman, M.D., James Fletcher, M.D., Jamshed Maddahi, M.D., C. Leon Partain, M.D., Ph.D.

TOPICS:
1. Radiopharmaceuticals
2. Brain imaging with single photon agents
3. Positron tomography
4. Monoclonal antibodies
5. Cardiac imaging
6. Therapy
7. Magnetic resonance
8. Computers
9. Instrumentation

9:00 Advances in Radiopharmaceuticals. Maria Liptplo, Ph.D., E. I. DuPont Diagnostic Imaging Division, Billerica, MA

9:45 Single Photon Imaging of the Brain. Richard Holmes, M.D., University of Missouri, Columbia, MO

10:15 Positron Emission Tomography: (The Impact on Clinical Decision Making). Michael Phelps, Ph.D., University of California, Los Angeles, CA

11:00 Monoclonal Antibodies: Diagnostic Imaging and Therapeutic Implications. Brian Gallagher, Ph.D., E.I. DuPont, Billerica, MA

11:30 New Frontiers in Nuclear Therapy. Richard Holmes, M.D., University of Missouri, Columbia, MO

1:00 Cardiac Imaging: The Role of Nuclear Medicine in a Multi-Modality World. Daniel S. Berman, M.D., Cedars-Sinai Medical Center, Los Angeles, CA

THE CHEMISTRY OF RADIOPHARMACEUTICALS IN VIVO:
Methods and State of Characterization
(Sponsored by the SNM Radiopharmaceutical Science Council)

8:10-4:30 Room 30

Educational objective:
The objective of the seminar is to present the chemical state of radiopharmaceuticals in vivo; metabolism, tissue binding at the molecular level, and methodology of characterization.

Topics:
1. Brain perfusion agent
2. Brain receptor agents
3. Uptake of cations by the heart
4. Organic cations
5. Tc-99m cations
6. Liver metabolism and binding
7. Misonidazole and analogs
8. Antibody metabolism
9. Labeled fatty metabolism

Summary: Recently developed radiopharmaceuticals have been designed to interact with biological systems in a specific manner. Organ specific transport, as well as intracellular binding and metabolism, are involved. Thus, it is important that the in vivo behavior of these radiopharmaceuticals be characterized in order to understand the chemical form the nuclear medicine image reflects. The faculty will review the methodology of metabolic and tissue binding characterization and the state of in vivo chemical characterization at the molecular level for different organs of interest to nuclear medicine. These include brain perfusion and receptor agents, cationic agents for the heart, antibodies that are acted upon by the liver. In addition, metabolism of labeled antibodies by tumor and liver will be discussed.

Program Chairman: Alan R. Fritzberg, Ph.D., NeoRx Corporation, Seattle, WA


8:10 Introduction. Alan R. Fritzberg, Ph.D., NeoRx Corporation, Seattle, WA

8:20 The Characterization of the In Vivo Chemistry of Brain Perfusion Radiopharmaceuticals. Ronald Blasberg, Ph.D., National Institutes of Health, Bethesda, MD
CURRENT ISSUES IN NUCLEAR MEDICINE:
Categorical Seminar on Marketing Nuclear Medicine Services and Update on Low-Level Waste (sponsored by the American College of Nuclear Physicians)

9:00–3:00 Room 38

Sponsor: American College of Nuclear Physicians (ACNP) Professional and Public Information Program

9:00–9:10 Introduction and Objectives. Ralph G. Robinson, M.D., Kansas University Medical Center, Kansas City, KS

9:10–9:30 The Importance of Marketing. Stuart J. Somerville, President, Medi-Physics, Inc., Richmond, CA

9:30–9:50 Identifying Market Segments. Jerome M. Smith, DuPont Diagnostic Imaging Division, Boston, MA


10:10–10:30 Break

10:30–11:00 Marketing to the Referring Physician. Ralph G. Robinson, M.D., Kansas University Medical Center, Kansas City, KS

11:00–11:30 Marketing Strategies That Work for Nuclear Physicians. Conrad E. Nagle, M.D., William Beaumont Hospital, Troy, MI

11:30–12:00 Cost Analysis: The Real Cost of Nuclear Medicine Procedures. Larry L. Heck, M.D., Methodist Hospital of Indiana, Indianapolis, IN

12:00–1:15 Lunch


1:45–2:15 Volume Reduction as an Approach to Low-Level Waste Management. Kerry Bennet, DuPont Diagnostic Imaging Division, Boston, MA

2:15–2:45 Alternative Technologies to Shallow Land Burial for Low-Level Waste. USCEA Representative

2:45–3:00 Discussion (Faculty)
NUCLEAR MEDICINE REVIEW COURSE

Sunday–Wednesday Room 29
(Refreshments compliments of Amersham Corporation.) This four day course is a review of selected topics for candidates for examination by the American Board of Nuclear Medicine, as well as for practicing nuclear medicine physicians and technologists. Residents in nuclear medicine or allied training programs should find these in-depth reviews helpful. The program is scheduled during the same time periods as the scientific sessions and categorical courses. Attendees are invited to participate in this course in its entirety, or in part. The faculty is composed of nuclear medicine physicians and scientists who are renown educators. They have donated their time and expertise to this review course. There is no additional fee for this course.

Chairmen:
Robert J. Lull, M.D., Letterman Army Medical Center, San Francisco, CA; Michael F. Hartshorne, M.D., Brooke Army Medical Center, San Antonio, TX.

