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CLINICAL EVALUATION OF REGIONAL MYOCARDIAL PERFUSION AT REST AND DURING PACING-INDUCED STRESS. Harry Agress, Jr., Alan S. Pearlman, William R. Brody, Richard W. Myers, Samuel B. Itscowitz, Michael V. Green, James J. Bailey, Gerald S. Johnston, David R. Redwood. National Institutes of Health, Bethesda, Maryland.

Coronary angiography defines anatomic defects in coronary arteries; however, this technique does not define abnormalities of myocardial perfusion. In the present study, a dual isotope technique is described that allows regional assessment of myocardial perfusion at rest and during stress, induced by atrial pacing.

Following coronary angiography in eleven patients with known or suspected coronary disease, Tc-99m labeled human albumin microspheres (HAM) and I-131 labeled macroaggregated albumin (MAA) were injected into the coronary arteries in random order at rest and during atrial pacing (to angina or 85% of maximum predicted heart rate). Scintigraphic images were collected in both the RAO and LAO views with an Anger camera/mini-computer system. Computer processing with image enhancement and EKG gating allowed detailed analysis of regional changes in perfusion. Myocardial images were divided into five areas. Thirty-four areas in eleven patients were normal at rest and pacing. In ten areas, perfusion defects at rest persisted unchanged with pacing, while in five areas such defects became worse with pacing. In six areas a perfusion defect was visible only during pacing. Scintigraphic abnormalities correlated closely with coronary and ventricular wall abnormalities as defined by angiography. Moreover, when a scintigraphic defect was observed that did not change with pacing, its presence and site correlated with the appropriate Q wave abnormalities on EKG. We conclude that this double isotope technique accurately delineates areas of both normal and diminished perfusion at rest and during stress and should therefore provide valuable information in the evaluation of patients with coronary artery disease.

THE USE OF THE BONE SCAN AS AN EARLY SIGN OF DEGENERATIVE ARTHRITIS OF THE KNEE. Naomi Alazraki, Roger Thomas, John Verba, Dale Daniel, Donald Resnick and Richard Greenfield. VA Hospital, San Diego and University of California, San Diego.

Clinical symptomatology and radiographic findings of degenerative arthritis of the knee may occur late in the disease, often after there is severe damage. Very sensitive tests are needed for pre-surgical evaluation for osteotomy, which unloads weight onto the opposite compartment, since success of surgery may depend upon normalcy of the apparently uninvolved side.

The sensitivity of the technetium polyphosphate bone scan in detecting early changes or degenerative osteoarthritis of the knee was compared to the clinical evaluation, plain x-rays, and arthrograms in 60 patients undergoing evaluation for surgery. Disease involvement in each compartment (lateral, medial and patellofemoral) was

graded in each modality by two independent observers trained in each field. Surgical and arthroscopic examination was obtained in 20 joints.

Many of the scans were also recorded on digital magnetic tape and analyzed with a computer program on a Nuclear Data Med II to quantitate degree of uptake in each compartment relative to a normal region of bone background.

The more involved compartments were graded abnormal by all methods. In the less involved compartments, the bone scan was most sensitive to pathology, with the arthrogram second and the plain x-ray third. Clinical examination was least sensitive.

A summary of the findings will be presented along with representative cases.

DETERMINATION OF GLOMERULAR FILTRATION RATE UTILIZING X-RAY FLUORESCENCE OF COLD IOTHALAMATE LEVELS IN PLASMA AND URINE. Naomi Alazraki, John W. Verba, James E. Henry, Richard Becker, Andrew Taylor, Jr., Samuel E. Halpern. VA Hospital, San Diego and University of California, San Diego.

The commonly used indicators of renal function in clinical medical practice give only gross estimates of renal function. Labeled iothalamate is probably the best inulin substitute for practical measurements of glomerular filtration rate. We are proposing the use of x-ray fluorescence to measure the non-radioactive iodine of iothalamate for GFR determinations.

