# Works-in-Progress

Abstracts in this section pertain to papers as Works-in-Progress at the 34th Annual Meeting of the SNM, June 2-5, 1987 at the Toronto Convention Centre, Toronto, Ontario, Canada. Scientific Program Chairman: Paul H. Murphy, Ph.D.

## BONE/JOINT

### Posterboard 837

STERNOCOSTOCLAVICULAR HYPEROSTOSIS: SCINTIGRAPHIC EVALUATION. A. Brassard, G. Bisson, P. Grondin, R.-Y. Lévesque Centre Hospitalier Universitaire, Sherbrooke, Canada.

Sternocostoclavicular Hyperostosis (SCCH) is a rare entity, more common in Japan. Only a few reports have been made in the Nuclear Medicine litterature. We report a retrospective analysis of 7 cases investigated in our hospital, 2 men and 5 women, all caucasian, ranging in age from 23-57 years old of whom 5 had pain and soft tissue swelling in the costo-sterno-clavicular region (CSCR). Dysphonia in one and pain in the right knee and tarsal bones in the other were the presenting symptoms of the other patients. 4 had cutaneous manifestations: palmoplantar pustulosis (2), acnea (1) and psoriatic pustulosis (1). The radiological evaluation of the CSCR in 6/7 pts showed abnormalities compatible with SCCH. The pt with dysphonia had a positive CT-scan of the larynx and the biopsies showed inflammatory changes. Elevated erythrocyte sedimentation rate was found in 6/7 pts. None had leucocytosis. 3 pts had bone biopsies with negative cultures. All pts had a bone scan (MDP-Tc 99m) and showed CSCR abnormalities. 4 had bilateral (asymetrical) lesions. Other sites included: mandible ("beard sign"), vertebra, sacro-iliac joints, tibia, calcaneum, tarsal bone, pubic symphisis and ribs. 3 pts also had a Ga-67 scan that showed generally less bony involvement, sometimes in an incongruent pattern.

In conclusion, the bone scan is a very useful tool in pts suspected of having SCCH: 1) with a typical scan, the diagnostic of SCCH can be made with reasonable confidence 2) in documenting the extent of the disease, 3) Ga-67 scan may be misleading (incongruency with the bone pattern suggesting osteomyelitis) and so its exact role remain to be defined.

## CARDIOVASCULAR—BASIC

### Posterboard 838

OPTIMAL BUTTERWORTH-WIENER FILTERING FOR Tl-201 MYOCARDIAL SPECT. N. HONDA, K. MACHIDA, J. TSUKADA, H. KAIZU, and M. HOSOBA*. SAITAMA MEDICAL CENTER, SAITAMA MEDICAL SCHOOL, KAWAGOE, JAPAN., *SHIMADZU CORPORATION, KYOTO, JAPAN.

The purpose of this study is to determine the optimal frequency characteristic of Butterworth-Wiener filter (BWF) for improving Tl-201 myocardial SPECT image quality. Thirty-two projection images of the phantom containing 11.1 MBq of Tl-201 with 4 different cold lesions were collected during 180-degree arc of a gamma camera. A set of the projection images were processed with each of the 27 BWF's of different characteristics. Twenty-seven sets of SPECT images were reconstructed by Shepp-Logan filtered backprojection after BW filtering. The SPECT images were evaluated for their lesion contrasts and noise level. The optimal combination of the parameters determining BWF characteristics for the data of about 100 counts/pixel at the myocardium is : 1) cutoff of 0.25 pixel, 2)FWHM of 3 pixels, 3) noise/signal ratio of 0.02. The contrast of the largest defect (2 x 2 cm transmural) was 80 % with the optimal BW filtering, compared with 58% with 3 x 3 smoothing, and 72% without filtering. FWHM and noise/ signal ratio affected lesion contrast much less than cutoff frequency. Clinical myocardial SPECT images processed with the optimal BWF showed less noise and sharper delineation of the myocardial contour.

### Posterboard 839

POLAR PRODUCTS ARE FORMED FROM METHYL-BRANCHED FATTY ACIDS BY ISOLATED LANGENDORFF RAT HEARTS.
F. F. Knapp, Jr.,[1] S. Kohlen,[2] J. Kolkmeier,[2] S. N. Reske,[3] M. M. Goodman,[1] K. R. Ambrose,[1] E. B. Cunningham,[1] D. E. Rice.[1] [1]Nuclear Medicine Group, Oak Ridge National Laboratory (ORNL), Oak Ridge, TN, USA, [2]Bonn, West Germany, [3]Aachen, West Germany.

Although β-methyl-substitution of 15-(p-iodophenyl)-pentadecanoic acid (IPPA) interferes with β-oxidation and results in delayed myocardial clearance in vivo, polar products are observed by chromatographic analysis of blood and urine of patients after injection of the 3-R,S-methyl-BMIPP and 3,3-dimethyl-DMIPP analogues. These results suggest alternate catabolic pathways producing short-chain products with subsequent conjugation. Since the behavior of IPPA in isolated hearts and release of p-iodobenzoic acid (IBA) is well known, [I-131]-IPPA and [I-125]-BMIPP or [I-125]-DMIPP dual label studies were performed to evaluate the relative clearance kinetics and analysis of released products in Langendorff rat hearts (n=5): 180-200 beats/min; $pO_2$ 550-650 mm; $pO_2$ 40-45 mm; pH 7.35-7.45; 8 ml/min. Relative rates of clearance correlate with in vivo behaviour (IPPA> BMIPP>DMIPP). Major polar components with the polarity of IBA were observed by TLC in Folch extracted perfusate samples (3-15 min) from IPPA and also BMIPP and DMIPP. These unexpected results suggest polar products may be formed from BMIPP and DMIPP analogues in vivo by unknown mechanisms.

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### Posterboard 840

GATED THALLIUM 201 FOR INFARCT SIZING IN AN ANIMAL MODEL.
A.C. Tweddel, W. Martin, E. Winslow*, J. Campbell*, R. Marshall*, I. Hutton. Department of Medical Cardiology, Royal Infirmary and *Organon Laboratories, Glasgow.

The coronary anatomy of a pig makes it a suitable model for the human situation. Gated Thallium scans were performed prior to and after medial sternotomy as control. In 20 small pigs (11.8 - 16.7 Kg) myocardial infarction was produced by 2 stage occlusion of the left anterior descending coronary vessel. 60 MBq of thallium 201 was injected intravenously 2, 4, 6 or 8 hours post infarction and scans were obtained gated to the electrocardiogram in the anterior and 45° left anterior oblique projections. Infarct size was expressed as a percentage of the whole left ventricle, from the end-diastolic image, as a mean of 2 views. Hearts were then extracted and counted whole, and infarct size estimated. The open left ventricle was counted from both the endocardial and epicardial surfaces and again infarct size was expressed as a percentage of the whole left ventricle. The infarct

size from the opened left ventricle correlated well with the intact heart (r=0.93). In vivo infarct size varied from 15-30% of the left ventricle. Estimated infarct size, in vivo correlated well with both the opened left ventricle and the intact ventricle, but was best from the intact ventricle (r=0.90). In infarcts of greater than 4 hours' duration were successfully stained with tetrazolium and infarct weights correlated well with infarct scans. In conclusion, in the pig model, infarct sizing from gated thallium scans would appear to be accurate. This technique can be performed in humans and holds promise as a method of infarct sizing acutely.

## CARDIOVASCULAR—CLINICAL

### Posterboard 841

THE USE OF ORAL DIPYRIDAMOLE THALLIUM SCINTIGRAPHY (ODTS) TO SCREEN FOR ISCHEMIC HEART DISEASE IN DIABETIC PATIENTS ABOUT TO UNDERGO ORGAN TRANSPLANTATION. RJ Boudreau, JT Strony, JS Schwartz, RP duCret, WR Castaneda-Zuniga, Y Wang, PE Carson, TB Levine, MK Loken. University of Minnesota Hospital and Clinic, Minneapolis, Minnesota.

Myocardial infarction and death following organ transplantation in patients with Type I diabetes occurs frequently (9-11%). It is extremely important to identify these high risk patients prior to transplantation. We have previously investigated TL-201 treadmill stress testing in this group of patients but the results were unsatisfactory due to the low levels of stress obtained. Only 6 of 86 patients reached 85% of their predicted maximum heart rates. We prospectively evaluated the efficacy of ODTS (300mg) to screen for ischemia. Diabetics suffer from gastroparesis and microvascular disease that could make this test less accurate than previously published.

After obtaining informed consent, CA and ODTS were performed, usually within one week of each other. The thallium scans were interpreted blindly by consensus reading. CA's were also read blindly using 75% cross-sectional narrowing as the criterion for a significant lesion. To date 29 patients have had both CA and ODTS with the following results:

| | ANGIO+ | ANGIO- |
|---|---|---|
| T1+ | 15 | 2 |
| T1- | 0 | 12 |

If CA is used as the standard, these results would give the visual assessment of ODTS a sensitivity of 100%, and a specificity of 86%. However, the long term follow-up of these patients will eventually serve as the "gold standard". These preliminary results indicate that ODTS shows great promise to identify high risk patients prior to transplantation.

### Posterboard 842

GATED Tc99m BLOOD POOL SCANS TO STUDY LEFT VENTRICULAR FUNCTION DURING WEANING FROM MECHANICAL VENTILATION. L.Cinotti*, G.Steg, E.Wirquin*, G.Giotto, J-L.Teboul, F.Abrouk, W.Zapol, F.Lemaire. Médecine Nucléaire* et Réanimation Médicale,CHU Henri Mondor,CRETEIL,France

Patients with chronic obstructive pulmonary disease (COPD) and ischemic heart disease can become completely dependent on mechanical ventilation (MV) after an episode of acute respiratory failure. We hypothetized that their unweanable character was due to the hemodynamic stress induced by spontaneous ventilation (SV) causing an acute left ventricular (LV) dysfunction.

We studied 12 patients, before and after a 10 minutes weaning period, using a right heart catheterization and Tc-99m gated scans to measure LV ejection fraction (LVEF). End diastolic volume index (LVEDV) was computed from cardiac index (CI), heart rate (HR) and LVEF. LV relative volume variations were calculated over a LV region of interest after background, decay and acquisition time corrections.

All patients showed a marked increase in transmural wedge pressure during weaning (7.5±5 to 24.5±13 mmHg). CI rose from 3.2±9 to 4.3±1.3 l/min-m² and HR from 97±12 to 112±16 per min. Gated scans showed a significant increase in LVEDV only in 4 cases (from 75.7±19 to 113±17 ml/m²). The other patients exhibited an acute drop in LV compliance (RV encroachment in 4 cases and regional dyskinesia in the other 4). After one week of fluid depletion and vasodilator therapy (blood volume went down from 4.6±8 to 3.6±6 l), weaning was successful in 8 patients.

Isotopic studies help separating mechanisms of acute LV dysfunction in COPD patients with heart disease, explaining weaning failure.

### Posterboard 843

TWO DIMENSIONAL POLAR REPRESENTATION OF CARDIAC SPECT IMAGE-A NEW METHOD TO DISPLAY LEFT VENTRICULAR WALL MOTION. K. Machida, N. Honda, T. Takishima, J.Tsukada, and H. Kaizu. Saitama Medical Center, Saitama Medical School, Kawagoe, Saitama, Japan

A new method was developed to display left ventricular wall motion using two dimensional polar representation of cardiac SPECT image. After intravenous administration of 20 mCi Tc-99m (in vivo labeling of red blood cell), ECG-gated SPECT image of cardiac pool was recorded( 32 directions, 180 degrees ). The short axis images of left ventricle were constructed at end-diastole(EDV) and end-systole(ES). Then the functional images of (ED-ES)/ED were calculated at each compatible slices and displayed in color according to the degree of wall motion. In 20 cases with cardiac diseases this method was applied and clinically useful functional images could be obtained. The area of akinesia or hypokinesia are successfully demonstrated clearly separated from the area of normokinesia. We conclude that this method is useful to show left ventricular wall motion and to evaluate the segment and grade of abnormal wall motion of left ventricle, as bull's eye view of Tl-201 images are useful clinically.

### Posterboard 844

PLATELET DEPOSITION DURING CARDIOPULMONARY BYPASS: EFFECTS OF PROSTACYCLIN. W. Martin, T. Spyt, L Walker*, J. Davidson*, K. McArthur, D.J. Wheatley. Departments of Cardiac Surgery and Haematology*, Royal Infirmary, Glasgow.

Platelet microaggregates are implicated in both cerebral problems and early graft closure following coronary artery bypass grafting. The present study was performed to assess the effects of prostacyclin (10ng/kg/min) on deposition of In-111 labelled platelets in the oxygenator and filter in the bypass circuits. 32 male patients were randomly allocated to placebo and active therapy, and their platelets labelled with 2-4 MBq of In-111 by standard methods and re-injected prior to commencement of bypass. At the end of the operation, the filter, oxygenator and reference standard were counted on a shadow shield whole body monitor large volume counter and a standard widefield gamma camera to quantitate deposition. Results obtained from the 2 counting techniques correlated well (r=0.91, n=26). The mean value for the oxygenator and filter deposition in the placebo group was 9.2 ± 5.0% (mean ± SD) and 4.8 ± 6.1% respectively; in the treated group values were significantly lower at 3.4 ± 2.3% ($p<.001$) and 0.6 ± 0.4% ($p<.05$) respectively. Images gave accurate localisation of deposits within the oxygenator and filters.

In conclusion, platelet deposition within the bypass circuit during coronary artery bypass grafting can be accurately quantitated by In-111 labelled platelets using either a shadow shield whole body monitor or a gamma camera. Significant reductions can be obtained by use of prostacyclin.