Tuesday, June 24
8:30 Review of Procedures for Evaluation of the Thyroid. N. David Charkes, M.D., Temple University Hospital, Philadelphia, PA
10:00 Break
10:30 Review of Procedures for Evaluation of the Gastrointestinal Tract. Leon S. Malmud, M.D., Temple University Hospital, Philadelphia, PA
12:00 Lunch
1:30 Radionuclide Therapy. William H. Blahd, M.D., V.A. Wadsworth Medical Center, Los Angeles, CA
3:00 Break
3:30 Radionuclide Evaluation of Renal Structure and Function. Eva V. Dubovsky, M.D., Ph.D., University of Alabama, Birmingham, AL

Sunday June 22
10:30 Development Administration, Psychometrics, and Evaluation of the American Board of Nuclear Medicine Certifying Examination. Joseph F. Ross, M.D., President, and I. Ross McDougall, M.B., Ch.B., Ph.D., Chairman, American Board of Nuclear Medicine, Los Angeles, CA
11:30 Thirty Things That They Didn’t Teach You During Residency. Myron L. Lecklitter, M.D., University of South Alabama, Mobile, AL
12:00 Lunch

Monday, June 23
8:30 Quality Assurance I: Radiopharmaceuticals. Richard E. Stotler, LTC, MS, Letterman Army Medical Center, San Francisco, CA
10:00 Break
10:30 Quality Assurance II: Instrumentation. L. Stephen Graham, Ph.D., V.A. Hospital, Sepulveda, CA
12:00 Lunch
1:30 Quality Assurance III: Radioassay. Martin L. Nysynowitz, M.D., University of Texas Medical Branch, Galveston, TX
3:00 Break
3:30 Nuclear Accident Management. Eugene L. Saenger, M.D., University of Cincinnati Medical Center, Cincinnati, OH
5:00 Session ends.

Wednesday, June 25
8:30 Radionuclide Evaluation Bone Abnormalities. Lawrence E. Holder, M.D., Baltimore, MD
10:00 Break
10:30 Radionuclide Evaluation of the Lung. William G. Spies, M.D., Northwestern Memorial Hospital, Chicago, IL
12:00 Lunch
1:30 Useful But Uncommonly Performed Procedures in Nuclear Imaging. George A. Wilson, M.D., University of Rochester Medical Center, School of Medicine, Rochester, NY
3:00 1986 Scientific Meeting Highlights. Henry N. Wagner, Jr., M.D., Johns Hopkins Medical Institutions, Baltimore, MD (Room 40)

ENDOCRINE EVALUATION USING RADIOASSAY & MULTIPLE IMAGING MODALITIES

10:30–12:00 Room 38

Educational Objective:
Review of current status of endocrine evaluation.

TOPICS:
1. Radioimmunoassay
2. Advances in endocrine imaging

Summary:
Clinical and laboratory evaluation of the endocrine system

Sunday–Wednesday
SPECT vs. PET vs. MRI: RELATIVE ROLES, COST, AND CAPABILITY

10:30-12:00 Room 40

Educational Objective:
To review the current and potential clinical capability of SPECT, PET, MRI and NMR Spectroscopy and their relative independent, correlative or competitive roles in clinical diagnosis.

Topics:
1. Single photon emission computed tomography
2. Positron emission tomography
3. Magnetic resonance imaging
4. NMR spectroscopy

Summary:
The current and potential capability, cost, and relative clinical roles of single photon emission computed tomography (SPECT), positron emission tomography (PET), magnetic resonance imaging (MRI), and nuclear magnetic resonance (NMR) in vivo spectroscopy will be compared and evaluated. Correlative, competitive, and independent roles will be identified and discussed. Presentation will include an open panel discussion in order to encourage audience participation.

Moderator: C. Leon Partain, M.D., Ph.D.

Faculty:
R. Edward Coleman, M.D., Duke University, Durham, NC; Robert Kessler, M.D., Vanderbilt University Hospital, Nashville, TN; Thomas Brady, M.D., Harvard University, Boston, MA; John C. Gore, Ph.D., Yale University, New Haven, CT

PICTURE ARCHIVING AND COMMUNICATION SYSTEM (PACS)—ALL DIGITAL NUCLEAR MEDICINE DEPARTMENT

10:30-12:00 Room 39

Educational objective:
These presentations will discuss the hardware and software requirements for an all digital nuclear medicine department, including image perception, displays, networks and storage needs. Cost and clinical advantages will be addressed in functioning PACS departments.

Topics:
1. Theoretical requirements for nuclear medicine all digital departments
2. Descriptions of currently functioning and developing all digital nuclear medicine departments

Summary:
The use of digital Picture Archiving and Communications Systems (PACS) in radiology departments provides three principal advantages over their analog counterparts. First by acquiring and viewing diagnostic images digitally, one can use a computer to manipulate the images, thus extending the diagnostic potential of the acquired data. Examples of computer enhancement are background subtraction, modifying the gray scale of the image, and creating movies, or “cines”. For instance, by expanding a portion of the gray scale, small differences can be accentuated revealing structures which otherwise might not have been visualized. Cines are particularly useful when viewing flow studies as they present the frames sequentially at a rate up to sixty frames/second. A second advantage of digital PACS systems arises from storing the data in a digital format. As a result of this, the ability to analyze images with a computer is retained. This means that at a later date, a study can be recalled either for comparison to a current study, or so that a new analysis algorithm can be applied. Finally, digital storage of the studies in a central archive prevents loss of studies and reduces the time to locate studies as compared to conventional filing systems. The ninety minute session will be divided into two sections. The first section with two 15 minute presentations will deal with some theoretical aspects and requirements of an all digital nuclear medicine department. Harold Kundel, M.D. of the University of Pennsylvania Hospital Department of Radiology will lead off with a discussion of image perception and diagnostic requirements of nuclear medicine. Samuel Dwyer, Ph.D. from the University of Kansas Hospital Department of Radiology will follow with a discussion of image perception and diagnostic requirements of nuclear medicine. Samuel Dwyer, Ph.D. from the University of Kansas Hospital Department of Radiology will follow with a discussion of image perception and diagnostic requirements of nuclear medicine. Samuel Dwyer, Ph.D. from the University of Kansas Hospital Department of Radiology will follow with a discussion of image perception and diagnostic requirements of nuclear medicine.