The classical method of GFR determination involves infusion of inulin and measurements of concentrations in plasma and urine. Various simplified approaches to measuring GFR include: the elimination of urine collections by measuring plasma levels of inulin or iothalamate, the elimination of infusion by substitution of a single injection, or utilization of a subcutaneous injection to simulate an infusion.

Because of the sensitivity of the x-ray fluorescence technique for detecting iodine (1 part per million), very small amounts of cold iothalamate may be used with any of the techniques described for measuring GFR. We have tested this technique in dogs, comparing the clearances obtained with cold iothalamate infusions to those obtained with C-14 labeled inulin infused simultaneously. The two techniques, measuring plasma and urine (C=UV/P) showed a high degree of correlation (r=0.99) based on 9 dog experiments with clearances ranging from 20 cc/minute to 100 cc/minute.

We also compared clearances obtained from x-ray fluorescence of iothalamate in plasma alone with classical C-14 inulin clearances calculated from urine and plasma measurements in 9 dogs. The correlation coefficient was excellent (r=0.98). Experiments comparing subcutaneous injection of iothalamate to simulate the infusion with classical measurements of clearances also indicate good correlation.

ABNORMALITIES OF PERFUSION AND VENTILATION-PERFUSION BALANCE IN PATIENTS WITH SURGICALLY CORRECTED TETRALOGY OF FALLOT. Philip O. Alderson, Supot Boonvisut, Robert McKnight, and Alexis F. Hartman, Jr. Washington University School of Medicine, St. Louis, Mo.

This study was designed to evaluate pulmonary perfusion and ventilation patterns in patients with surgically corrected tetralogy of Fallot. Twenty-two children were studied. Each had a Tc-99m MAA perfusion lung scan and 16 also had a Xe-133 ventilation study. The studies were done using a gamma camera interfaced to a small computer, and quantitative analysis of perfusion and ventilation was performed. Pulmonary angiograms were reviewed and the findings were compared with the results of the radionuclide studies. Fifteen of the children had surgical corrections after removal of a temporary aortic-pulmonary shunt (Waterston or Potts-Smith). The interval between installation of the temporary shunt and the complete correction averaged 6 years. The interval between the corrective surgery and the radionuclide study averaged 22 months. Seven children had corrective surgery, but no temporary aortic-pulmonary shunt; 4 had initial complete corrections and 3 had previous Blalock shunts. Asymmetric pulmonary perfusion was found more frequently in the children who had previous aortic-pulmonary shunts ($p < .05$). Decreased perfusion was present in the lung which had received the shunt in 11 of 13 patients. The decrease in perfusion was mild (10-20%) in 4 patients, moderate (20-30%) in 4, and severe (>30%) in 3. Two patients were excluded because Xe-133 studies showed evidence of abnormal ventilation. Xe-133 studies were normal in other patients. Therefore, relative ventilation-perfusion ratios were abnormally high in the lung which received the shunt. The findings suggest that temporary aortic-pulmonary surgical shunts may lead to permanent alterations in pulmonary perfusion. Early complete correction seems preferable in children with tetralogy of Fallot.

THE VALUE OF RAPID SEQUENCE SCINTIGRAPHY IN PEDIATRIC BRAIN SCANNING. Philip O. Alderson, David L. Gilday and Arnold Wilkie. Washington University School of Medicine, St. Louis, Mo. and the Hospital for Sick Children, Toronto, Canada.

The value of rapid sequence studies (RSS) in pediatric brain scanning is disputed. Some feel these studies should be done routinely, while others feel they should be done only in selected cases. To assess the value of RSS, a prospective study was done. 500 children referred for Tc-99m brain scans had RSS, including immediate post injection blood pool images. Standard 4 view static images were performed and delayed views were obtained in many cases. Pertinent history and physical findings were recorded at the time of the scan. Confirmation of scan findings was obtained from other diagnostic procedures including EMI scans, angiography, pneumography, and subdural taps. 97 of 191 children who presented with signs, symptoms, or a history suggesting focal disease (trauma, tumor, A.V.M., C.V.A., focal seizures, a large head, or abnormal transillumination) had positive scans. 70 of these children had positive RSS and in 27 (14.1%) the RSS was essential in making the diagnosis. The RSS was especially helpful in diagnosing hypovascular lesions like porencephaly and in detecting subdurals. Only 23 of 309 children with non-focal presentations (nonfocal seizures, headache, psychomotor retardation, etc.) had positive scans. Ten had a positive RSS and in 5 (1.5%) a positive RSS prevented a false negative diagnosis. The RSS detected hydrocephalus in 3 of these patients, a porencephalic cyst in one, and showed asymmetric cerebral perfusion in the other. RSS are more likely to be positive and more likely to provide essential information in patients whose presentation suggests focal disease. However, if maximum accuracy is desired, RSS should be performed with all pediatric brain scans.