**Posterboard 845**

FOCALLY INCREASED THALLIUM UPTAKE BY THE VENTRICULAR SEPTUM: SIGNIFICANCE IN CARDIAC ARRHYTHMIA. M.W. Montgomery, P.S. Sirotta, M.M. Graham, G.H. Bardy, G.C. Adhar, P.J. Kudenchuk, H.L Greene. University of Washington; Harborview Medical Center, Seattle, WA.

In tomographic thallium scans performed on patients with supraventricular tachycardias (SVT) prior to accessory pathway or AV node ablation, we have observed focal regions of apparently increased perfusion in the ventricular septum. To determine whether this is a significant observation, 46 scans were reviewed, comprising 16 patients with Wolff-Parkinson-White syndrome, 7 with atrial tachycardias, 12 with coronary artery disease and 12 others with no perfusion defects on thallium scan.

Four experienced observers graded the relative intensity of septal thallium uptake on a scale of 1 to 5 for each scan, using the reoriented short axis tomographic images only. For each observer at each grading level 2-5 (as the minimum discriminator for positivity), sensitivity and specificity were calculated.

For 89% of scans the observers' intensity grading differed by no more than 2 levels. Receiver operator curves (ROC) identified the best discrimination for presence/absence of SVT at level 2 for 2 observers (sens/spec = 83%/82% and 79%/64% respectively), and at level 3 for 2 observers (sens/spec = 71%/91% and 71%/73% respectively).

These results show that increased septal uptake probably reflects the presence of SVT in these patients. This finding, in these patients with recurrent SVT, may be due to increased perfusion, myocardial hypertrophy, increased metabolism and/or early relaxation in diastole. The potential diagnostic or prognostic value of this finding, however, remains to be explored.

**Posterboard 846**

EFFECT OF SUBOPTIMAL EXERCISE PERFOMANCE ON SENSITIVITY OF THALLIUM CARDIAC IMAGING. W.H. Moore, S.E. Long, R.D. Dhekne, E.J. Ladwig. St. Luke's Episcopal Hospital and Baylor College of Medicine, Houston, TX.

Symptom-limited treadmill stress testing (TMT) is the standard study to evaluate patients for coronary artery disease (CAD). Adjunctive Tl-201 imaging increases the sensitivity of CAD detection in patients performing adequate exercise. Experience has shown that the sensitivity of TMT decreases significantly when the patient's peak heart rate is <85% of the maximum predicted rate (MPHR). We studied the effect of heart rate on sensitivity of Tl-201 SPECT imaging in 70 consecutive patients referred for evaluation of CAD who had cardiac catheterization within 2 weeks of TMT. In this group, the sensitivity of ECG monitoring was 31% and thallium imaging was 88%. Further breakdown of sensitivities by the %MPHR achieved revealed the following.

| %MPHR | 50-64% | 65-74% | 75-84% | >84% |
|---|---|---|---|---|
| # of Pts. | 11 | 17 | 18 | 24 |
| Tl sens. | 86 | 90 | 93 | 87 |

These preliminary results indicate Tl-201 imaging is a sensitive indicator of CAD even in patients reaching levels of stress which are well below those necessary for adequate TMT-ECG interpretation.

**Posterboard 847**

CRITICAL EVALUATION OF AN AUTOMATED SPECT TL QUANTITATION METHOD "COMPARISON WITH SELECTIVE CORONARY ARTERIOGRAPHY". J.C.Price, M.L.Cianci, R.C. Reba, A.G. Wasserman, and W. Kong. George Washington University Hospital, Washington,D.C.

A method of thallium Single Photon Emission Computerized Tomography (SPECT) quantitation recently developed at Cedars-Sinai Medical Center is being evaluated. At this time, the results of 17 patients have been tabulated. Selective coronary arteriography was performed on 14 of these patients and used as a standard. The remaining 3 patients were judged as normal using strict clinical criteria and a thallium stress test. The results follow:

| | Overall | LAD | LCX | RCA |
|---|---|---|---|---|
| TRUE+ | 12 | 3 | 7 | 3 |
| TRUE- | 3 | 8 | 4 | 8 |
| FALSE+ | 1 | 1 | 5 | 3 |
| FALSE- | 1 | 5 | 1 | 3 |

One unusual case involved a patient with a prior apical infarct. The arteriogram was normal but the polar map displayed abnormalities which identified an apical defect, which was confirmed by ventriculography. When the SPECT study is used in a screening mode, for example, abn'l test=any abn'l vessel, there is high sensitivity. However, there is poor individual artery specificity and LCX/RCA overlap may cause single vessel disease to appear as multiple vessel disease.

**Posterboard 848**

REPRODUCIBILITY OF PEAK FILLING RATE MEASUREMENTS EMPLOYING FRAME MODE ACQUISITION WITH CYCLE-DEPENDENT BACKGROUND CORRECTION AND FOURIER ANALYSIS. R.G. Schwartz, J. Benhorin, K. Hopkins, G.A. Wilson, D.A. Weber, R.E. O'Mara and J.F. Richeson. University of Rochester Medical Center, Rochester, NY.

Peak filling rate (PFR) of the left ventricle can be measured employing radionuclide angiocardiography (RNA) with technetium-99m-pertechnetate and may be abnormally low in a variety of pathological cardiac states associated with impaired diastolic filling. However, the reproducibility of PFR measurements by RNA employing frame mode acquisition at different framing rates using commercially available software (TAC-F) which utilizes cycle-dependent background correction and Fourier analysis has not been established. We therefore measured inter-observer variability at both 16 and 21 frames per cycle acquisition rates in 50 consecutive patients (Group A), and also assessed same day, inter-study variability of PFR in an additional 25 patients (Group B). Mean PFR of studies acquired at 16 frames per cycle in Group A (N=28) was 2.24 ± 0.97 end-diastolic vol/sec (EDV/sec). There was an excellent inter-observer agreement of PFR measurements on these studies (R=0.95). In studies acquired at 21 frames per cycle (N=22), mean PFR was 2.33 ± 0.87 EDV/sec and excellent inter-observer agreement was also noted (R=0.95). In Group B, same day inter-study reproducibility of PFR measurements was excellent (R=0.84, PFR = 2.52 ± 1.10 EDV/sec). We conclude that frame mode acquisition with the use of the TAC-F software permits excellent inter-study and inter-observer reproducibility of PFR measurements at both 16 and 21 frames per cycle. These findings suggest the utility of this program for clinical studies.

## COMPUTERS AND DATA ANALYSIS

**Posterboard 849**

MRI-PET CORRELATION USING AN ADJUSTABLE ROI ATLAS A.C. Evans, C. Beil, S. Marrett: Brain Imaging Center, Montreal Neurological Institute, Montreal, Canada

Exact anatomical localization is needed for the proper assessment of brain function with PET, particularly where normal function is disrupted, as in infarcted or neoplastic tissue. Whereas most approaches assume normal cerebral morphometry, this work used individual MRI sets to provide structural information in pathological brains. Using a fast-hardening foam mould with an MRI-PET compatible head holder and a fiducial framework for confirmation of image registration, 18 matched MRI-PET slices, separated by 6mm, were obtained in 4 volunteers to provide an anatomical ROI atlas. Slice correspondence was achieved by superposing PET

slice positions, obtained with a lateral skull X-ray and radio-opaque markers, on to a mid-saggital scan during the MRI slice selection procedure. 410 ROIs, grouped into 62 brain regions, were defined on 18 'pages'. Any page could be called up and subjected to geometric transformation or local re-definition to obtain a customized ROI set for every patient. For 10 patients with ischemic infarction, Huntington's disease or myoclonus epilepsy, 6 matched slices were obtained and the MRI data used to map the atlas ROIs on to the PET data. The method allows rapid analysis of a series of metabolic parameters from one patient using a fixed ROI template and the automatic adjustment of physiological model parameters, e.g. FDG rate constants, with respect to underlying brain structure. We are currently defining volumes-of-interest within the MRI-PET image volume to allow arbitrary slice selection.

## DOSIMETRY/RADIBIOLOGY

### Posterboard 850

KILLING OF HUMAN CANCER CELL WITH CELL-CYCLE PHASE BY IN-111-BLEOMYCIN COMPLEX. D.-Y. Hou, J.V. Ordonez, R.J. Cross, D.D. Ross, and Y. Maruyama. University of Kentucky, Lexington, KY and University of Maryland Cancer Center, Baltimore, MD.

A new In-111-Bleomycin Complex (In-111-BLMC) was superior to Ga-67-citrate for animal tumor imaging. It produced tumor regression in transplanted gliomas, and was effective for killing human small cell lung cancer (SCLC) cells. In-111-BLMC localized mainly in the nucleus and induced bizarre chromosome aberrations in SCLC cells. Efficacy of killing SCLC cells with cell-cycle phase ($G_1$, S, $G_2$-M) was therefore investigated. SCLC cells (N417, H526, NCI) were synchronized by double thymidine (d-Thd, 1 mM/ml) block. The cell-cycle phase distribution of the population was assessed by cell DNA content with flow cytometry. The percentage of cell-cycle phase at each time point were ascertained by gated histogram analysis, and the periods for largest population of S, $G_1$, $G_2$-M phase for cells was determined. Cells were exposed by 0.9% NaCl, BLM (15-20 μg/ml) or In-111-BLMC (30-40 μCi/15-20 μg BLM/ml) for 1 hr at 37°C, and observed for colony formation. The survival of H526 cells for In-111-BLMC group was 71% (highest population for S phase), 46% ($G_1$) and 31% ($G_2$-M). For N417 cells, survival was 25% (S), 20% ($G_1$) and 8% ($G_2$-M) for the In-111-BLMC group; and 33% ($G_1$), 18% (S) and 10% ($G_2$-M) for the BLM group. These results indicated that SCLC cells in $G_2$-M were most sensitive, S phase was the least sensitive to In-111-BLMC; and $G_1$ phase was the least sensitive to BLM. These results provide additional data for planning therapy using In-111-BLMC in cancer patients.

### Posterboard 851

BETA PARTICLE DOSE POINT KERNELS. W.V. Prestwich, McMaster University, and C.S. Kwok, Hamilton Regional Cancer Centre, Hamilton, Ont., Canada L8V 1C3.

Knowledge of the spatial dose distribution produced by beta-particles emmitted from an inhomogeneously distributed source is important in radioimmunotherapy using labelled monoclonal antibodies. The relation between the dose and source distributions is determined by the dose point kernel. Currently tabulated values for this quantity (such as appear in MIRD pamphlet 7) are based upon calculations which ignore energy fluctuations. Progress in developing dose-point kernels for radionuclides based upon previous results of more realistic Monte Carlo calculations is presented here. It is shown that the inclusion of energy fluctuations leads to more disperse dose/point kernels than those presently in use. In the case of P-32, agreement with experimental results is improved. Analytic approximations giving closed form expressions for dose-point kernels both for mono-energetic electrons and beta spectra of specific radionuclides will be discussed.

### Posterboard 852

DOSIMETRY MODELS FOR RADIOIMMUNOTHERAPY. V.K. Langmuir and R.M. Sutherland. University of Rochester Medical Center, Rochester, NY.

One of the major problems encountered in radioimmunotherapy (RIT) is determining the dosimetry when the isotope is not uniformly distributed throughout the tissue. Two theoretical dosimetry models have been developed to aid in both the calculation of dose rates and the choice of the appropriate isotope for RIT. The first model is based on the multicellular tumor spheroid which is being used for the in vitro study of RIT. Dose rates for I-131 and Y-90 have been determined at varying distances in from the surface of the spheroid. The second model, for tumors in vivo, assumes the presence of multiple small blood vessels in parallel with the radioactivity being deposited around the vessels. Dose rates for a single vessel and additive dose rates from multiple vessels have been determined. Initial calculations have made the assumption that all activity is on the surface of the spheroid or the vessel. Future work will study the effects of a decreasing density of radioactivity as the distance from the surface of the spheroid or vessel increases.

These models demonstrate that, for non-vascularized micrometastases over 600μ diameter, Y-90 would be a better isotope than I-131 for RIT, assuming that the viable clonogenic cells are within 250μ of the surface of the tumor. In vascularized tumors, Y-90 would be the better isotope because of the enhanced effect of overlapping dose distributions.

### Posterboard 853

QUANTITATIVE SPECT IN ONCOLOGICAL NUCLEAR MEDICINE. APPLICATION IN DOSE PLANNING FOR RADIONUCLIDE THERAPY. M Ljungberg, S-E Strand, Radiation Physics Department, University of Lund, Lasarettet, S-221 85 Lund, Sweden

In nuclear medicine imaging, SPECT is being used with increasing frequency for routine studies of different organs. A new approach is to use quantitative SPECT for dose planning in radionuclide therapy. The most important parameters to estimate in a dose planning, are described.

Proper dose planning requires an absolute quantification of the activity of the therapeutic radiopharmaceutical uptake in different tissues. In order to calculate the absorbed dose the specific activity (MBq/g) must be determined with high accuracy.

Using SPECT, the specific activity can be determined if the activity in and the volume of the target can be estimated. An essential parameter in SPECT images to consider is the photon attenuation. A new method for attenuation correction based on measured attenuation charts of the actual object is described. Using the attenuation chart, the emission image is corrected pixel by pixel for photon attenuation. With this method it is possible to reduce the margin of error due to attenuation to less than 5% for 140 keV photons.

By using quantitative SPECT with attenuation correction, for dose planning in radionuclide therapy, it is possible to calculate the absorbed dose to the target volume, with an margin of error better that 10%.

## ENDOCRINE

### Posterboard 854

SPECT IMAGING OF THE THYROID. J.J.S. Chen, N.D. LaFrance, R. Rippin, D.W. Koller, P.D. Cole, A.C. Civelek, M.D. Allo, H.N. Wagner, Jr. The Johns Hopkins Medical Institutions, Baltimore, Maryland.