Moderator: Gerald M. Kolodny, M.D.

Faculty:
Harold Kundel, M.D., University of Pennsylvania Hospital, Philadelphia, PA; Samuel Dwyer, Ph.D., University of Kansas Hospital, Kansas City, KS; John A. Parker, M.D., Ph.D., Beth Israel Hospital, Boston, MA; Jack Juni, M.D., University of Michigan Hospital, Ann Arbor, MI; Theodore J. Stahl, M.D., Middlesex General University Hospital, New Brunswick, NJ; Stephen Bacharach, Ph.D., National Institutes of Health, Bethesda, MD; Jason Zielonka, M.D., Veterans Administration Medical Center, Milwaukee, WI

Background of the Kinetic Approach

10:30-12:00 Room 31

Educational objective:
Fundamental and basic ideas underlying kinetic modeling are presented with actual examples of progressively more com-
plex systems starting with the microsphere model and including the method for calculating the rate of constant and lumped contrast for the fluorodeoxyglucose model. The specific topics to be discussed are:

**Topics:**
1. Types of flow tracers
2. Models appropriate for emission data
3. Method for quantitating receptors
4. Power and pitfalls of inferring metabolism of glucose, amino acids and fatty acids using emission tomography

**Moderator:** Thomas F. Budinger, M.D., Ph.D., University of California, Berkeley, CA; Albert Gjedde, Ph.D., Panum Institute, Copenhagen, Denmark

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**Societal Considerations in Nuclear Medicine**

1:30–3:00 Room 31

**Educational objective:**
To review a variety of current societal concerns impacting medicine in general and nuclear medicine in particular.

**Topics:**
1. Preserving the biomedical research establishment
2. Legislative initiative/AAMC
3. Antitrust and organized medicine
4. Cost of imaging technology
5. Effect of DRG's on imaging procedures

**Summary:**
Multiple societal stress points are impacting with increasing significance on the evolution of health care in this country. Sources of stress include governmental control, legislative initiatives, increasing frequency of litigation, and cost of medical care (including imaging technology). Special attention will be paid to the impact of these societal concerns on the practice of medical imaging.

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**FUNCTIONAL BRAIN IMAGING: NEW RADIOPHARMACEUTICALS**

10:30–12:00 Room 33

**Educational objective:**
To review the history of radionuclide brain imaging techniques for the detection of blood-brain-barrier abnormalities, brain blood flow and cerebral metabolism and receptor distribution with SPECT and PET, with special attention to the chemical development, in vitro and in vivo testing and preliminary clinical experience with the new I-123 and Tc-99m labeled agents for rCBF including HM-PAO.

**Topics:**
1. Early radionuclide brain imaging techniques, Xe-133 for detection of BBB abnormalities, the need for rCBF measurements, and the use of I-123 IMP.
2. Development and testing of HM-PAO.
3. Current and potential clinical utility of rCBF measurement, receptor binding, and metabolic radionuclide studies.

**Summary:**
This session will summarize the history of nuclear medicine, brain scanning techniques, namely Xe-133 washout technique for detection of blood-brain-barrier abnormalities and the new techniques to measure brain function through evaluation of blood flow, cerebral metabolism, and receptor distribution using PET and SPECT. Special attention will be paid to I-123 and Tc-99m labeled agents for rCBF measurements. The chemical development, in vivo and in vitro evaluation of preliminary clinical experience with HM-PAO will be described. The potential applicability of these agents will be discussed.

**Moderator:** R.D. Neirinckx, PhD

**Faculty:**
Neils Lassen, MD, Bispebjerg Hospital, Copenhagen, Denmark; R.D. Neirinckx, PhD, Amersham, Buckinghamshire, England; Peter Ell, MD, Middlesex Hospital, London, England.

**Moderator:** A. Everette James, Jr., J.D., M.D.

**Faculty:**
A. Everette James, Jr., J.D., M.D., Vanderbilt University, Nashville, TN; Otha Linton, M.S., American College of Radiology, Reston, VA; Terry Calvani, J.D., Federal Trade Commission, Washington, DC; Seymour Perry, M.D., Georgetown Institute for Health Care Policy, Washington, DC; Caroline Davis, M.D., Health Care Financing Administration (HCFA), Washington, DC

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**PRESENTATION OF AWARDS, SNM BUSINESS MEETING AND WINE & CHEESE RECEPTION**

5:00–6:00 Room 40

Presentation of Awards by Leonard M. Freeman, M.D., Chairman, Awards Committee and Walter Wolf, Ph.D., President, Education and Research Foundation.

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**COMPUTERS FOR THE COMPUTER-SHY WORKSHOP**

6:00 Location to be announced

(Buses leave from front entrance of the Convention Center after the SNM Business Meeting.)

**Purpose:**
To educate the computer novice in some basic aspects of computer usage and how to use some practical nuclear medicine programs.

**Presented by:**
The SNM Computer Council and Barbara Y. Croft, Ph.D.

(Limited audience, register early on registration form.)

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**MONDAY**

**CONSIDERATION OF IMAGING MODALITIES TO EVALUATE MYOCARDIAL ISCHEMIA DURING STRESS: THE POTENTIAL IMPACT OF EXERCISE ECHOCARDIOGRAPHY**

8:30–10:00 Room 40

**Educational objective:**
We seek simply to familiarize the nuclear physician with the growing body of work supporting the advantages of the
application of echo-Doppler methods for the identification and quantitation of stress-induced myocardial ischemia. These methods will be described and their capabilities noted. Scintigraphic methods will be briefly summarized and a comparison drawn between echocardiographic and scintigraphic methods. The relative clinical utility and specific applications of each technique will be considered.