DETECTION AND QUANTITATION OF LEFT-TO-RIGHT CARDIAC SHUNTS IN CHILDREN: A CLINICAL COMPARISON OF COUNT RATIO AND AREA RATIO TECHNIQUES. P. O. Alderson, R.G. Jost, A.W. Strauss, S. Boonvisut, and J. Markham. Washington University School of Medicine, St. Louis, Mo.

A comparison of several reported methods for detection and quantitation of left-to-right shunts by radionuclides was performed in 50 children. Count ratio (C2/C1) techniques were compared with exponential extrapolation and gamma function area ratio techniques. Children were positioned supine under a gamma camera interfaced to a small digital computer. An intravenous injection of Tc-99m pertechnetate was made using the saline flush technique and digitized data frames were collected at 0.4 sec intervals. A pulmonary time-activity curve was generated from an area of interest over the peripheral lung fields and this data

was subjected to each of the methods of shunt quantitation. These results were then compared with standard oximetry determinations. Count ratio calculations were performed by hand using the inspection and 10% methods, and automatically by a short computer formula. The area ratio calculations were performed by algorithms which fit pulmonary time-activity curves with the appropriate mathematical functions. C2/C1 ratios accurately detected shunts and reliably separated shunts from normals, but there was a high rate of false positives in children with valvular heart disease. The exponential fitting method provided more accurate shunt quantitation and a better separation of patients with valvular heart disease than did the C2/C1 ratio. The gamma function method provided a slightly better separation of shunts from valvular heart disease and a more accurate reflection of oximetry values than the exponential method. However, the results of the two area ratio methods were not significantly different when tested statistically. For accurate shunt quantitation and separation of patients with valvular heart disease from those with shunts, area ratio calculations are preferable to the C2/C1 ratio.

BONE IMAGING IN EVALUATION OF JAW LESIONS. John M. Alexander, Abass Alavi, John R. Hansell. Veterans Administration and University of Pa. Hospitals, Philadelphia, Pa.

Because little attention has been given to lesions and conditions involving the jaw it was the purpose of this study to evaluate the comparative findings on radiographs with those on bone scans of common dental lesions.

Thirty patients were studied having a variety of diseases of the jaws utilizing the scintillation camera and the rectilinear scanner. The radiopharmaceuticals used were Tc-99m polyphosphate and Tc-99m diphosphonate. The malignant tumors were cases of squamous cell carcinoma, chondrosarcoma, and multiple myeloma. Included in the benign conditions were fibrous dysplasia, cementifying fibroma, central giant cell lesions, odontomas, various dental cysts and osteomyelitis of the jaws. Also studied were evaluation of bone grafts. The diagnosis were confirmed by tissue biopsies.

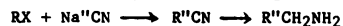
We found the conditions to be detected earlier and more accurately with bone scans than on radiographs. The studies have lead to a better understanding of the pathophysiology, the aggressiveness, and the extent of many disease processes of the jaws.

The nuclear bone imaging proved to be a superior technique for diagnosis and treatment planning of lesions of the jaws.

LUNG UPTAKE AND METABOLISM OF C-11 LABELED ALIPHATIC AMINES. A. Ansari, H. Atkins, J. Briggs, D. Christman, J. Fowler, B. Gallagher, R. MacGregor, A. Wolf, Chemistry and Medical Depts., Brookhaven National Lab, Upton, N.Y.