To examine whether SPECT offers advantages over planar imaging, both SPECT and planar imagings of the thyroid were performed in 45 consecutive patients with a variety of thyroid diseases. After the administration of I-123 (n=38), Tc-99m (n=5) or Thallium-201 (n=2), transaxial, sagittal and coronal tomographic images were obtained using a slant hole collimator and 180° sampling. SPECT involves relatively short data acquisition (20 min.) and processing (5 min.) times. Transaxial sections of 6/12 patients with multinodular goiter showed tracheal compression which was confirmed by neck X-ray or surgery in all six cases. The finding of retrotracheal extension of the goiter, shown in transaxial and sagittal slices, assisted in preoperative evaluation. The tracer uptake of 5 palpable nodules with completely normal I-123 planar scan, was increased (n=1), normal (n=3) or decreased (n=1) as compared to the rest of gland on SPECT images. Following thyroid hormone suppression, the nodule with increased uptake and one nodule with normal uptake on SPECT became nonsuppressible and suppressible, respectively, on follow-up SPECT images. 4/4 cold nodules were equally well shown on both SPECT and planar images. Physical exam correlation of nodule location was as important in SPECT as with pinhole studies. Our preliminary observations suggest that SPECT is a useful adjunct to pinhole imaging in the decision-making for managing multinodular goiter and palpable nodule with normal I-123 pinhole imaging.

### Posterboard 855

BONE SCANNING: USE IN DETECTING THE EFFECT OF FLUORIDE IN OSTEOPOROTIC PATIENTS. B.A.Clive, T.A.Bayley, N.D.Greyson, J.E.Harrison, T.M.Murray, University of Toronto Bone and Mineral Group, Toronto.

Sodium fluoride (NaF) treatment for osteoporosis (OP) is associated with a histological bone picture of hyperosteoidosis (HO), i.e. increased percentage of trabecular bone surfaces covered with abnormally thickened osteoid seams. Development of HO appears to be a precursor of an increase in bone mass (measured by neutron activation) and is used as our criterion for adequate F dose. To avoid the necessity of bone biopsy, the value of a bone scan to predict onset of the histologic fluoride response of HO was investigated. Tc-99mMDP bone scans and biopsies were obtained from 13 patients before and after NaF a treatment period (3.25 ± 1.4 years) for postmenopausal osteoporosis. Qualitative assessment of bone scans was performed by a nuclear medicine physician given no clinical information. Two patients had hyperkinetic OP with positive scans pre and post therapy. While on NaF 9 patients developed HO indicative of F response. 9/11 scans predicted the histologic effect. There were 2 false negative scans.

Bone scans appear to be helpful in the diagnosis of fluoride effect in patient with involutional osteoporosis treated with NaF.

The use of bone scanning in the diagnosis of NaF side effects will also be discussed.

### Posterboard 856

PARATHYROID ADENOMA: COMPARISON OF PREOPERATIVE EVALUATION BY RADIONUCLIDE, ULTRASOUND, COMPUTED TOMOGRAPHY AND MAGNETIC RESONANCE TECHNIQUES. W. Erdman, J. Weinreb, P. Weatherall, N. Breslau, W. Snyder, J. Cohn, H. Setiawan. University of Texas Health Science Center at Dallas, Texas.

This study was undertaken to compare the accuracy of non-invasive imaging techniques in the prospective evaluation of surgically proven parathyroid adenomas. Pre-operative Thallium 201-Technetium 99m Pertechnetate substraction studies were evaluated in a blinded fashion and compared to high resolution ultrasonography (US) and computed tomography (CT). Magnetic resonance imaging (MRI) was performed in all patients however the interpreters were not blinded to the previous diagnostic examinations. Thirteen mass lesions found at surgery were correlated with the pre-operative interpretative reports. Nine mass lesions were less than 500 mg (average 236mg) and 4 mass lesions were greater than 500 mg (average 3300mg). In the group with the lesions greater than 500mg the sensitivity was 100% for all of the modalities. The non-specificity was 0% in all cases. The second group consisting of the smaller lesions showed a sensitivity of 57% for nuclear medicine as compared to 75% and 70% for CT and US respectively. The non-specificity was 0% for nuclear medicine as compared to 37% for CT and 16% for US. MRI showed an 83% sensitivity and a 28% non-specificity. We conclude that lesions greater than 500mg are equally well evaluated by all of the modalities. Radionuclide studies are less sensitive to smaller lesions however offer the greatest specificity of the modalities evaluated.

## GASTROENTEROLOGY

### Posterboard 857

GASTRIC EMPTYING (GE) STUDIES IN THE OBESE PATIENT WITH AND WITHOUT THE GARREN INTRAGASTRIC BUBBLE. N. Gemayel, N. Arnstein, L. Laine, H. Cohen, D.C.P. Chen, and M.E. Siegel. USC School of Medicine, Los Angeles, CA.

Double-blinded GE studies using liquid and solid test meals were performed in 15 female obese patients, mean age 40±3 yr and body-mass index 39.5±2 kg/M$^2$. All patients underwent endoscopy; 8 were randomized to receive a 200 cc Garren intragastric bubble and 7 served as controls. Pre- and 2 week post-endoscopy GE studies were performed using 200 µCi In-111 DTPA in 150 cc water for liquid and 2 mCi of Tc-99m sulfur colloid in 2 scrambled eggs for solid meals. The curves were analyzed to yield T½ (min), % residual gastric activity (%RA) at 30 min for liquids and 2 hr. for solids, and time (min) from oral administration to duodenal visualization (DL).

| | LIQUID | | | SOLID | | |
|---|---|---|---|---|---|---|
| | T½ | %RA | DL | T½ | %RA | DL |
| BUBBLE Pre | 19±3 * | 33±5 * | 7±1 * | 73±5 | 27±5 | 30±4 |
| (n=8) Post | 11±2 | 17±3 | 3±1 | 170±80 | 40±8 | 24±5 |
| CONTROLPre | 19±3 | 30±5 | 7±1 | 70±5 | 29±3 | 27±5 |
| (n=7) Post | 19±5 | 35±7 | 7±2 | 73±5 | 32±5 | 29±6 |

* $p<0.05$ pre-bubble vs. post-bubble

All parameters of liquid GE were significantly reduced following bubble insertion. Comparison of patients post-endoscopy revealed a significantly lower %RA in the bubble group as compared to controls. After bubble insertion, 6 of 8 patients developed wide fluctuations in the solid GE curve, making T½ calculation difficult.

In conclusion, the gastric bubble significantly hastens GE of liquids in obese patients 2 weeks after insertion. Although the pattern of the solid GE curve changed after bubble insertion, quantitative parameters of GE of solids were not significantly altered.

### Posterboard 858

IMPROVED DELIVERY METHOD FOR TREATMENT OF HEPATIC METASTASES USING INTRA-ARTERIAL YTTRIUM 90. MJ Herba, FF Illescas, MP Thirlwell, L Rosenthall, PM Bret. Montreal General Hospital, Montreal, Que. Canada

A new improved method of utilizing Yttrium 90 to treat hepatic malignancies by intrahepatic arterial injection was investigated.

Yttrium 89 oxide is incorporated into the matrix of glass microspheres and rendered radioactive as Yttrium 90 following neutron

bombardment. Immediately prior to arterial injection of Yttrium 90, TcMAA perfusion and lung scans are obtained to assess for possible gastric or bowel perfusion or AV shunting to the lungs.

In 3 patients, appropriate catheter embolization was done to redistribute flow in the presence of replaced hepatic arteries or to embolize the gastroduodenal artery to prevent radiation effects in the GI tract. 8 patients (1 primary hepatoma 5 colorectal, 1 carcinoid and 1 islet cell tumor) were treated in Phase I with 5,000 rads to the liver. 3 additional patients with metastatic colorectal ca. were treated in Phase II with 7,500 rads.

Unlike previous reports, no procedural hematological, GI or pulmonary complications occurred. Early follow up studies reveal the liver disease to be stable.

This method of intra-arterial administration of Yttrium 90 is feasable, safe and efficient. Further studies using higher doses are warranted.

## HEMATOLOGY

### Posterboard 859

DETECTION OF FOCAL SEPSIS WITH Tc-99m LABELLED POLYMORPHO NUCLEAR LEUKOCYTES. A.A.Driedger, F. Gojmerac, A.G. Mattar, G.A. Hurwitz and G.J. Morrissey, Department of Nuclear Medicine, Victoria Hospital, London, Ontario.

We have used Tc-99m-HMPAO to label polymorphonuclear leukocytes (PML) of patients referred for leukocyte scintigraphy regarding suspected focal infection. The purpose of this presentation is to demonstrate selected cases from the initial experience which illustrate the advantages and disadvantages of technetium labelled PML compared to In-111 labelled cells and to speculate on the future clinical role of Tc-99m-labelled PML in clinical practice.

Our initial series of 17 cases includes cases of confirmed sinusitis, infected intraabdominal dialysis catheter, osteomyelitis, infected joint prosthesis, avascular necrosis of bone, infected renal cyst,abdominal wall fasciitis, pneumonia, ischemic small bowel and decubitus ulceration.

The major differences in biodistribution between Tc-99m and In-111 are in the variable appearance of Tc-99m in the proximal large bowel after several hours and also of urinary excretion. It is possible that Tc-99m will not completely replace In-111 labelled PMLs in cases of suspected intraabdominal disease, especially those with inflammatory bowel disease.

The potential advantages of Tc-99m PMLs are those of statistically improved images with concurrently reduced radiation dosage. Critically ill patients may be studied with mobile cameras. Definitive interpretation of the studies within 4 or 5 hours is frequently possible.

### Posterboard 860

SCINTIGRAPHIC MODEL FOR EVALUATING FIBRINOLYTIC THERAPY. P. Hollett, I.D. Greenberg, R. Prewitt, R. Papadimitropoulos, I. Hasinoff, and J. Ducas. Health Sciences Centre, Winnipeg, Manitoba, Canada.

Recent advances in fibrinolytic therapy, such as streptokinase (SK) and human tissue plasminogen activator (t-PA) have great potential in the treatment of thromboembolic disease including acute myocardial infarction and pulmonary embolism.

To determine optimal dosage regimens, a canine model was developed which allowed combined scintigraphic, hemodynamic and hematologic monitoring.

Autologous clot was formed by combining dog blood, thrombin and Tc-99m sulfur colloid (SC). This was infused via a femoral vein until multiple pulmonary emboli caused an elevation of mean pulmonary arterial pressure (PAP) to at least 55.0 mmHg.

After stabilization, all ten animals were randomized to bolus therapy with either SK or heparin (HP). With breakdown, the rapid serum clearance of SC allowed very low activity blood samples to be taken for clotting factor evaluation. Lysis was monitored by a mobile gamma camera and computer, and quantified by lung clearance and liver accumulation.

Mean clot lysis after SK 16.4% $\pm$ 7.0% was significantly improved ($p < 0.01$) over HP 7.3% $\pm$ 8.6% as was the drop in PAP to 25.8 $\pm$ 6.4 mmHg vs. 36.4 $\pm$ 5.6 mmHg respectively. Thrombolysis was three times more rapid with SK vs. HP for the first 30 minutes after therapy.

This scintigraphic model allows direct quantitation of clot lysis and shows good correlation with hemodynamic data. For this system bolus SK is superior to HP in inducing clot breakdown. Preliminary work with t-PA will also be discussed.

### Posterboard 861

WBC LABELING WITH Tc-99m HM-PAO. J.G. McAfee, G. Gagne, G. Subramanian, R.S. Schneider. SUNY Health Science Center, Syracuse, NY.

To find out if Amersham and "in-house" preparations of Tc-99m HM-PAO irreversibly label WBC suspensions (similar to brain tissue), their in vivo distribution was compared with In-111 oxine labeled WBC in 3 control dogs, and 15 with E coli abscesses. The leukocyte saline suspensions were prepared before the Tc-99m complexes, and the latter immediately added to the cells for 30 minutes at 37°C. The Tc-99m and In-111 labeled cells were washed and injected IV. Serial blood and plasma samples and camera images were obtained at and prior to sacrifice at 18 hours, tissue concentrations were measured by well counting, and 1 hour blood samples were elutriated to determine the concentration in circulating granulocytes.

With 25 ug, d,l HM-PAO irreversibly labeled $10^8$ WBC in 2 ml in vitro with a yield of 80-90% in saline, 60-70% in plasma, and the label did not wash off by elutriation of blood after circulating 1 hour. The "in-house" meso form of HM-PAO labeled WBC with a yield of 30-40%, and about 20% of the circulating activity was associated with blood cells. However, only a small fraction was not removed from WBC by elutriation.

The detectibility of abscesses on camera images with Tc-99m d,l HM-PAO varied widely, even with the same preparations, and the abscess concentrations by direct assay were usually one third of the In-111 concentrations. Although this is the best Tc-99m agent for WBC labeling we have tested, it quickly deteriorates in aqueous solution, and better quality control will be required for more consistent abscess localization.

## INSTRUMENTATION

### Posterboard 862

A METHOD FOR POST-INJECTION PET TRANSMISSION MEASUREMENTS WITH A ROTATING PIN SOURCE. RE Carson, ME Daube-Witherspoon, MV Green. National Institutes of Health, Bethesda, MD.

The feasibility of acquiring PET transmission (TR) information after tracer injection using a rotating pin source was studied. A combined transmission/emission (TR+EM) study is taken, followed by an emission (EM) scan, used to subtract the EM counts from the TR+EM data. The ratio of EM count rate (FDG brain scans) to TR count rate (5 mCi pin) is less than 5% compared to 50-100% for a ring. Furthermore, sinogram windowing, which rejects most randoms and scatter, also eliminates most EM counts.

To test the method, a device was constructed to hold a pin source (1x2x15 cm) at 60 positions on the circumference of the Scanditronix PC1024-7B tomograph.