**Topics:**
1. Stress echocardiography and Doppler methods
2. Scintigraphic methods for the evaluation of stress-induced myocardial ischemia
3. A comparison of echocardiographic and scintigraphic methods and a consideration of their relative clinical benefits

**Summary:**
We seek here to familiarize the audience with the current and potential advantages, as well as disadvantages, of stress echocardiography and Doppler techniques for the evaluation of stress-induced myocardial ischemia. A comparison will be made with other imaging modalities currently employed for this purpose and the relative clinical advantages will be discussed. The specific benefits of application of individual modalities to specific patient subgroups will be considered, and the potential interaction of modalities sought. Finally, issues of cost-effectiveness, diagnostic accuracy and overall clinical utility will be considered as speculation and is given to the developing and future role, as well as the breadth of clinical application, for each modality.

**Moderator:** Elias H. Botvinick, M.D.

**Faculty:**
William F. Armstrong, M.D., Indiana University, Indianapolis, IN; Miguel Quinones, M.D., Baylor University, Houston, TX, Alan Rozanski, M.D., Cedars-Sinai Medical Center, Los Angeles, CA

**Panelist:**
Robert Jones, M.D., Duke University, Durham, NC

An evaluation of noninvasive modalities for the assessment of myocardial ischemia during dynamic stress

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**MONOCLONAL ANTIBODIES IN THE MANAGEMENT OF THE CANCER PATIENT**

8:30–10:00 Room 39

**Educational objective:**
At the completion of the session the attendee should be able to outline the major characteristics of antibody structure and function, define the steps involved in the antigen-antibody reaction and list the major areas of antibody imaging as applied to patient evaluation.

**Topics:**
1. Introduction to immunology—basic concepts
2. Clinical imaging with monoclonal antibodies
3. Appropriate radiolabels
4. Routes of administration

**Summary:**
This session is directed to the clinician and technologist interested in expanding their knowledge of immunology and the application of antibodies to patient evaluation. An in-depth presentation at the introductory level will cover basic concepts of immunology, fundamentals of nomenclature, antibody-antigen reactions and a look at future uses. The session will also include a review of monoclonal imaging applications emphasizing clinical results as function of radiolabel, routes of administration, injected doses, and antibody specificity.

**Moderator:** William D. Kaplan, M.D.

**Faculty:**
Jeffrey Schlom, Ph.D., National Institutes of Health, Bethesda, MD; Ronald D. Neumann, M.D., National Institutes of Health, Bethesda, MD; William D. Kaplan, M.D., Dana Farber Cancer Institute, Boston, MA

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**ACCEPTANCE TESTING AND QUALITY CONTROL OF CAMERAS (INCLUDING SPECT)**

8:30–10:00

**Educational objective:**
To review the performance parameters of scintillation cameras that are appropriate for routine quality and acceptance testings.

**Topics:**
1. Acceptance testing
2. Quality control of scintillation cameras
3. Quality control of SPECT systems

**Summary:**
The performance characteristics of a scintillation camera should be checked upon receipt and periodically thereafter to ensure appropriate performance. The acceptance testing criteria are generally more extensive than those for routine quality control. Quality control on cameras that are used for SPECT imaging include all of those appropriate for planar imaging in addition to those that are unique to SPECT data acquisition. Recommendations for acceptance and QC testing will be presented.

**Moderator:** Paul Murphy, M.D.

**Faculty:**
L. Stephen Graham, Ph.D., University of California, Los Angeles, CA; Anthony R. Benedetto, Ph.D., University of Texas Medical Branch, Galveston, TX; Jon J. Erickson, Ph.D., Vanderbilt University, Nashville, TN

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**KINETICS WITH SINGLE PHOTON EMITTING RADIOTRACERS: I**

8:30–10:00 Room 31

**Educational objective:**
To review the kinetic approach to analyzing images using $^{123}$I-HIPDM and $^{123}$I-IQNB.

**Topics:**
1. The critical analysis of a "chemical microsphere"—HIPDM
2. The effect of the critical analysis of HIPDM on clinical studies
3. The analysis of IQNB data

**Summary:**
HIPDM, an iodinated diamine, has been suggested as a
“chemical microsphere” to measure cerebral perfusion. Other investigators have shown that the constant retention of HIPDM is a result of various balancing factors and is not indicative of a pure “chemical microsphere.” This information will be reviewed and the effect of these complications on clinical studies will be addressed.

Recently, an iodinated ligand that binds to the muscarinic cholinergic receptor has been developed. The pharmacokinetics of 3-quinolciidinyl 4-iodobenzilate (IQNB) will be discussed and estimates made of the binding parameters. These two single photon-emitting radiotracers, one for the measurement of flow (HIPDM) and one for the measurement of a biochemical reaction (IONB) can both be used with SPECT.

Moderator: William C. Eckelman, Ph.D.

Faculty:
Giovanni Luciquani, M.D., Ospedale S. Raffaele, Milano, Italy; B. Leonard Holman, M.D., Brigham and Women’s Hospital, Boston, MA; Ronald Blasberg, M.D., National Institutes of Health, Bethesda, MD

PEDIATRIC NUCLEAR MEDICINE UPDATE

10:30–12:00 Room 33

Educational objective:
Update on pediatric nuclear medicine techniques, urinary tract and skeletal scintigraphy.

Topics:
1. Techniques in pediatric nuclear medicine
2. Urinary tract updates
3. Skeletal scintigraphy update

Summary:
Pediatric nuclear medicine techniques differ in many aspects from adult routine techniques. Not only immobilization of the patient and resolution play a vital role in obtaining meaningful results but the spectrum of diseases and many protocols are different. The nuclear medicine physician has to be familiar with the techniques and the interpretation of the results.