The uptake and metabolism of C-11 labeled aliphatic amines by the lung as a function of variation in the carbon chain length has been studied preliminary to evaluation of their usefulness in lung scanning and lung function studies.

The C-11 labeled amines were produced in ca. 30% radiochemical yield (not optimized) using the following sequence:



The C-11 labeled C-4 through C-8 amines were synthesized by using alkyl halides (RX) of appropriate chain lengths. The uptake and metabolism of these amines was studied in mice by serial sacrifice and by identification of tissue metabolites and excreted metabolites. The monoamine oxidase (MAO) inhibitor, iproniazid, was used to determine the effect of MAO on amine metabolism.

The results of this study are summarized:

1. Lung selectivity of C-11 aliphatic amines increases with increasing chain length.
2. C-11-n-octylamine is much more selective for lung tissue than are the other C-8 compounds C-11-caprylonitrile and C-11-caprylic acid (prepared by hydrolysis of R¹¹CN).
3. Carbon-11 is largely excreted as ¹¹CO₂ shortly after injection of C-11-octylamine.

4. The $^{14}C_2$ excretion 40 minutes after i.v. injection of C-11 octylamine decreases from 60% in control animals to 8% in animals pretreated with MAO inhibitor.

One of the recently recognized roles of the lung is the regulation of vasoactive substances, many of which are amines (i.e. noradrenaline). This suggests that C-11 octylamine may be taken up and metabolized by the lungs by a similar mechanism to the one(s) responsible for the uptake of these physiologically active amines. Thus the C-11 labeled aliphatic amines may be useful as indicators for this aspect of lung function.

CLINICAL APPLICATION OF THE BNL TECHNETIUM-99m RED CELL LABELING KIT. A.N. Ansari, H.L. Atkins, T. Smith and P. Richards. Brookhaven National Laboratory, Upton, N.Y.

A simple kit method for labeling red blood cells with technetium-99m (J. Nucl. Med. 15: 534, 1974) was used to explore and evaluate various applications of Tc-99m red blood cells. A labeling yield of 97% was regularly achieved and high concentrations of radioactivity of greater than 15 mCi/ml were possible. In four patients, comparison with Cr-51 in a double tagging experiment showed excellent correlation. The ratio of red cell mass determination with the Tc-99m and Cr-51 was 1.01 ± 0.03 at 15 minutes, 0.98 ± 0.03 at 30 minutes, 1.04 ± 0.02 at 60 minutes and 1.09 ± 0.03 at 2 hours.

The Tc-99m labeled cells were used for measurement of ejection fraction in cardiac angiography, for cerebral perfusion imaging (dynamic and static) and for peripheral vascular imaging. Heat damaged red cells were used for spleen imaging. These were prepared by heating at 49° C for 15 minutes.

The ability to label small volumes of red cells was advantageous for two reasons. A comparison of dynamic and static imaging for peripheral vascular studies was possible after a small bolus injection. In spleen imaging nearly 2/3 of the injected dose localized in the spleen with a $T_{1/2}$ of uptake of about 30 minutes. This rapid and high uptake was felt to be due to the small volume of injected cells. Comparison with Tc-99m colloid imaging showed that the labeled cells allowed a much clearer presentation of the spleen without interference from liver activity.

RATE OF Tc-99m PYROPHOSPHATE CONCENTRATION IN MYOCARDIAL INFARCTS AND BONE. James S. Arnold, W. Earl Barnes, Leon Frazin, and Ervin Kaplan. Hines V.A. Hospital, Hines, Illinois.

Since Bonte et al. reported that recent myocardial infarcts can be visualized by Tc-99m pyrophosphate, the problem of differentiating between infarct and overlying ribs has been frequently mentioned. If the rate of activity concentration or release were different for bone and infarct, the two should be distinguishable on the basis of their differences in behavior as a function of time.

Since the rate of Tc-99m pyrophosphate buildup in bone and infarcts had been not measured in man, we first developed suitable technics to make these measurements from sequential images in the course of performing routine myocardial infarct scans as described below.