A 20 cm phantom with 3 internal regions (air, lucite, and water with twice the background activity) was studied. The emission count rate was 50% higher than average FDG brain studies and the pin activity significantly lower than 5 mCi due to decay (a worst case condition). 60 blank scans and 60 TR+EM scans were acquired with the pin source, followed by an EM scan. Attenuation data were produced by subtracting the EM data (after correction for decay and pin attenuation) from the TR+EM data, and windowing. Regional TR and EM measurements from the pin study were within 2% of values derived from conventional TR ring measurements with less than a 10% increase in SD. Without subtraction of the EM data, attenuation values were underestimated by 8-17%. This study demonstrates that quantitative TR measurements can be made with a TR+EM scan and a rotating pin source.

**Posterboard 863**

THE IMPORTANCE OF COLLIMATOR HOLE ALIGNMENT IN CALCULATING SPECT CENTER-OF-ROTATION. M. Cerqueira, D. Matsuoka and G. Harp, VA Medical Center and University of Washington, Seattle, WA.

Single photon emission computed tomography (SPECT) requires exact alignment between the electrical and mechanical center of rotation (COR). Collimators must have perpendicular alignment between the collimator face and the holes across the entire field-of-view. Since a single point source measurement of COR examines only a limited area of the field, we tested 7-14 point sources across the entire field-of-view with 4 different collimators - 2 general all purpose (GAPA&B) and 2 high resolution (HRA&B). The mean COR, S.D. and range, in pixels, are:

| | GAP-A | GAP-B | HR-A | HR-B |
|---|---|---|---|---|
| Mean COR | 64.89 | 65.82 | 66.79 | 66.24 |
| S.D(±) | 0.31 | 0.27 | 0.51 | 0.17 |
| Range | 0.82 | 0.80 | 1.36 | 0.47 |

The mean COR for the multiple points was different for each collimator and the range within each collimator varied from .47 to 1.36 pixels. Since misalignment greater than .5 pixels will result in keyhole or ring artifacts, only GAP-B and HR-B are acceptable for SPECT acquisition across the entire field-of-view. Thus, initial acceptance testing of collimators should verify perpendicular alignment between the holes and face across the entire field-of-view.

**Posterboard 864**

**HIGH COUNT RATE IMAGING CAPABILITY AND LINEARITY OF A DUAL CRYSTAL WHOLE-BODY POSITRON TOMOGRAPH.** H. Ostertag, W.K. Kübler, J. Doll, P. Schmidlin, L.G. Strauss, S. Holte*, W. Maier-Borst.
Institute of Nuclear Medicine, German Cancer Research Center, Heidelberg, FRG, *Scanditronix, Uppsala, Sweden.

When using high activities of short-lived radionuclides positron cameras are exposed to very high, and rapidly changing, count rates. The capability of a system to handle these count rates without image distortion and uncorrectable losses is a prerequisite for the quantitative determination of the activity concentrations. The count rate capability of the tomograph was assessed by following the decay curve of $^{13}N$ homogeneously distributed in a water phantom with 20 cm diameter . The initial activity concentration was 10 $\mu Ci/cm^3$. At a total true coincidence rate of $10^5$/s from all three slices (act. conc. 2.4 $\mu Ci/cm^3$) the dead time loss was 10%. Even at the highest activity concentration the reconstructed image of the 20 cm phantom was without artifacts. Possible distortions of both spatial resolution and linearity were tested at high count rates using line source patterns of $^{64}Cu$-wires distributed in the whole field of view (52 cm diam.) and an additional strong $^{13}N$-source. The reconstructed images at various count rates are presented and discussed.

## NEUROLOGY

**Posterboard 865**

MORPHINE DECREASES REGIONAL CEREBRAL GLUCOSE UTILIZATION IN HUMAN POSTADDICTS. E. Broussolle, E.D. London, J. Links, D.F. Wong, R.F. Dannals, H.N. Wagner, Jr., L.R. Rippetoe, B. Holicky, R.I. Herning, W.B. Pickworth, F.R. Snyder, N. Cascella, J.K.T. Toung, and J.H. Jaffe. NIDA Addiction Res. Ctr. and Johns Hopkins Univ., Balto., MD.

Regional cerebral metabolic rates for glucose (rCMRglu) provide indices of brain function under various conditions. To further clarify the mechanisms or pathways mediating opioid euphoria, we initiated a double-blind, placebo-controlled, crossover study to determine the effect of morphine (M) on rCMRglu by the PET [F-18]fluorodeoxyglucose (FDG) method. Seven men (21- 45 yr) with a history of opioid abuse completed the study. EEG and subjective responses (self-reports on questionnaires, visual analogue scale) to 15 & 30 mg M and placebo (P) i.m. were recorded on 4 test days before PET. The subjects underwent two FDG scans, with 30 mg M or P 15 min before FDG. Rates of rCMRglu were measured in 22 brain regions. M generally reduced rCMRglu, with significant reductions (10-15% from P) in 8 regions (anterior cingulate cortex, superior and middle frontal gyri, insula, amygdalohippocampal complex, midbrain, putamen, medial thalamus; Hotelling's $T^2$ = 43.234, $p \leq .0001$). M did not alter arterial blood gases or pH at the FDG injection time, indicating that rCMRglu decreases did not result from hypercapnia. A significant correlation was obtained between temporal pole rCMRglu in the M state and integrated euphoria scores during the FDG incorporation period ($r = -.80$, $p = .05$). The results indicate M-induced decreases in cerebral oxidative metabolism and have implications for neuroanatomical substrates of opioid euphoria.

**Posterboard 866**

N-ISOPROPYL-[I-123]-P-IODOAMPHETAMINE IN EVALUATING PRECLINICAL AIDS RELATED DEMENTIA. M.S. Humayun, N.D. LaFrance, G. Pearlson. The Johns Hopkins Medical Institutions, Baltimore, MD.

The clinical syndrome of AIDS in general and HIV+ status in patients in particular is becoming of increasing concern in clinical medicine. In addition to opportunistic infections and certain malignancies, an HIV dementia behaving similar to an Alzheimer's dementia, but occuring in a more rapid temporal sequence, is thought to occur in HIV+ patients with AIDS. To further evaluate this finding we tested the hypothesis that a perfusion related brain agent might be helpful in the evaluation of preclinical AID's related dementia. After the IV administration of 5 millicuries of N-Isopropyl-[I-123]-p-Iodoamphetamine (IMP), two patients having recently been identified as HIV+ and having no neurological or physical exam complaints, and two age and sex matched controls were studied using tomographic acquisition. The SPECT images were reconstructed and subsequently qualitatively and quantitatively analyzed [the latter was accomplished using Von Schulthess' noninvasive quantification equation and assumptions (G.K. Von Schulthess, et al. Regional quantitative noninvasive assessment of cerebral perfusion and function with N-isopropyl-[I-123]-p-iodoamphetamine. J Nucl Med, vol. 26, Jan. 1985)]. The preliminary results suggest marked assymetries between right and left occipital lobes (the mean difference between right and left occipital lobes in the patient population = 14.5

counts/pixel compared to 1.9 counts/pixel in normal controls). These results suggest that tomographic iodoamphetamine studies may be a sensitive measure to evaluate the preclinical dementia in HIV+ patients.

**Posterboard 867**

180 DEGREES FACIO-VERTEX-OCCIPITAL BRAIN I-123 IMP SPECT. K. Machida, H. Honda, T. Takishima, J. Tsukada and H. Kaizu. Saitama Medical Center, Saitama Medical School, Kawagoe, Saitama, Japan

In order to save scan time of I-131 IMP brain SPECT, we performed 180 degrees facio-vertex-occipital SPECT (FVO) in 18 cases with normal and cerebrovascular diseases. And those SPECT images were compared with conventional 360 degrees transaxial SPECT images. After intravenous administration of 4mCi of I-131 IMP, in 180 degrees FVO, data were collected from 32 directions and each image was recorded for 30 seconds, and in 360 degrees conventional SPECT data were collected from 64 directions and each image was recorded for the same 30 seconds.

Five doctors analyzed the quality of images for each parts of brain, that is frontal, parietal, temporal, occipital lobe, brain stem and cerebellum, and classified the quality of images into excellent, good and poor, and read the both images separately.

It was found that there was no significant difference in the quality of images and in sensitivity and specificity of diagnosing abnormal findings between both methods. We conclude 180 degrees FVO is useful and could be used clinically for I-123 brain SPECT.

**Posterboard 868**

USE OF UPTAKE KINETICS TO IMPROVE SPECT IMP BRAIN IMAGING. H.T. Pretorius, D.S. Rimkus, and W.A. Dillon. University of California, San Diego, CA.

Current brain imaging protocols with I-123 iodoamphetamine (IMP) have relied on reports of rapid uptake of intravenously injected IMP from the cerebral circulation and achievement of stable brain activity within 30 minutes. We found very different kinetics in certain patients, and computer correction for these kinetics has improved their SPECT images.

Our technique involved imaging of patients injected with 3 to 4 mCi (111 to 148 MBq) IMP in a quiet room with immediate dynamic acquisition of counts over the head or the lungs. SPECT imaging began at 30 to 40 minutes post injection.

The period of 40 minutes was definitely not sufficient to obtain stable cerebral activity in all cases. For example, one hypothyroid did not develop stable activity for over 100 minutes. In fact, this patient's brain activity increased by 12.3% from 35 to 103 minutes. In another patient who had a similarly prolonged cerebral uptake, the release of activity from the lungs was slow, with a half time of 64 minutes. We estimated that in as many as half of all our patients (n=20) such effects would have a significant impact upon validity of the SPECT brain image reconstruction. To compensate for such effects, we applied an exponential correction to the acquired images based on an estimate of the washin rate from the SPECT acquisition data. If uncorrected, delayed uptake may result in reconstruction artifacts, which would be of special concern in quantitative analysis.

**Posterboard 869**

COMPARISON OF SPECT IMAGING USING Tc-99m HM-PAO TO HEAD CT IN STROKE AND TIA PATIENTS. P.K.Rehm, E.O.Smith, S.L. Bridgers, L.Soldano, I.G.Zubal, A.Gottschalk and P.B.Hoffer, Yale University, New Haven, CT

SPECT imaging using Tc-99m HM-PAO (Ceretec), a new cerebral blood flow radiopharmaceutical was compared to head CT with respect to identification of abnormalities. 13 patients (4f,9m) ranging in age from 53-83 with a clinical diagnosis of transient ischemic attack (5), stroke (7) or both (1) were studied. All patients except one had both studies within 5 days of each other. All HM-PAO studies on patients with TIAs were done more than 48 hours and all CT's except one were done less than 48 hours after the episode. In stroke patients all HM-PAO studies were done more than 5 days after onset of symptoms. 20 mCi Tc-99m HM-PAO were administered i.v. in each patient; 360° SPECT imaging was performed using 64x64 matrix resolution. SPECT images were analyzed visually; areas of decreased activity were identified as lesions. Conventional CT criteria were used as a standard for comparison. On the basis of the overall reading of the HM-PAO study on each patient, there were 5 TP, 6 TN, 1 FP, 1 FN (sens. 83%; spec. 86%). On a lesion-by-lesion basis in the stroke patients, there were 5 TP, 3 TN, 1 FP, 0 FN (sens. 100%; spec. 75%). The "false positive" finding was an example of crossed cerebellar diaschisis. In the TIA patients there were 0 TP, 4 TN, 1 FP, 1 FN (sens. 0%; spec. 80%).

We conclude that SPECT imaging using Tc-99m HM-PAO shows good correlation with CT evidence of stroke. The relative insensitivity of HM-PAO in TIA patients probably results from the transient nature of the abnormalities.

**Posterboard 870**

TRANSITION FROM ICTAL TO POSTICTAL STATES DEMONSTRATED BY Tc-99m-HMPAO BRAIN SPECT. E. SUESS, W. LANG, I. PODREKA, J. ZEITLHOFER, M. STEINER, and L. DEECKE. Neurological University Clinic Vienna, Austria.

This study is in progress to investigate rCBF patterns related to ictal and postictal states in patients with partial complex seizures. SPECT studies were started 15 minutes after iv. injection of 20 mCi Tc-99m-HMPAO. A double head rotating scintillation camera equiped with HRES collimators was used. In all patients (n=4) the isotope was injected at the onset of the seizure. Successive SPECT studies were performed in different time intervals when the patients did not show any clinical and electroencephalographic equivalents of seizure activity. All ictal SPECT studies showed patterns of rCBF increase corresponding to the clinical symptomatology indicating both, the origin of seizure activity, its spreading to adjacent cortical areas as well as to distant brain regions via neuronal pathways. In spite of the absence of ictal signs, successive SPECT investigations (3 to 4 days later) showed still an increase of tracer deposition, but only in the focus and adjacent cortical areas. Late SPECT studies (4 to 12 days after the seizure) revealed hypoperfused brain regions corresponding to the seizure focus. These results obtained in four patients indicate that regional hyperperfusion can be detected despite absence of seizure symptoms. This phenomenon might be related to persistent pathologic neuronal activity, which seems to be blocked or compensated by unknown mechanisms and, therefore, remains clinically inapparent.

**Posterboard 871**

IMAGING OF SEROTONIN 5-HT2 RECEPTORS IN THE LIVING HUMAN BRAIN USING N1-([11C]-Me)-2-Br-LSD: A MORE SELECTIVE RECEPTOR LIGAND. D.F. Wong, J.R. Lever, P.R. Hartig, R.F. Dannals, V. Villemagne, A. Wilson, H. Ravert, J. Links, U. Scheffel, B.J. Hoffman, H.N. Wagner, Jr. Johns Hopkins Med. Inst., Balto., MD.