Renal scintigraphy provides regional functional information with sufficient resolution to achieve specific diagnosis. The use of multiple radiopharmaceuticals, pharmacologic interventions and quantitation amplifies the usefulness of renal scintigraphy in pediatrics. The function and pathology of the ureters is studied during renal scintigraphy and by retrograde methods. Factors such as pressure and volume, which influence the function and pathology of ureters and bladder may be monitored with nuclear medicine techniques.

Bone scintigraphy remains a useful imaging approach for the study of the pediatric patient with musculoskeletal problems. New modalities influence the spectrum and the specific indications of bone scintigraphy. Quantitation techniques, the three phase approach and high resolution skeletal scintigraphy help in making the specific diagnosis of diseases and in studying the normal and abnormal functional characteristics of the growing skeleton.

Moderator: George Sfakianakis, M.D.

Faculty:
James J. Conway, Children’s Memorial Hospital, Chicago, IL; George N. Sfakianakis, M.D., University of Miami, Miami, FL; Howard T. Hartke, M.D., Alfred I. DuPont Institute, Wilmington, DE

Note: The Pediatric Nuclear Medicine Club will convene immediately following this session. Room 33, 12:00-1:30.
Continuing Education

Topics:
1. How to be a successful nuclear medicine physician
2. How to develop a nuclear medicine product
3. Organization of practice finances

Summary:
In order to be a successful nuclear medicine consultant, certain factors must be included as follows: 1) Provide imaging excellence. 2) Be available. 3) Be courteous. 4) Be visible. 5) Give prompt service. 6) Be relevant in your reports. 7) Provide personal contact. 8) Practice cost and price containment. 9) Provide diagnostic accuracy.

Nuclear medicine services should be regarded as a product. Consideration will be given to the development of a quality product, the establishment of the clinical value of that product, and the integration of that product into clinical practice. Such factors as quality control, quality assurance, the nuclear medicine physician as a consultant and an imaging specialist, the non-imaging nuclear medicine services, and the involvement and education of the referring physician will be reviewed. Lastly, certain elements of financial management of the nuclear medicine office will be presented.

Moderator: Howard J. Dworkin, M.D.

Faculty:
Philip Matin, M.D., Sierra Nuclear Medicine Group, Roseville, CA; Lawrence E. Holder, M.D.; Donald L. Holmquest, M.D., Houston, TX

NEW CARDIOVASCULAR TRACERS AND TECHNIQUES ON THE HORIZON

8:30–10:00 Room 29

Educational objective:
To update status of new radiopharmaceuticals suitable for cardiac imaging.

Topics:
1. Clot imaging (antifibrin, anti-platelet antibody)
2. Myocardial damage (antimyosin)
3. Myocardial perfusion (Tc-99m isonitriles)
4. Fatty acids
5. Cardiac SPECT

Summary:
This course is designed to update the current status of new radiopharmaceuticals suitable for cardiac imaging. The emphasis will be on assessment of:
1. Intravascular thrombosis with monoclonal antibodies,
2. Myocardial damage in myocardial infarction, cardiac transplantation, and inflammatory myocarditis with monoclonal antibodies,
3. Myocardial perfusion with technetium-99m isonitrile analogs,

The goals of this course will be to define the clinical utility of these agents and the feasibility of new clinical applications. Cardiac single photon emission computed tomography, with these agents as well as with more conventional agents such as thallium-201, will also be addressed.

Moderator: Harvey J. Berger, M.D.

Faculty:
Harvey J. Berger, M.D., Centocor, Inc., Malvern, PA; H.

BONE DENSITOMETRY

INSTRUMENTATION

8:30–10:00 Room 38

Educational objective:
To summarize the physical principles of bone mineral quantification by photon absorptiometry and to review the available instrumentation with regard to clinical efficacy.

Topics:
1. Summary of absorptiometry modalities
2. Principles of absorptiometry
3. Comparison of instrumentation
4. Discussion of requisite instrumentation specifications with regard to clinical applications

Summary:
Bone mineral density may be measured by planar imaging instruments utilizing either single photon absorptiometry (SPA) or dual photon absorptiometry (DPA) and by CT scanners equipped with appropriate reference standards. SPA is generally applied to appendicular bone sites having minimal interposed soft tissue whereas DPA provides direct access to sites such as the lumbar spine and the proximal femur. The various modalities differ in their inherent precision (reproducibility), accuracy, radiation exposure, and cost. These and other factors, which are reviewed in depth in this session, are particularly relevant to the needs of screening and therapy monitoring and in the selection of appropriate instrumentation.

Moderator: Stuart G. Mirell, Ph.D.

Faculty:
Stuart G. Mirrell, Ph.D., Nuclear Medicine Service/UCLA School of Medicine, Los Angeles, CA; Richard B. Mazess, Ph.D., Lunar Radiation Corporation and University of Wisconsin, Madison, WI; William L. Dunn, M.S., Mayo Clinic, Rochester, MN; Heinz W. Wahner, M.D., Mayo Clinic, Rochester, MN

SIMULTANEOUS IMAGING MEASUREMENTS OF BLOOD FLOW AND RECEPTOR CONCENTRATION

8:30–10:00 Room 31

Educational objective:
To demonstrate the potential of receptor radioligands for simultaneously measuring flow and receptor concentration. To emphasize the importance of separating flow and biochemical effects when analyzing receptor-based images.