N1-([11C]-Me)-2-Br-LSD (11C-MBL) selectively labels serotonin 5-HT2 receptors (SR) in vivo in mice (J. Nucl. Med. P27, 1985). We have now examined the kinetics of 11C-MBL in baboons and human beings with and without ketanserin blockade. The cerebellum was used to correct for non-specific binding. Without blockade, high levels of activity were observed in the frontal cortex in accord with the known distribution of SR. Administration

of ketanserin (0.5 mg/kg/i.v.) prior to 11C-MBL resulted in a significant decrease in the ratio of activity in the frontal cortex to cerebellum (FR/CB) which suggests selective labeling of SR in baboon brain. PET studies were performed in 5 normal human volunteers utilizing 11C-MBL (15mCi; 0.1 μg/kg). At 45 min. p.i., FR/CB ratios ranged from 2.7 for a 34 y.o. male to 1.2 for a 52 y.o. male. Multiple dynamic scans and plasma sampling allowed the application of kinetic modeling to these studies. In FR, the K1/k2 ratio ranged from 0.2-0.6 while the bound/free ratio (k3/k4) ranged from 0.5 for the 52 y.o male to 1.0 for the 28-35 y.o. males. These FR/CB and rate constant values are comparable to those obtained in studies of SR with ([11C]-N-methyl) spiperone (11C-NMSP); however, caudate/CB for 11C-MBL were 2-3 fold lower than for 11C-NMSP which suggests selective labeling of SR in caudate. Thus, the selectivity of 11C-MBL for SR over α-1 adrenergic and D2 dopamine receptors will prove advantageous for studies of SR in brain.

**Posterboard 872**

C-11 AND I-125 IODOBENZAMIDE: A NEW LIGAND FOR PET AND SPECT IMAGING OF D2 DOPAMINE RECEPTORS. D.F. Wong, A.A. Wilson, R.F. Dannals, H.T. Ravert, R. Gungon, V. Villemagne, J. Links, H.N. Wagner Jr. Johns Hopkins Med. Inst. Baltimore, MD.

We have carried out the radiolabeling, rodent biodistribution and preliminary baboon imaging of I-125 and C-11 iodobenzamide (IBZ), synthesized with high specific activity (avg. 350 and 1570 Ci/mmole, resp.). Distribution studies in mice with C-11 IBZ (2 μg/kg injected) and with I-125 IBZ (0.07 μg/kg) demonstrate a maximum striatal/cerebellum ratio approximately 4 to 1 at 90 minute post injection. Striatal dissociation of the tracer had a t 1/2 of 33 min. One mg/kg haloperidol (HAL) pre-injected IV resulted in significant blockade of the uptake of the tracer of 74% at 45 min. post injection. The striatal unblocked and blocked activity curves of the C-11 and the I-125 compound were essentially superimposable, while frontal cortex uptake was low. In baboon studies with C-11 IBZ maximum uptake in the striatum occurred 20 minutes post injection, which were comparable to those with C-11-3-n-methylspiperone. Competition studies with HAL 1 mg/kg injected 49 min. post injection (PI) in a second PET study demonstrated specific displacement of the C-11 IBZ with an increase in dissociation rate of >20% compared to the control PET scan. The studies show that IBZ can be used to image D2 dopamine receptors in vivo and allows equilibrium state modelling. Its kinetics are comparable to C-11-raclopride. Furthermore, since it can be labeled isotopically with either C-11 or I-123, studies can be performed with both SPECT and PET with this new ligand.

**Posterboard 873**

INTRAOPERATIVE MONINTORING OF CEREBRAL BLOOD FLOW (CBF). W.L. Young, I. Prohovnik, T. Wang, J.W. Correll, P.O. Alderson. Columbia University, New York, N.Y.

To determine the feasibility of regional (r) CBF monitoring using Xe-133 during operative procedures on the cerebral circulation, rCBF determinations were performed on 20 patients (pts) during carotid endarterectomy. For intraoperative use in surgical procedures where physiologic conditions change rapidly, rapid determination of rCBF is necessary. The most commonly employed methods for determining rCBF such as the Initial Slope Index (ISI) are compartmental models that require at least 10 minutes of data collection. Accordingly, we comapred the ISI derived from 2 such compartmental models (ISI-1, ISI-2) and 1 non-compartmental model, the Wyper index, which requires only three minutes of clearance monitoring. Data were collected from 20 pts after approximately 20 mCi of Xe-133 in saline was injected i.v. for each measurement. All pts were under general anesthesia. The rCBF device consisted of 5 Na-I detectors per hemisphere and an end-tidal gas detector. Flow values for the 10 detectors were averaged for each measurement to obtain a global mean value for rCBF. Data were analyzed from a total of 83 measurements. The rCBF values ranged from 7 to 50 ml/100g/min (mean values 23-25,SD=1.6-1.7). The values determined by the 3 methods correlated closely ($r>0.94$, $p<0.001$). The slopes of the regression lines (between 1.101 and 0.068) also were similar. The results indicate that the rapid, non-compartmental Wyper index is well suited to provide information about intra-operative changes in cerebral perfusion.

## NUCLEAR MAGNETIC RESONANCE

**Posterboard 874**

ISCHEMIC VERSUS NON-ISCHEMIC HEART FAILURE: DIAGNOSIS BY P-31 NMR. P.G. Carlier, M.D. Jacobstein, R. Gilles, and T.A. Gerken. Case Western Reserve University, Cleveland, OH, and Université de Liège, Belgium.

We were interested in determining if P-31 NMR spectroscopy can distinguish heart failure caused by inadequate supply of energy precursors (O2, glucose) from cardiac depression resulting from negative inotropic drugs or cardiotoxins, i.e. ethanol (ET).

P-31 NMR spectra and physiological parameters were collected from Langendorff perfused rat hearts. The first protocol consisted of five 12 min steps: baseline, insult 1, recovery, insult 2, recovery. Group 1 hearts were subjected to ET first and anoxia second while Group 2 hearts were studied in the reverse order. ET depressed cardiac function in a dose-related manner until cardiac arrest occurred in both groups. The inorganic phosphate/creatine phosphate ratio (Pi/CP), an index of phosphorylation status, remained normal during ethanol infusion (ET:$0.16\pm0.15$ vs baseline:$0.21\pm0.13$; NS). In contrast, Pi/CP increased during anoxia in each group ($1.29\pm0.85$;$p<0.001$) as function progressively decreased. Anoxia was more detrimental after ET (Group 1) than before ET (Group 2) ($1.71\pm0.89$ vs $0.87\pm0.58$; $p<.05$).

In a second protocol, we depressed cardiac function by using different combinations of ET and anoxia while maintaining cardiac function at 30% of baseline. We found the Pi/CP ratios varied over a wide range, from 0.33 to 4.54, demonstrating a dissociation between cardiac mechanics and high energy phosphate status.

In conclusion, P-31 NMR spectroscopy can distinguish hypoxic contractile failure from that due to negative inotropic cardiotoxins.

**Posterboard 875**

EARLY DETECTION OF CARDIAC HYPERTROPHY BY F-19 NMR. P.G. Carlier, R. Gilles, T.A. Gerken, M.D. Jacobstein, and G.L. Rorive. Université de Liège, Belgium, and Case Western Reserve University, Cleveland, OH.

Myocardial polyamine levels increase at a very early stage during the development of cardiac hypertrophy. Ornithine decarboxylase, the rate-limiting enzyme of the polyamine pathway, is specifically blocked by difluoromethylornithine (DFMO), a "suicide" inhibitor. This study was to determine whether myocardial levels of DFMO could be detected by F-19 NMR and would reflect the intensity of the cardiac hypertrophy process.

Rats received DFMO in drinking water; cardiac hypertrophy was induced in some of them by catecholamine injections. After 2 and 4 days, heart fragments were taken and studied by NMR on a spectrometer operating at 9.4 T. The F-19 NMR spectrum of DFMO shows 8 peaks at 8.77, 8.92, 9.52, 9.70, 14.23, 14.39, 14.99 and 15.12 p.p.m. relative to freon. Spectra of the cardiac samples were obtained in 20 min (500 scans). DFMO levels were

2.50±.71 higher in rats having received catecholamines than in control, unstimulated animals (n=8 in each group, p<.001). Wash-out studies revealed that this difference could not be accounted for by DFMO accumulation in the vascular space.

One of the earliest biochemical changes in the course of cardiac hypertrophy is the activation of the polyamine pathway, that can be blocked by DFMO. The in vitro data show that the cardiac levels of DFMO are increased in the hypertrophying myocardium after a short-term, oral administration of non-toxic dose of this compound. As the acquisition time is short, F-19 NMR of DFMO might be useful in vivo for very early and non-invasive detection of cardiac hypertrophy.

### Posterboard 876

MRI AS A DETECTOR OF EARLY HEART TRANSPLANT REJECTION IN RAT MODELS. R.J.Kurland*, S.Kelley*, J.West*, J.D.Shoop* E.A.Carr†, J.M. Bergsland†, M.Carrol†;*Geisinger Medical Center, Danville, PA 17822; †SUNY/Buffalo School of Medicine and V.A. Medical Center, Buffalo, NY 14214.

To determine the most useful MRI parameters for indicating early cardiac transplant rejection, we are carrying out MRI studies on the following model. Heterotopic heart transplants are given to male Lewis rats by established procedures (1). Previous studies (2) have shown that rejection in allograft transplants for this model are evident at 5 to 6 days post-transplantation, whereas isografts do not usually reject at this time. Male or female ACI rats are donors for allografts, and male Lewis rats for isografts. MRI studies (1.5 Tesla) have been done at 5 and 6 days post-transplantation on 13 rats (to date) to determine the relaxation times T1 and T2 and the effect of the contrast agent GdDTPA. Histological examinations of the transplanted hearts, obtained from animals sacrificed after the MRI exams, provide graded measures of rejection. T2 values of the transplanted heart (measured in vivo) correlate well with histological rejection grades, while T1 values do not. GdDTPA is effective in showing rejection: the intensity increase of rejecting transplants, following injection of GdDTPA, is much greater than for non-rejecting hearts.

(1) K Ono and ES Lindsay (1969): J.Thor.Cardiovasc.Surg. 87, 913-919.
(2) JM Bergsland et al (1987): Fed.Proc. 46, 1115.

### Posterboard 877

THE USE OF GADOLINIUM LABELED HUMAN SERUM ALBUMIN FOR QUANTITATIVE CEREBRAL BLOOD FLOW MEASUREMENT USING MR IMAGING. A. Najafi, E. G. Amparo, University of Texas Medical Branch, Galveston, Texas.

Paramagnetic metal chelates, such as gadolinium DTPA have been studied as contrast agents for magnetic resonance imaging. We have begun a series of studies using Gd-DTPA human serum albumin (Gd-DTPA HSA) to develop techniques for functional imaging of cerebral blood volume. HSA was coupled with 5 x 40 molar ratio of DTPA bicyclicanhydride in 5 steps in 1.0N phosphate buffer pH = 7.0. After each step the pH was adjusted back to 7.0 by addition of dilute sodium hydroxide. An aliquot sample of this protein was first labeled with In-111. HPLC analysis using size exclusion column chromatography on the labeled protein showed a coupling efficiency of about 8 percent with little polymer formation. The rest of the DTPA coupled HSA was dialyzed twice against 0.1 N phosphate buffer pH = 7.0. The dialyzed product was than labeled with "Carrier Added" Gd-153 gadolinium citrate. Electrophoretic analysis on this product showed 1) all of the gadolinium is bound to HSA and 2) little high molecular weight protein was present. "Carrier Added" Gd-153 Gd-DTPA HSA is currently being used for measurement of CBV in rats using a 4.7 T NMR scanner.

## ONCOLOGY

### Posterboard 878

RADIOIMMUNOTHERAPY OF LYMPHOMA WITH FRACTIONATED I-131 LYM-1: PHASE I/II STUDY. S.J. DeNardo, G.L. DeNardo, L.F. O'Grady, D.J. Macey, S.L. Mills, J.P. McGahan, A.L. Epstein, J.P. McGahan. U.C. Medical Center, Sacramento CA and U.S.C. Medical Center, Los Angeles, Supported by CA. DOE Grant #DE FG03- 84ER60233.

In order to develop effective radioimunotherapy for patients with B-cell lymphoma we initiated a phase I/II trial of intravenously injected I-131 Lym-1, an IgG2a MAb produced against African Burkitt's lymphoma, and labeled at one I/Ab with immunoreactivity greater than 80%. Ten patients with aggressive lymphoma who had failed standard Rx have been accessed, and greater than 40 doses of I-131 Lym-1 have been delivered, at 2 to 6 week intervals, 2 to 9 doses per patient, up to 300 mCi. Each treatment consisted of 5 mg unlabeled Lym-1 immediately prior to 30 -60 mCi of I-131 Lym-1 (3-6 mg). Tumor volumes were followed by CT and caliper measurements. Seven of ten patients had objective tumor regression of greater than 30%, and three of these patients greater than 75% tumor regression. Three patients expected to live less than 6 months are clinically well 6-20 months after access to the protocol. No toxicity ocurred; one patient had transient myalgia and nausea temporally related to tumor response. There was no change in liver or renal functions. One patient developed HAMA after three doses.

Calculated tumor dose has ranged from 10-200 rads per mCi, whole body dose from 0.3-0.5 rads per mCi, marrow dose from 0.5-1.0 rads per mCI. The lack of toxicity and the documented tumor response, suggest this to be an effective approach for treating B-cell lymphoma.

### Posterboard 879

EXPERIENCE WITH THALLIUM-201 IMAGING IN HEAD AND NECK CANCER A.H. El-Gazzar, H.M. Abdel-Dayem, R. Halker, H. Kubasik, M.Jamil, A. Rageb, S.M. Abdul-Rahim, A.Mahmoud, Y.T. Omar. Dept. of Nucl. Med., Fac. of Med., Kuwait Univ., Kuwait Cancer Control Center, Kuwait.

Advanced head and neck cancer (H & N Ca.) has not achieved significant improvement in 5 year survivals inspite of aggressive combined surgical, chemo and radiotherapy. Evaluation of response to treatment (Trt), detection of residual tumor, local and distant metastasis is a clinical problem. Thallium-201 chloride has been used for tumor imaging. It has the advantage over Ga-67 of better sensitivity and early imaging. The aim of our presentation is: (1) to show the normal appearance of Tl in the H & N region in a group of patients imaged for non malignant reasons. (2) To show examples of H & N Ca. patients before Trt., with residual tumor after Trt. and with recurrent tumors or distant metastasis. (3) Negative Tl uptake in inflammatory lesions in the H & N.

We evaluated Tl-201 in a group of H & N Ca. patients excluding thyroidal region. All were imaged in the ant. projection after i.v. injection of 2 mCi Tl-201 chloride. Data were acquired in dynamic modes every 5" for 300" followed every 1' for 60'. Static images in ant., Rt & left laterals for 10' each were then acquired. In all Tl-201 was positive for residual, recurrent tumor or distant bony metastasis.

We conclude that Tl-201 is a useful imaging agent in H & N Ca. cancer to evaluate response to therapy and in verifying the presence of local recurrence or distant metastasis.

### Posterboard 880

THE ASSESSMENT OF Tc-99m-HMPAO AS A BRAIN TUMOUR IMAGING AGENT. AT Irvine, MA Flower, JW Babich, S Fielding, A Fullbrook and VR McCready. RMH, Sutton, Surrey UK.

It is well documented that computed tomography (CT)and angiography demonstrate both good anatomical detail and pathological vasculature of brain tumours. However angiography is invasive & CT gives little information about the physiology of tumour circulation. Contrast

enhancement at CT not only reflects vascularity but also alteration in the blood brain barrier. The purpose of this study was to evaluate the uptake of the cerebral blood flow tracer Tc-99m-HMPAO in patients with pathologically proven gliomas. Ten patients were studied using SPECT imaging, performed 15 minutes after the administration of 15-20 mCi of Tc-99m-HMPAO. A comparison of tumour perfusion patterns was made with CT appearances; specifically, the size of the tumour, its pathological characteristics i.e. (well defined, ill-defined, cystic or necrotic) along with the degree of contrast enhancement. Five out of six lesions greater than 2cm were identified, while only one of four tumours less than 2cm were seen. We found a correlation between increased tracer uptake and increasing tumour size. Ill-defined tumours took up tracer more readily than contralateral normal tissue, compared with well defined lesions. There was no specific relationship with tumour uptake and contrast enhancement. The oedematous area around the tumour showed decreased uptake while necrotic or cystic areas exhibited no uptake. These results suggest that Tc-99m-HMPAO can distinguish between tumour and oedema. In addition, it appears most gliomas have an increased nutritional perfusion suggesting that the increased vascularity seen on angiography does in fact reflect increased metabolic demand. This has implications both for radiosensitivity and drug delivery.

### Posterboard 881

**I-123 IMP AND MALIGNANT MELANOMA**

P.Lecouffe, G.Demonceau, P.Delvoye, C.Foucher, M. Deveaux, X.Marchandise, G.Merchie. Associated Service of Nuclear Medicine, Lille, FRANCE - Cyclotron Center, Liège, BELGIUM

The aim of this study was to assess the usefulness of N-isopropyl-(I-123)-p-iodoamphetamine (I-123 IMP) in melanoma as previously reported by HOLMAN and WADA.

I-123 IMP studies were performed in 32 patients : 6 had ocular melanoma and 7 had cutaneous nevocarcinoma; a nevocarcinoma had been excised in 12 patients, 9 with metastases; in addition 7 patients with benign cutaneous lesions (6 ulcers and 1 case of benign nevus) were studied. Total body and localized images were obtained in each patient at 3 hrs after i.v. administration of 100 to 150 MBq of I-123 IMP ; delayed images (24 hr) were often obtained. In addition, a kinetic study was performed on 14 patients : dynamic acquisition during 90 min was followed by serial static images and a blood pool study (370 MBq of Tc-99m labeled RBC).

We observed a significant uptake of I-123 IMP by only 1 ocular melanoma and a slight asymmetry in 3 patients. None nevocarcinoma was imaged (but in one case, an uptake around the tumor). Metastases were visualized in 4 of 9 patients. The scan was normal in the case of benign nevus and in all patients excised without metastase. Moreover, all patients with ulcer showed I-123 IMP uptake in their lesion. The best time for imaging was different according to localization.

These data on large series did not show a clear usefulness of I-123 IMP in management of melanoma. Debatable specificity adds to a low sensibility which is altered by an important physiologic noise. Uptake seems to us mostly vascular and inflammatory. There is lack of correlation between the uptake, and the tumor type (SSM, NM, ...), the tumoral size or a previous chemotherapy. Studies were positive when evolution was pejorative, but reverse was not true.

### Posterboard 882

POSITRON IMAGING OF NEUROBLASTOMA TUMORS WITH I-124/ I-123 LABELLED MONOCLONAL ANTIBODY 3F8.

F. Miraldi, A.D. Nelson, M.S. Berridge and N-K.V.Cheung. University Hospitals of Cleveland, Cleveland, OH.

In previous studies we showed that tumors with surface antigen GD2 can be successfully imaged with I-131 labelled monoclonal antibody 3F8. The advantages of cross-sectional imaging and, in particular, the potential for positron techniques to obtain quantitative pharmokinetic data led to this study.

Some commercially purchased I-123 contains I-124 as a contaminant (approximately 4%). 3F8 labelled with the I-123/I-124 isotopes using a modified chloramine T method retained its immunoreactivity and was intravenously administered to nude rats bearing xenografts of neuroblastomas. Planar images were obtained at 24 and 48 hours using scintillation cameras set for the I-123 peak and positron images were obtained on the Scanditronix SP 3000 using the annihilation gammas from I-124. Planar images with the I-123 show excellent uptake and delineation of the tumor similar to those previously shown with I-131 labelled 3F8. The I-124 images correspond well with the planar images, but show considerably more detail. Using standard positron techniques, accurate quantitative dosimetry and pharmokinetic data is obtained more easily than with planar techniques.

### Posterboard 883

IMMUNOSCINTIGRAPHY OF A HUMAN OVARIAN TUMOUR IN THE NUDE MOUSE USING In-111 LABELLED MONOCLONAL ANTIBODY.

*R.M. Reilly, †K. Sheldon, *G.N. Ege, †A. Marks. †Banting and Best Department of Medical Research, University of Toronto, *The Princess Margaret Hospital, Toronto, Ont., Canada.

This study was carried out to evaluate monoclonal antibody 10B for immunoscintigraphy of carcinoma of the ovary. 10B which reacts with 36% of epithelial adenocarcinomas of the ovary was labelled with In-111 to a specific activity of 40-80 KBq/ug. The immunoreactive fraction of In-111 10B was 30% as measured by a cell binding assay against a human ovarian adenocarcinoma cell line (HEY). Ten N:NIH(s)/nu mice bearing subcutaneous HEY tumours were injected intravenously with 2.6 MBq/50 ug of either In-111 labelled 10B or control antibody 2G3. Whole body images were obtained at 4-96 hours p.i. The animals were then euthanized and the biodistribution of the In-111 antibodies determined by scintillation counting of various organs.

The tumours were visualized well at 24 hours p.i. with In-111 10B but not with In-111 2G3. At 96 hours tumour uptake for In-111 10B was 16.23 ± 6.06% and for In-111 2G3 was 4.64 ± 2.03%. Other organs which showed uptake of In-111 10B were liver (10.50 ± 2.63%), intestine (3.86 ± 1.19%) and kidneys (3.23 ± 0.83%). Analysis of the images by computer showed that maximum tumour uptake occurs at 24-48 hours p.i. then remains relatively constant.

We conclude that In-111 10B can specifically image a subcutaneous human ovarian tumour grown in the nude mouse and the kinetics of uptake indicate that the optimum time of imaging is 24-48 hours p.i.

### Posterboard 884

RADIOIMMUNOSCINTIGRAPHY IN EYE MELANOMA

K. Scheidhauer, G. Leinsinger, E. Moser, U. Schumacher, A. Markl, O. Scheiffarth, and F.H. Stefani Depts. of Radiology and Ophthalmology, University of Munich, FRG

Eye melanoma is generally diagnosed in early stages with a tumor size of less than 10 mm; so this tumor represents a suitable model for in-vivo radioimmunoscintigraphy (RIS) of small lesions. 24 patients with primary eye melanoma were studied. Lesions' size ranged from 3.5 to 12 mm (mean: 7.5 mm) measured by ophthalmoscopy and ultrasound. RIS was performed between 10 and 22 hours after i.v.-administration of 0.2 - 0.3 mg $F(ab')_2$ fragments of an $IgG_{2a}$ monoclonal antibody (MAb: 225.28S), labelled with 400 - 600 MBq Tc-99m. The antibody recognizes a high-molecular-weight melanoma-associated antigen. Specificity of accumulation was studied in two cases by additional injection of a CEA-specific antibody labelled with In-111. Planar scintigrams and SPECT-images were performed using a rotating double head gamma camera with an acquisition time of up to 40 minutes.

17/24 documented intraocular melanomas showed in-vivo accumulation; 13 lesions were visualized by planar images, for the remainder SPECT was necessary. In one specificity test, accumulation of the anti-melanoma MAb was seen, but none of the CEA-specific antibody. The

other one was negative with both antibodies. In the enucleated tumors, the recognized melanoma antigen was also proven by immunohistochemistry.

These data confirm the potential of RIS for specific detection of small (<12 mm) eye melanoma lesions. SPECT improves the results.

### Posterboard 885

CAN THE BIODISTRIBUTION OF A MONOCLONAL ANTIBODY (KS1/4) BE MODULATED BY RADIOPHARMACOKINETICALLY TIMED ADMINISTRATION? J. Shani, S. Mohd, W. Wolf and L.E. Walker, Radiopharmacy Program, Univ. Southern Calif., Los Angeles, CA, and Scripps Res. Inst., La Jolla, CA

KS1/4, a monoclonal antibody (MoAb) specific against the UCLA P3 human lung adenocarcinoma, was radiolabeled with either In-111 or I-131. Studies of the kinetics of the biodistribution of both the intact antibody and its F(ab')2 and F(ab) fragments were conducted in nude mice bearing the human tumor, following both IV and IP administrations. A maximum ratio of tumor-to-blood of 15 was reached on the 9th day of the IV adminstration of the intact antibody. A comparison of the kinetics of clearance of the intact MoAb and its fragments from the whole body and from blood, as well as HPLC analysis of the plasma were carried out. The results obtained revealed the absence of any measurable amounts of either metabolites or of the Ag-Ab complex present in plasma, documenting that the antigen to KS1/4 does not shed into the circulation. Further preliminary results have shown that increased (e.g, doubling) tumor retention of the labeled MoAb can be obtained by preloading the mice with a proper dose of the unlabeled MoAb. This complex effect appears to be controlled not only by the dose, but also by the dose-rate and the timing of administration of the labeled vs the preloading dose, suggesting that proper manipulation of the degree of non-specific binding of the MoAb to the liver and other tissues, as opposed to its specific binding to the tumor, may be kinetically manipulated so as to achieve a more selective deposition of this MoAb in the tumor. Further studies of this model system may provide better tools for greater selectivity in tumor localization of specific MoAbs.

### Posterboard 886

**POSITRON EMISSION TOMOGRAPHY WITH N-13-GLUTAMATE AND F-18-URACIL IN PATIENTS WITH LIVER METASTASES. L.G. Strauss, J.H. Clorius, U. Räth, M.E. Heim, F. Helus, F. Oberdorfer, H. Ostertag, W.K. Kübler, J. Doll, G.Wolber, P. Schmidlin**

Ten patients with liver metastases from colorectal tumors were examined in an ongoing study, to assess tumor metabolism and uptake of the cytostatic agent. All patients were studied prior to the chemotherapy with 5-FU. A positron emission tomograph was used to assess both the N-13-Glutamate, and F-18-Uracil distribution following i.v. injection of the tracers. Serial transversal scans (3 slices simultaneously) were obtained at 5 min intervals for a total of 30 min. Furthermore, late images were acquired 2 hours after i.v. injection of the F-18 labeled Fluoruracil, to evaluate the metabolic turnover. The reconstructed cross sections were quantitatively evaluated using a region-of-interest technique. The Glutamate and Fluoruracil uptake of the metastases was expressed as percentage of the tracer concentration in the normal liver parenchyma. A significant correlation was noted between relative Glutamate and Fluoruracil accumulation in the metastases. These preliminary results indicate, that the uptake of the cytostatic agent may depend on tumor metabolism.

## PULMONARY

### Posterboard 887

I-123 HIPDM HIGH LUNG UPTAKE IN PULMONARY HYPERTENSION: A RAT MODEL. WJ Shih, CM Cotrill, JJ Coupal, MS Shryock. VA and University of Kentucky Medical Centers, Lexington, KY.

The lung as a metabolic organ accumulates a large amount of lipophilic amines. Therefore, lipophilic amines such as I-123 HIPDM may also be used as a pulmonary agent. A well established pulmonary hypertension model in male rats (300-400 gm) was used in this experiment: One sided pulmonary vein constriction was developed by a #24 Jellco plastic sheath as a sizer knot tied encompassing both the Jellco and the pulmonary vein; then the Jellco was removed. Pulmonary-vein-constricted rats at 1,2,4, and 8 wks underwent imaging study using pinhole collimator. Rats anesthetized with IP pentobarbital were imaged in ventral position; lung images were recorded at 5, 15, and 30 min by gamma camera interfaced with a PDP computer. The images of the treated lung in 12 rats demonstrated much higher activity than that of non-treated lung. The activity ratio of treated and nontreated lung was computed and ranged from 1.2-2.2 (average 1.5). The sham-operated group had homogeneous uptake in both lungs and the ratio of left lung to right lung, or reverse is 1. The increased accumulation of the I-123 HIPDM in the treated lung may be hypothesized that induction of pulmonary hypertension by constricted pulmonary vein may activate "receptors" or increase in number of receptors to allow more HIPDM localization in the lung. While pulmonary accumulation of HIPDM is considered a drawback for optimal concentration of brain, I-123 HIPDM as a lung imaging agent may be an ideal agent for detection of pulmonary hypertension. Current noninvasive diagnosis of pulmonary hypertension is sometimes difficult and nonspecific and this radionuclide study using I-123 HIPDM may thus be potentially used.