Topics:
1. Goals for kinetic models of receptor-based tracers
2. Models need to account for known molecular biopsy
3. Simultaneous measurements of flow & receptor concentration are useful in the clinic
4. New biochemical radiopharmaceuticals require new models that describe dynamic bimolecular processes

William Strauss, M.D., Massachusetts General Hospital, Boston, MA; John McAfee, M.D., Update Medical Center, Syracuse, NY; B. Leonard Holman, M.D., Brigham and Women’s Hospital, Boston, MA

The Journal of Nuclear Medicine
FEDERAL REGULATORY ASPECTS REGARDING THE USE OF INVESTIGATIONAL RADIOPHARMACEUTICALS

Summary:
The presentation will inform the participant of the various FDA regulatory differences between labeled monoclonals and labeled drugs. Further, the presentation will include instructions and requirements (including preclinical) regarding IND submissions and studies carried out under the Radioactive Drug Research Committee. Comments from the NRC and a discussion will be included.

Topics:
1. Introduction, overview, timeframes, unapproved uses
2. Requirements regarding INDs (for drugs)
3. Requirements regarding INDs (for antibodies)
4. Preclinical requirements and clinical protocols
5. Studies carried out under the Radioactive Drug Research Committee
6. The NRC's requirements regarding radioactive investigational drugs
7. Panel discussion and questions

Moderator: Neil M. Abel
Faculty:
Neil M. Abel, Robert West, M.S., Samuel K. Ackerman, M.D., Alfred E. Jones, M.D., Norman L. McElroy, Food and Drug Administration, Rockville, MD

STRATEGIES FOR A SUCCESSFUL NUCLEAR MEDICINE PRACTICE THE CUSTOMER'S PERSPECTIVE

Educational objective:
To have participants understand and appreciate the needs of the people they serve. By understanding and working to meet these needs, practices will improve and grow.

Topics:
1. What the hospital wants from nuclear medicine
2. What referring physicians want from nuclear medicine

Summary:
Almost every book on contemporary management practice stresses the importance of knowing the customer and his or her needs. This presentation is designed to increase your insight into the real needs of the individuals whose decisions result in the growth or decline in the utilization of nuclear medicine services. Presentations by the panelists will express their needs and expectations of nuclear medicine. Subjects addressed will include service, clinical support and financial components.
Continuing Education

Moderator: Henry L. Ernstthal, CAE, Society of Nuclear Medicine, New York, NY

Faculty: will include a hospital administrator, a physician from a department of medicine, a physician from a department of surgery.

Please Note

The Education and Research Foundation of the Society of Nuclear Medicine Technologist Section has presented an award to Gordon E. Wynant, CNMT for his paper “Experimental and Clinical Validation of a Radiouclide Angiographic Method for Assessing Myocardial Dyskinesis.”

Mr. Wynant will make a special presentation of the paper on Tuesday, June 24 at 2:30 in Room 13-14.

WEDNESDAY

RADIONUCLIDE FUNCTIONAL BRAIN IMAGING

8:30–10:00 Room 39

Educational objective:
To review the techniques and radiopharmaceuticals used in development for SPECT imaging of the brain and the data it reveals and adds to the diagnosis of several neurologic diseases (e.g., cerebrovascular disease, dementia, psychiatric disease, seizure disorder).

Topics:
1. The method and use of radioxenon tomographic imaging in cerebrovascular accidents (CVA) and neuropsychiatric disorders.
2. Application of iodoamphetamine SPECT imaging in CVA, seizure disorders and dementia
3. Assessment of the new Tc-99m-labeled amine for cerebral blood flow (CBF) imaging in CVA, and other neurologic diseases

Summary:
Radionuclide conventional brain imaging has all but been replaced by x-ray computed tomography (CT) and NMRI but studies employing positron labeled radiopharmaceuticals and PET imaging has served as a catalyst in developing new gamma-emitting radiopharmaceuticals that normally cross the intact BBB and are readily imaged by SPECT. Xenon-133 has long been used to evaluate rCBF but recent tomographic instrumentation has improved its detection accuracy. The redistribution of the iodoamphetamines may be useful in determining the selection of shunt surgery patients with extracranial carotid occlusion and in differing various forms of organic dementia. The new Tc-99m labeled tetraamine hexamethyl-propyleneamine oxime can be used to monitor the course of infarction and compare its functional changes to the anatomical lesions detected on the CT.

CLINICAL APPLICATIONS OF BONE MINERAL ESTIMATION BY SINGLE AND DUAL PHOTON ABSORPTIOMETRY

8:30–10:00 Room 40

Educational objective:
To provide a sound basis for clinical use of bone mineral measurements to detect bone disease and measure bone response to therapy and disease.

Topics:
1. Peripheral extremity measurements
2. Lumbar spine measurements
3. Hip and femur measurements
4. Epidemiologic inferences
5. Whole body measurements

Summary:
This course is intended to compliment a preceding session on the physical and technical aspects of bone absorptiometry. Succinct discussions of the applications of bone mineral measurement by planar absorptiometry technique will be given by speakers who have long experience with peripheral extremity measurements, lumbar spine measurements, and hip and femur measurements. Site to site correlations will be presented and the bone mineral at each site will be related to osteoporotic fracture prevalence. For the purposes of this discussion, osteoporotic fractures will be defined as fractures occurring in the wrist, spine, hip and ribs with no or limited trauma in individuals who have bone demineralization. Epidemiologic studies offer some insight into the significance of these correlations, the appropriate definition of fracture thresholds, and even the distinction of abnormals from normals. Last, although whole body measurements have not yet enjoyed widespread utilization, early data on the clinical relevance will be discussed with the thought that whole body bone mineral measurements will detect bone disease and measure bone response to therapy and disease.

Moderator: Richard A. Holmes, M.D.

Faculty:
Michael D. Devous, Ph.D., University of Texas, Dallas, TX; David B. Collier, M.D., Milwaukee County Medical Complex, Milwaukee, WI; Richard A. Holmes, M.D., University of Missouri, Columbia, MO; R.D. Neirinckx, Ph.D., Amersham, Buckinghamshire, England

John M. Vogel, M.D., University of California Davis Medical Center, Sacramento, CA; Malcolm R. Powell, M.D., University of Texas, Dallas, TX; Heinz W. Wahner, M.D., Mayo Clinic, Rochester, MI; J. Chris Gallagher, M.D., Creighton University School of Medicine, Omaha, NE

The Journal of Nuclear Medicine
KINETICS WITH POSITRON EMITTING RADIOTRACERS

8:30–10:00 Room 38

Educational objective:
An understanding of methods for the kinetic analysis of neuroreceptor binding studies and their application.