### Posterboard 888

RADIOAEROSOL CLEARANCE FOLLOWING GRADED DOSES OF OLEIC ACID. D.L. Waldman and D.A. Weber. University of Rochester School of Medicine and Dentistry, Rochester NY.

Oleic acid pulmonary emboli in experimental animals provide a model for acute lung injury that resembled acute respiratory distress syndrome. The sensitivity of the radioaerosol clearance procedure to measure respiratory epithelial permeability was evaluated in the rat following graded I.V. doses of oleic acid. Oleic acid was prepared in different concentrations using propylene glycol as a solvent. Doses of 6.0, 12.5, 25.0 and 40 mg/kg were given to 4 groups of 8 animals each. There were two control groups. One received 0.2 ml of propylene glycol; the other was a sham control. Tc-99m DTPA radioaerosol clearance was measured 1 day prior to injection. Clearance from the lungs was evaluated with NaI(Tl) probe. Static compliance and histologic sections were obtained in each animal.

The radioaerosol clearance in the lungs showed a dose dependent decrease in aerosol clearance half-times (14-40% decrease) compared to control values immediately following oleic acid administration. The rate of aerosol removal is best described by the sum of two exponentials in the treated animals as compared to one exponential in the control animal. One day following oleic acid injection, biologic half-times increased significantly and static compliance decreased, on day 7 both approached control levels. Histologic studies showed severe damage in oleic acid treated animals. The results indicate that radioaerosol clearance from the lungs may provide a useful index of injury and repair in the respiratory epithelium in this animal model for lung injury.

## RADIOPHARMACEUTICAL CHEMISTRY

### Posterboard 889

TECHNETIUM-99m MERCAPTO SUCCINYL TRIGLYCINE COMPLEX: A POTENTIAL RENAL FUNCTION AGENT. L.R. Chervu, K.K. Bhar-

gava, S.B. Chun, and M.D. Blaufox. Albert Einstein College of Medicine, Bronx, NY.

Mercaptoacetylglycyl-glycyl-glycine ($MAG_3$) based on triamide monomercaptide tetradentate set of donor groups is reported to yield a Tc-99m complex which has renal clearance similar to I-131 hippuran. The tedious method of preparation and purification of the Tc-99m-$MAG_3$ complex by HPLC prior to its clinical use is the main drawback for this agent. The synthesis and biological properties of mercaptosuccinylglycyl-glycyl-glycine ($MSG_3$) is herewith reported as a replacement for $MAG_3$ for forming Tc-99m complexes.

$MSG_3$ is prepared by reacting equimolar amounts of glycyl-glycyl-glycine and S-acetyl-mercapto succinic anhydride in DMF overnight and crystallization from water and structure confirmed by CHN analysis and NMR. Stable Tc-99m complex with this agent is readily achieved via Sn(II) reduction and reacting with 2 mg of the complexing agent at room temperature. Radiochemical purity is established by ITLC and HPLC. The percent administered dose data (mean $\pm$1 SD) of Tc-99m-$MSG_3$ in mice at 120 minutes post injection in blood, GI tract, kidney and liver are $0.5\pm1.5$, $1.5\pm0.2$, $1.8\pm0.5$ and $1.1\pm0.2$ respectively whereas corresponding values of Tc-99m-$MAG_3$ are $0.3\pm0.05$, $6.6\pm1.6$, $1.1\pm0.7$ and $0.3\pm0.06$ respectively. Preliminary experiments on single injection clearances for Tc-99m-$MSG_3$ in rats yield data comparable to those of I-131 OIH.

HPLC separation is not required for Tc-99m-$MSG_3$ preparation unlike in the case of TC-99m-$MAG_3$ complex and this offers a definite advantage in a clinical setting. The present results suggest the potential use of $MSG_3$ and its derivatives for complexing with Tc-99m for renal secretory function studies.

### Posterboard 890

N-HYDROXYSUCCINIMIDE-HIPPURAN ESTER: APPLICATION FOR RADIOLABELING OF MACROMOLECULES. L.R. Chervu, S.B. Chun, and K. K. Bhargava. Albert Einstein College of Medicine, Bronx, NY.

Specific antibodies labeled with radioiodine are widely used for visualization of tumors and metastases. A major problem encountered with radio-iodinated antibodies for imaging of tumors and metastases is the deiodination of the macromolecule. This would lead to relatively high circulating levels of iodine activity in blood masking the tumor uptake particularly at early imaging intervals. A method of coupling labeled hippuran (OIH) via the N-hydroxysuccinimide ester to macromolecules and its application is reported here which would reduce the high background levels.

The N-hydroxysuccinimide ester of OIH (OIH-OSU) is prepared by reacting molar equivalents of OIH, N:N-disuccinimidyl carbonate and pyridine in DMF overnight. The OIH-OSU active ester is isolated with 87% yield in pure form: M.P.186-187°C, CHN analysis and NMR spectroscopy. The active labeled ester is obtained using high specific activity OIH in a similar synthetic protocol. Conjugation of OIH-OSU to human serum albumin is effected by incubating the reactants (10:1 mole ratio) for half an hour at room temperature followed by purification of the labeled protein on a Sephadex G-100 column or dialysis at 5°C with an activity yield of 44.3%.

Organ distribution in mice and rats for the labeled albumin preparation when compared with commercial RISA shows identical biodistribution. However, at 4 hr circulation time, urinary excretion of radioactivity for the labeled preparation is greater than that of RISA reflecting the rapid urinary clearance of the OIH moiety released into the blood stream. HPLC analysis of urine confirmed the presence of the active OIH metabolite.

Further work based on the OIH labeling method for radioiodo labeling of antibodies for diagnostic nuclear medicine applications is in progress.

### Posterboard 891

MYOCARDIAL PERFUSION: COMPARISON OF SQ 30217, THALLIUM-201 AND MICROSPHERES IN DOGS. R.E. Coleman, M. Maturi, A.D. Nunn, W.C. Eckelman, F.R.Cobb. Duke University Medical Center, Durham, NC, and Squibb Institute for Medical Research, New Brunswick, NJ.

SQ 30217 [J.N.M. 27 (1986) 893] is a myocardial imaging agent which gives good images of the myocardium in dogs and humans. This study determined the relationship between the distribution of SQ 30217 (SQ), Tl-201 (Tl) and Sn-113 microspheres (MS) in a canine model of ischemia. One week prior to the study, a pneumatic cuff occluder was positioned around the circumflex coronary artery and polyvinyl catheters were inserted into the left atrial appendage and the aortic arch. On the day of the study, the occluder was inflated, 30 seconds later SQ, Tl and MS were injected into the left atrium. Blood was withdrawn using a Harvard pump. 5 minutes after occlusion, the animal was sacrificed. The left ventrical was sectioned into 44 1-2 g samples.

Dogs 1-6 were studied as described, blood flows ranged from 0.004-2.5 ml/min./g, dog 7 received adenosine to increase blood flow. The correlation (r) of flow was determined between MS, SQ and Tl.

| <-Dog-> | <-MS Vs SQ-> | <-MS Vs Tl-> | <-SQ Vs Tl-> |
|---|---|---|---|
| | <----------r----------> | | |
| 1-6 | 93-99 | 98-99 | 91-99 |
| 7 | 90 | 99 | 93 |

We conclude that SQ 30217 and Tl-201 both correlate well with microsphere-determined myocardial blood flow over a wide range of blood flow which extends into the flows commonly experienced during exercise studies.

### Posterboard 892

SYNTHESIS AND EVALUATION OF 6-BROMO-L-DOPA AS A POTENTIAL TRACER FOR CEREBRAL L-DOPA. O.T. DeJesus, M. Wong, and J. Mukerjee, Argonne National Laboratory, Argonne, IL, University of Chicago, Chicago, IL and Princeton University, Princeton, NJ

A previous study has shown that 6-bromo-L-dopa (6-BD) can mimic L-dopa and become part of the dopamine pool in the rat brain (Friedman et al., J. Label. Comp. Radiopharm. 16: 66, 1979). Thus, 6-BD may be a viable alternative to 6-fluoro-L-dopa (6-FD) as a tracer for cerebral L-dopa. In this study, we confirm that the direct bromination of L-dopa with molecular bromine gives 6-BD as the sole product. This identification was made using NMR, mass spectrometry, and HPLC. Although we found that 6-BD is a substrate of an isolated decarboxylase enzyme to form 6-bromo-dopamine, its rate of conversion was measured to be about 260 times slower than that for L-dopa. If a similar relative rate is also true in mammalian brain, 6-BD may be useful in measuring local rates of L-dopa transport similar to the use of the well transported, poorly phosphorylated glucose analogs. Also if a greater fraction of 6-BD crosses the blood brain barrier without the need for a peripheral decarboxylase inhibitor, counting statistics may be better compared to that obtained with the same does of 6-FD. Current efforts are underway in our laboratory to synthesize Br-75 or Br-77-6-BD using electrophilic radiobromine generated *in situ* and the diacetate of L-dopa as starting material. The *in vitro* and *in vivo* characteristics of this radiotracer would be studied in the rat brain before proceeding to PET or SPECT scanning of the dopamine system in the primate brain. Research supported by the U.S. DOE OHER Contract No. W-31-109-ENG-38.

### Posterboard 893

IODINE-125 17$\alpha$-IODOVINYL-11$\beta$-ETHYLESTRADIOL: A HIGH AFFINITY RECEPTOR-RADIOTRACER FOR THE ESTROGEN RECEPTOR. R.E. Gibson, R.N. Hanson*, V. Sood, and R.C. Reba. The George Washington Univ. Med. Ctr., Washington, D.C. 20037 and *College of Pharmacy, Northeastern Univ., Boston, MA, 02115.

Radiolabeled derivatives of estradiol have been used to image estradiol receptor rich tissues, e.g. breast and ovarian carcinoma, and may be used as adjunctive radiotherapy with a suitable isotope which can deliver a high radiation dose to the tumor. Both 16$\alpha$-haloestradiols and 17$\alpha$-iodovinyl-11$\beta$-methoxy estradiol have been shown to localize specifically in receptor rich tissues, but the affinities of these compounds are not sufficient to give high tumor to blood ratios in tumors with low to intermediate receptor concentrations, nor to provide sufficiently long receptor occupancy for radiotherapy. Estradiol derivatives with lipophilic 11-beta substituents have been shown to have higher affinity for the receptor than estradiol (Shook, et al., J. Nucl. Med. 27 [1986] 916). We have prepared I-125 17$\alpha$-iodovinyl-11$\beta$ethyl-estradiol via the tributylstannyl intermediate in high specific activity (S.A. 1500 Ci/mmole) and found its affinity to be 14-fold higher than estradiol. Tissue

distribution studies in female weanling rats (21-25 days old) showed high initial localization (6.9% dose/g tissue, uterus/plasma ratio = 30) at 2 hrs which was blocked 85% by coinjection of 20 μg of unlabeled estradiol. At 24 hrs and 48 hrs post-injection, the concentration in the uterus was 3.7% dose/g and 2.3% dose/g, respectively, with respective uterus to plasma ratios of 51 and 79, indicating good retention. These results are consistent with the potential for tumor imaging and radiotherapy.

### Posterboard 894

A RADIOSYNTHESIS OF F-18-FLUOROMISONIDAZOLE. J. Grierson C. Mathis, E. Shankland, J. Link, Z. Grunbaum, J. Rasey, and K. Krohn. Univ. Washington, Dept. Radiology, WA and Lawrence Berkeley Laboratory, Berkeley, CA.

Misonidazole and its congeners are metabolically trapped in cell that are alive but at low oxygen concentrations. Studies with H-3-fluoromisonidazole (1-(2-nitro-1-imidazolyl)-3-fluoro-2-propanol) have shown the potential of this drug, if labeled with F-18, for imaging hypoxic tissues in tumors, stroke and ischemic myocardium. Recently a report by Jerabek et al. (IJARI, 37:599(1986) has described the radiosynthesis of F-18-fluoromisonidazole in sufficient quantities to permit biodistribution studies. In pursuit of a method for a higher yielding radiosynthesis of this compound we have investigated the F-18 fluoride displacement of glycidyl o-tosylate to prepare F-18 epifluorohydrin and its subsequent nucleophilic ring opening with 2-nitroimidazole to afford F-18-fluoromisonidazole. Exploratory reactions with the stable iosotope F-19 as the tetrabutylammonium salt were undertaken and reaction mixtures examined by F-19 NMR. Reaction TBAF (1 eq) with glycidyl O-tosylate (2 eq) in DMSO (80C, 20min) provided good yields of epifluorohydrin (90%). Further, the synthesis of fluoromisonidazole from epifluorohydrin (1 eq) and 2-nitroimidazole (2 eq) in the presence of 1,8-bis(dimethylamino)naphthalene (0.5 eq) in DMSO (80C, 20min) was efficient and rapid (50%). Radiosynthesis of F-18-fluoromisonidazole from nca F-18-fluoride using Kryptofix 2.2.2/potassium carbonate in DMSO as a one pot-2-step reaction with glycidyl o-tosylate followed by 2-nitroimidazole with 1,8-(dimethylamino)naphthalene at 80C (20min per step) afforded F-18-fluoromisonidazole in 5% radiochemical yield (EOB).

### Posterboard 895

[C-11]N-METHYLATION OF SECONDARY AMIDES BY A CAPTIVE SOLVENT APPROACH: APPLICATION TO THE BENZODIAZEPINES, 4'-CHLORO-DIAZEPAM AND FLUNITRAZEPAM. Douglas Jewett, Leonard Watkins, Keith Mulholland. University of Michigan Medical Center, Ann Arbor, MI.