Topics:
1. Modeling of kinetic studies
2. Implementation of kinetic studies
3. Results

Summary:
Kinetic modeling of neuroreceptor binding using positron emitting radionuclides will be discussed. Several different methods requiring different assumptions have been proposed for analysis of these positron emission tomographic (PET) data. These different approaches will be presented and compared. The potential advantages and disadvantages of the different analysis methods will be addressed. Results of studies with these methods in humans will be demonstrated.

Moderator: Martin Reivich, M.D.

Faculty:
Henry Wagner, M.D., Johns Hopkins University, Baltimore, MD; Joel S. Perlmutter, M.D., Washington University, St. Louis, MO

NUCLEAR MEDICINE MILESTONES

10:30–12:00 Room 13

The Historian of The Society of Nuclear Medicine will present a lecture and an interesting collection of historical slides. William G. Myers, Ph.D., M.D., Ohio State University, Columbus, OH
He plans to emphasize the impact of the discovery of radioactivity in Paris, just 90 years ago, and to interrelate it with the discussion of a dozen and a half Nobel Laureates on the emergence of nuclear medicine.

SCIENTIFIC MEETING HIGHLIGHTS

3:00–4:30 Room 40

For the ninth consecutive year, Henry N. Wagner, Jr., M.D., of the Johns Hopkins Medical Institutions, will present his views of papers at the Annual meeting. As in the past, he will relate current advances to previous work and future directions of the field of nuclear medicine.
All Scientific Exhibits to be presented at the 33rd Annual Meeting of the Society are listed by the title and author. Exhibits will be on display in the Washington Convention Center in Washington, D.C. For full abstracts, exhibit numbers and locations, and times for viewing, please consult the Show Directory, which will be distributed on site.

### BONE JOINT

**Posterboard No. 733**  

**Viewbox No. 734**  
OPTIMIZATION OF MR IMAGING OF THE KNEE JOINT. M. Mesgarzadeh, C.D. Schneck, A. Bonakdarpour, A.H. Maurer, L.S. Malmud. Temple University Hospital, Philadelphia, PA

**Viewbox No. 735**  
ANATOMY OF THE WRIST AND CARPAL TUNNEL SHOWN BY MRI. M. Mesgarzadeh, C.D. Schneck, A. Bonakdarpour, A.H. Maurer, L.S. Malmud. Temple University Hospital, Philadelphia, PA

**Posterboard No. 736**  
GASTRIC ACTIVITY ON Tc-99m OXIDRONATE BONE SCANS CAN BE CAUSED BY ISOPROPYL ALCOHOL. E.M. Peterson, J.W. Ryan, and W.B. Martin. University of Chicago, Chicago, IL

**Posterboard No. 737**  

**Viewbox No. 738**  
SKELETAL TUMORS AND INFECTIONS: A COMPARISON BETWEEN MRI AND OTHER MODALITIES. S. Rindsberg, M. Mesgarzadeh, A. Bonakdarpour, A.H. Maurer, L.S. Malmud. Temple University Hospital, Philadelphia, PA.

**Viewbox No. 739**  
GALLIUM UPTAKE IN MYOSITIS OSSIFICANS: POTENTIAL PITFALLS IN DIAGNOSIS. L. Salzman, V.W. Lee, and P. Grant. Lahaye Clinic Medical Center, Burlington, MA and Boston City Hospital, Boston, MA.

**Viewbox No. 740**  
OS CALCIUM BONE MINERAL MEASUREMENTS: AN EVALUATION OF THEIR CLINICAL UTILITY. J.M. Vogel, P.D. Ross, and R.D. Wasnich. Kucikin Medical Center, John A. Burns School of Medicine, Honolulu, HI and U.C. Davis, Sacramento, CA.

**Posterboard No. 741**  
SKELETAL PHOTOPERIC LESIONS IN IN-111 LABELED LEUKOCYTE IMAGING OF PAGET’S DISEASE. William T. C. Yuh, Joan M. Hartnell, Theodore J. Hahn, William H. Blahd West Los Angeles V.A. Medical Center, Wadsworth Division, Los Angeles, CA.

### CARDIOVASCULAR

**Posterboard No. 742**  
RUBIDIUM-82 AND PET FOR EVALUATION AND MEASUREMENT OF REGIONAL MYOCARDIAL BLOOD FLOW AND NONINVASIVE DETECTION OF BIOCHEMICAL DERANGEMENT. E. McKay, E.J. Hoffman, S.C. Huang, M.E. Phelps, H.R. Schelbert. UCLA School of Medicine, Los Angeles, CA.

**Posterboard No. 743**  
FIVE-SEGMENT DISPLAY FORMAT FOR MYOCARDIAL THALLIUM SPECT ANALYSIS: A NEW METHOD FOR "INFARCT MAP". K. Imai, S. Yumikura, T. Ando, S. Saot, Y. Ozawa, M. Hatano, T. Takemoto, H. Abe, R. Kami. Nihon University, Tokyo, Japan

**Posterboard No. 744**  
SINGLE PHOTON EMISSION COMPUTERIZED TOMOGRAPHY OF THALLIUM-201 DURING EXERCISE IN THE DIAGNOSIS OF CORONARY ARTERY DISEASE: COMPARISON WITH QUANTITATIVE PLANAR IMAGING. J.J. Mahman, A. Ian, R. Roberts, and M.S. Verani. Baylor College of Medicine, Houston, TX.