In the captive solvent approach to radiosynthesis, a substrate to be labeled is dissolved in an appropriate solvent and absorbed in a porous solid in a column. A volatile species carrying the radiolabel is then trapped in the absorbed liquid phase, where the desired reaction occurs. This method has the advantage of requiring a very small amount of solvent, ie., 20-70 μl. Thus the reaction can be done in the injection loop of a liquid chromatograph, followed by direct injection on a column for purification. For the N-methylation of a secondary amide with [C-11]methyl iodide, this results in a synthesis which is particularly easy to do by remote control. In the case of the benzodiazepine, 4'-chloro-diazepam, 20 mg of acrylic yarn is packed in a 3 x 20 mm teflon column. The column is saturated with sodium hydroxide in methanol. After evaporation of the methanol, 1 mg of desmethyl 4'-chloro-diazepam in 70 μl of 5% aqueous acetone is added. The column is installed in the injection loop of a liquid chromatograph. During the radiosynthesis, the loop is maintained at -50°C to trap the [C-11]methyl iodide. The loop is then pressurized with nitrogen to 3 atmospheres to prevent volatilization of the acetone and methyl iodide, and heated at 60°C for 5 min. After cooling, the contents of the loop are injected directly onto an alumina column for final purification. The identical procedure has been applied to the synthesis of [C-11]flunitrazepam. Modifications of the method appear to be applicable to most alkylations of amides and secondary amines with [C-11]methyl iodide.

### Posterboard 896

AUTORADIOGRAPHY OF MONKEY BRAIN WITH SQ 32097: A NEW Tc-99m-LABELED BRAIN IMAGING AGENT. B.L.Kuczynski, D.Silva, T.Feld, C.Ita, R.K.Narra, A.D.Nunn, W.C.Eckelman. The Squibb Institute for Medical Research, New Brunswick, NJ. R.E.Coleman. Duke University Medical Center, Durham, NC.

SQ 32097, [Bis[2,3-butanedione dioximato(1-)-0]-[2,3-butanedionedioximato(2-)0]2-methyl,1-propylborato(2-)-N,N',N'',N''',N'''',N''''']-chlorotechnetium, is a member of the BATO family of neutral lipophilic technetium complexes.

We have used autoradiography to obtain data on the distribution of SQ 32097 in the Cynomologous monkey brain, which is structurally closer to the human brain than the rat but still too small to give high definition SPECT images.

Autoradiographs of 30-40 u sections of brain show excellent substructural detail at 10 minutes post injection with distribution proportional to blood flow. Preliminary standardized optical density measurements of the autoradiographs show a gray/white ratio of 3.9 at 10 minutes.

In monkeys the maximum brain activity is 2.68 + 0.57% ID (n=4) at 5 minutes post injection; pharmacokinetic analysis shows that SQ 32097 has a brain clearance half-time of approximately 85 minutes. In rats it has a Cerebral Extraction Efficiency of >90% at 15 s after intracarotid injection. SPECT images of the calf brain clearly delineate the gray and white matter.

The autoradiographic data show that the distribution of SQ 32097 in the brain is in proportion to blood flow. The properties of SQ 32097 make it a potentially useful agent for cerebral perfusion imaging in man.

### Posterboard 897

Tc99m CITC GABA, A NEW COMPOUND WITH HIGH TUMOR AFFINITY. M.Lichtenstein, D.Goodwin, C.Meares, N.Salehi, M.McTigue, and M.McCall. VA Medical Ctr., Palo Alto, CA; Chemistry Dept., U.C. Davis, CA; Royal Melbourne Hospital, Australia.

We set out to study the biodistribution of Tc99m chelates in tumor bearing mice with and without preinfusions of monoclonal antibodies specific to the chelates.

Five mCi NaTcO4 was mixed with 15 nmole CITC GABA (a conjugate of paraisothiocyanato benzyl EDTA and glycine paraamino benzoic acid) and passed through a polypropylene catheter which had been previously precoated with SnC12 according to the new method of Salehi et al. (JNM, in press).

The product was analyzed by Silica Gel and acetone chromatography as well as paper saline chromatography suggesting > 50% binding with small amounts < 10% of possible colloid and pertechnetate.

Up to 2mCi were injected into Balb/C mice bearing KHJJ tumors and images obtained at 0,1,3,5 and 24 hours; biodistributions at 5 and 24 hours were made.

| | % Dose/gm Mean ± SD N=3 Mice | | | | | | |
|---|---|---|---|---|---|---|---|
| | Blood | Tumor | Liver | Spleen | Gut | Kidneys | Muscle |
| 5 hrs | 1.36 ±.27 | 10.1 ±3.5 | 29.5 ±5.4 | 4.03 ±.49 | 10.6 ±1.62 | 9.6 ±1.25 | 0.45 ±0.25 |
| 24 hrs | 0.6 ±0.14 | 1.43 ±.40 | 4.7 ±1.47 | 2.42 ±2.2 | 0.59 ±0.36 | 6.77 ±1.77 | 0.15 ±.02 |

Images at 4 and 24 hours show the tumor clearly, thyroid faintly, as well as considerable renal, billiary and fecal excretion.

Pre-injection of BA14B6 antibody, specific to the benzoic acid moiety of the chelate, 24 hours prior to chelate injection increased tumor uptake by 1.45 ± 0.35.

### Posterboard 898

A NEW AUTOMATED Xe-123/I-123 PRODUCTION UNIT AT BROOKHAVEN. S. Mirzadeh, L.F. Mausner, and S.C. Srivastava. Brookhaven National Laboratory, Upton, NY.

To improve the yield, purity and availability of I-123 at BNL, a computer controlled, on-line production system of Xe-123/I-123 has been installed at the Brookhaven Linac Isotope Producer (BLIP). The process has been designed to operate with minimum attendance for 6-8 h daily, for five days per week. Reliability and flexibility were the most important criteria used in the design of the system. Close attention was also paid to the design of safety interlocks for personnel and equipment protection. The gas collection setup consists of 60 solenoid valves, 2 mass flow meters, 3 flow controllers, 4 vacuum gauges, 8 liquid nitrogen level sensors, 5 heaters, 3 thermocouples, a metering liquid pump, and 3 radiation monitors. The process is not limited to the production of I-123, but can be used for the production of any radionuclide with sufficient vapor pressure at 25°C, e.g. the Kr-75/Br-75 system. Custom graphics are used to monitor and control the process and are dynamically linked to the system devices. Special features include alarm call-out devices in the case of failures and emergencies. I-123 can be prepared either in 0.01 M NaOH solution or in an anhydrous form adsorbed on the wall of a glass ampoule. Alternatively, the bulk of Xe-123 itself can be shipped. The target, which is compatible with the BLIP, consists of two concentric stainless steel disks housed in a square frame. The inner disk holds the molten NaI target salt and contains heating elements and a thermocouple, and a line for He to flow across the salt surface. The outer disk is primarily for secondary containment and thermal insulation. (Research supported under U.S. Department of Energy Contract #DE-AC02-76CH00016.)

### Posterboard 899

ENTRY INTO FLUORINE-17 (t 1/2 = 65 sec) RADIOPHARMACEUTICALS. ON LINE ELECTROPHILIC SYNTHESIS OF THE BLOOD FLOW AGENT [F-17]FLUOROMETHANE. G.K. Mulholland, G.D. Hutchins, S.A. Toorongian, D.M. Jewett. Univ. of Michigan Medical Center, Ann Arbor, MI 48109

Efforts are underway in this laboratory to develop [F-17]fluoromethane ($CH_3F$) as a very short halflife regional cerebral blood flow (rCBF) agent which might find special value in PET studies of seizure or other transient brain phenomena in which sequential rCBF measurements taken over a short time frame would be the protocol. The positron energies of O-15 and F-17 are the same but the more rapid F-17 decay permits repeat F-17 rCBF images every 6 min as opposed to every 12 min for O-15 agents. Thus F-17 could provide greater temporal resolution.

The approaches under study begin with electrophilic F-17 which we have found is easily produced by the 16-O(d,n) F-17 reaction in large amounts (>1 Ci) through bombardment of $O_2$/<1% $F_2$ carrier in the same nickel gas target system as used in routine 18-$F_2$ production. F-17 and F-18 production have been run consecutively in this system without adversely affecting yields of either radioisotope. The produced F-17 is radiochemically pure and appears to be mainly in the chemical form of $F_2$ based upon several tests including formation of characteristic $F_2$ adducts with t-stilbene and triacetyl glucal, and conversion to [F-17]acetyl hypofluorite. Preparation of [F-17]$CH_3F$ in yields sufficient for animal studies has been achieved by two different on-line approaches, first, by Hunsdiecker-like decomposition of F-17 acetyl hypofluorite and second, by passage of F-17 gas through $CH_3HgCl$. [F-17]Fluoromethane was analyzed by radio-GC on Porapak Q. Labelled $CF_4$ and $NF_3$ were also present but the levels were less than 5% of the $CH_3F$ radioactivity.

### Posterboard 900

FACILE PRODUCTION OF ANHYDROUS F-18 HYDROGEN FLUORIDE DURING COMMITTED DEUTERON BOMBARDMENT SCHEDULES. G. Leonard Watkins, Steve Toorongian, G. Keith Mulholland. Univ. of Michigan, Cyclotron/PET Facility, Ann Arbor, MI.

At our institution the growing use of oxygen-15 and F-18 fluorodeoxyglucose (FDG) in positron emission tomographic (PET) studies of disease states, particularly those in which oxygen extraction and glucose utilization have been uncoupled, e.g. malignant tumors, is placing great demands on available beam time and limiting the choice of particle for bombardment. Currently, our O-15 and F-18 FDG are produced via deuteron bombardment of N-14 and Ne-20, respectively, rather than the alternate proton bombardment of scarcer N-15 and O-18. In order to carry out exploratory chemical studies involving nucleophilic displacement with F-18 fluoride we examined ways of converting the electrophilic F-18 fluorine, obtained via the Ne-20 (d,α) F-18 target used for FDG, into usable fluoride during the frequent idle cyclotron periods in the clinical studies.

We found that if the irradiated target gas on emptying the target is combined with an equal flow of hydrogen, in the radiochemistry laboratory, followed by passage of the mixture through a nickel coil (4.5 ft x 0.125 in i.d.) at 250-300°C, then complete conversion of fluorine to hydrogen fluoride results, as evidenced by the lack of oxidation of potassium iodide. The generated HF can be used directly or trapped in a polyethylene coil at -78°C. The method provides more than adequate quantities of low specific activity fluoride, useful for preliminary radiochemical studies, without the need to change particle or target during idle periods of concurrent clinical studies using deuteron bombardment.

## RENAL

### Posterboard 901

THE DETECTION OF RENAL ARTERY STENOSIS WITH CAPTOPRIL RENOGRAPHY IN PATIENTS ON ANTIHYPERTENSIVE THERAPY. A.N. Ansari, G.L. Hung, M.E. Siegel, C. Lundell, and M. Akmal. University of Southern California, Los Angeles, CA.

Captopril, a converting enzyme inhibitor (CEI), is reported in the presence of renal artery stenosis (RAS) to greatly reduce I-131 Hippuran and I-125 Thalamate excretion after a single dose of 50 mg. Animal work and limited patient studies suggest that the detection of RAS may be improved by noting this phenomenon using Radionuclide Renography (RNR) with Tc-99m DTPA (TC) and I-131 Hippuran (I-131). All studies, however, were performed in a selected population of patients with single RAS and after discontinuing antihypertensive medication (AHM). In that some patients with severe hypertension due to RAS cannot be taken off medication to perform the study, we studied 15 patients still on various AHM except CEI.

Patients had baseline Tc-RNR followed by I-131 RNR. Follow-up RNR were performed within 10 days, patients receiving 50 mg Captopril about 45 min. before the studies.

7/15 patients had an angiography. 6/14 renal arteries were normal angiographically and showed no change in time to peak (TP) on pre and post CEI RNR. 3/14 completely stenosed RA's demonstrated non-functioning kidneys on RNR. 2/14 renal arteries had moderate stenosis (30% and 50%) and increased TP by at least 8 min. between pre and post Captopril Tc-RNR. Two diffusely stenosed intrarenal arteries showed no change on Tc-RNR but significant increase of TP on I-131 RNR. One moderate stenosed RA with high grade stenosis of aorta above and below the RA showed no change in CEI RNR.

The preliminary data on the ongoing project suggests that CEI RNR may be useful in detecting moderate RAS even when patients are on AHM.

### Posterboard 902

RADIONUCLIDE DETERMINATION OF GFR IN CHILDREN. S.E. Long, R.D. Dhekne, E.T. Gonzales, D.R. Roth, B.K. Pounds, and W.H. Moore. St. Luke's Episcopal and Texas Children's Hospitals and Baylor College of Medicine, Houston, TX.

The method derived by Gates for the determination

of GFR has not been well validated in children with either Tc-99m DTPA or Tc-99m glucoheptonate (GHA). Included in the study were 62 children ages 4 days to 18 years referred for renal imaging who had a serum creatinine (Cr) or endogenous creatinine clearance (CrCl) determination. GFR'S were determined using the Gates method (2-3 min time interval and semilunar and extended background ROI'S) and either Tc-99m DTPA or Tc-99m GHA. All patients had GFR's (in ml/min/1.73 mm BSA) estimated using formulae based on Cr, height, and age. Correlation coefficients comparing estimated GFR's and CrCl's with the semilunar/extended ROI's are as follows: < 1 year (n=20) .860/.924; females 1-18 years (n=14) .757/.806; males 1-18 years (n=28) .795/.781; all patients (n=62) .853/.848; DTPA (n=43) .823/.803; GHA (n=43) .860/.882, and CrCl (n=10) .933/.921.

In conclusion, the preliminary data suggest that GFR can be accurately determined in children using the Gates method and that the GFR values obtained do not require correction for BSA.