**Viewbox No. 746**  
CARDIAC REJECTION MONITORED BY RADIOISOTOPE BIVENTRICULAR EJECTION FRACTIONS AND WALL MOTION STUDIES. N.L. Martin, D.F. Preston, R.G. Robinson, and M.P. Hlantakoon. The University of Kansas College of Health Sciences and Hospital, Kansas City, KS.

### DOSEMISTRY/RADIOBIOLOGY

**Posterboard No. 753**  
RADIATION DOSEMISTRY OF Sm-153-EDTMP IN HUMANS. K.W. Logan, W.A. Volkert, R.A. Holmes, University of Missouri, and H.S. Truman Memorial Veterans Hospital, Columbia, MO.

### ENDOCRINE

**Posterboard No. 754**  
ASSESSMENT OF THYROID MASS FROM SCINTIGRAPHIC THYROIDAL DIMENSIONS. R.E. Choi, R.P. duCret, S. Roe, H.M. Park, Indiana University, Indianapolis, IN.

**Posterboard No. 755**  
THYROID ABNORMALITIES DETECTED IN PATIENTS WITH PARATHYROID DISEASE: HISTOPATHOLOGICAL CORRELATION WITH DUAL ISOTOPIC PARATHYROID STUDIES. S. Lottenberg, R.C. Brunken, M.E. Phelps, R.A. Hawkins, K.H. Anders, R.K.J. Brown. UCLA School of Medicine, Los Angeles, CA.

**Posterboard No. 749**  
A MICROCOMPUTER IMAGE ANALYSIS SYSTEM: DEVELOPMENT AND APPLICATION TO QUANTITATIVE AUTORADIOGRAPHY. T.J. Hoffman, W.A. Volkert, and R.A. Holmes. Research Service—Harry S. Truman Memorial Veterans Hospital and Nuclear Medicine—University of Missouri, Columbia, MO.

**Posterboard No. 750**  

**Posterboard No. 751**  
OPTIMIZED DISPLAY FOR EVALUATION OF PLANNAR EXERCISE TL-201 WASHOUT AND REDISTRIBUTION. D.G. Pavl, O. Oola, G. Kondos, P. Brandet, M. Gons, Univ. of Illinois Hospital, Chicago, IL and Stanford Univ. Hosp., Stanford CA.

**Viewbox No. 752**  

### COMPUTER AND DATA ANALYSIS

**Posterboard No. 748**  
A MATHEMATICAL LIVER PHANTOM AND ITS APPLICATION TO SYSTEM EVALUATION. E. B. Cargill, R. D. Fiete, H. H. Barrett, W. E. Smith, A. V. Clough. University of Arizona, Optical Sciences Center, and University Medical Center, Tucson, AZ.

**Posterboard No. 747**  
TISSUE MANGANESE LEVEL AS AN INDICATOR OF BIOCHEMICAL DERANGEMENT OF METABOLISM IN MYOCARDIAL ISCHEMIA AND INFARCTION. M.A. Quaife, R.A. Quaife, J.W. Dirksen, R.S. Markin, S.C. Augustine, R.A. Stratbucker. Un. Nebraska Medical Center, Omaha, NE.
MELANOMA. E.L. Kramer, A. Postle, J. Sanger, F. Golomb. Bellevue Hospital/NYU Medical Center, NY, NY.

Posterboard No. 786

PEDIATRICS
Booth No. 787
PLANAR AND SPECT IMAGING OF NEUROFIBROMATOSIS WITH TECHNETIUM-99m DIETHYLENE TRIAMINE PENTAACETIC ACID. G.A. Mandell, H.T. Harcke, C.A. Sharkey, K.M. Brooks, G.D. MacEwen, A.I. duPont Institute, Wilmington, DE.

Posterboard No. 789
NUCLEAR MEDICINE IMAGING OF CO-JOINED TWINS STUDIED AT THE HOSPITAL FOR SICK CHILDREN, TORONTO, CANADA. R. Puntito, D.L. Gilday, M. Green, J. Ash

Viewbox No. 790
AN APPROACH TO INFECTIONS OF THE EXTREMITIES IN CHILDREN (OSTEOMYELITIS OR NOT?). L.E. Swischuk, C.K. Hayden, Jr., H.D. Fawcett, University of Texas Medical Branch, Galveston, TX.

PULMONARY
Posterboard No. 791

Posterboard No. 792

RADIATION SAFETY
Posterboard No. 793
A GUIDE TO BETTER NRC INSPECTIONS. R.E. Burgin and C.C. Casey. United States Nuclear Regulatory Commission, Glen Ellyn, IL.

RADIOPHARMACEUTICAL CHEMISTRY
Posterboard No. 794
A NEW GENERATOR FOR THE PRODUCTION OF PB-212 AND ITS ALPHA-EMITTING DAUGHTERS. R. Atcher, A. Friedman, J. Hines. National Cancer Institute, Bethesda, MD and Argonne National Laboratory, Argonne, IL.

Posterboard No. 795
VOLATILITY OF THERAPEUTIC I-131 SODIUM IODIDE SOLUTIONS FOR ORAL ADMINISTRATION. J. Clanton, J. Seibert and D. Nunn. Vanderbilt University, Nashville, TN.

Booth No. 796

Posterboard No. 797

RENAL/ELECTROLYTE/HYPERTENSION
Viewbox No. 801

Viewbox No. 802

Viewbox No. 803
PRINCIPLES AND PITFALLS OF PERITONEAL SCINTIGRAPHY. L.S. Witanowski, E.J. Urrutia, F.D. Thomas, M.P. Bartlett, R. Kopecky and D. Ewing. Department of Radiology, Division of Nuclear Medicine and Department of Medicine, SUNY Health Science Center at Syracuse, NY.