With patients supine, the camera was positioned for a left anterior oblique view, images were collected in the form of 100 X 100 matrices at 1 minute intervals for up to 60 minutes, and stored on a digital magnetic disc using an Elscint CDP-2 data collection and processing unit. Areas of interest were defined for sternum, rib, right and left ventricles, as well as abdominal background. Using a small computer, the data for each area of interest was corrected for blood and body wall contribution, as well as decay, and plotted.

The shapes of the bone and infarct Tc-99m uptake curves were comparable differing only in magnitude. The kinetics are consistent with an irreversible binding of Tc-99m on mineral surfaces from perfusing blood.

The above technics of measurement and data reduction are currently being validated in dogs.

These studies demonstrated that there was no difference in the time course of Tc-99m concentration or release in bone and infarcts so that a differentiation was not feasible.

Tc-99m OR I-123 FOR THYROID IMAGING: A COMPARATIVE STUDY. John E. Arnold and Steven Pinsky. Michael Reese Hospital & Medical Center, Chicago, Ill.

From over 1000 patients predisposed to the development of thyroid tumors by prior radiotherapy to the neck, 65 were re-evaluated because of a possible abnormality on initial clinical examination or Tc-99m thyroid image. Normal patients or those with readily detected thyroid abnormalities were excluded. With Nuclear Chicago HP camera and pinhole collimator the thyroid was imaged 30 mins. after 5mCi Tc-99m pertechnetate I.V. and 18 hrs. after 250-400µCi I-123 orally. Oblique views were obtained when necessary.

51 of 65 patients had equivalent Tc and I-123 images - 32 were within normal limits, 15 showed cold area(s), 3 showed a hot area and one patient had a palpable isthmus nodule not delineated by Tc or I-123. In 14 patients some disparity between the Tc and I-123 image was seen - relative to the remainder of the thyroid 7 had a localized area of increased Tc but apparently normal I-123 concentration, 3 had cold area(s) more obvious with Tc than I-123, one had an area which concentrated I-123 but not Tc plus multiple cold areas with both nuclides, one with apparently normal Tc image showed an indefinite cool area with I-123 and 2 patients with poor uptake had a much clearer I-123 than Tc thyroid image. Oblique views proved extremely valuable to better define areas questionably abnormal on the anterior view. While the I-123 images often showed better contrast than the Tc images they required a longer imaging time and usually did not provide useful additional information.

We conclude that I-123 provides no advantage over Tc-99m for routine thyroid imaging except in patients with very poor thyroid uptake or with suspected retrosternal thyroid tissue. Patients with areas of increased Tc concentration should be re-imaged with radioiodine as disparity may be found, but the significance of this is uncertain.

Tc-99m GAMMA CAMERA THYROID IMAGING IN PATIENTS PREDISPOSED TO THYROID NEOPLASMS BY PRIOR X-RAY THERAPY. John E. Arnold, Steven Pinsky, U. Yun Ryo, Martin Colman, Lawrence A. Frohman, Arthur Schneider, Murray Favus, Maximillian Stachura and Margaret Arnold. Michael Reese Hospital & Medical Center, Chicago, Ill.

Radiotherapy for benign conditions of the head or neck is known to predispose to the later development of thyroid neoplasms. We have evaluated 1500 patients with a history of such irradiation 18-35 years previously by obtaining a relevant history, clinical examination and thyroid image. The latter was obtained with a gamma camera and pinhole collimator 30 mins. after I.V. 5mCi Tc-99m pertechnetate.

331 were found to have palpable thyroid nodule(s) and/or discrete areas of decreased Tc-99m uptake. 9 had a palpable nodule which showed increased Tc uptake. Of the remaining 322 (21% of all those evaluated), 310 (96%) had discrete cold area(s) demonstrated by the Tc imaging procedure while only 188 (58%) had thyroid nodule(s) which 2 or more clinicians could detect by palpation before knowing the scintigram result. Of the 322 abnormal patients 49 (15%) had 2 or more palpable nodules while 116 (36%) had 2 or more cold areas on the Tc thyroid image.

182 have been surgically explored and thyroid malignancy was found in 49 (27%). Papillary or mixed papillary-follicular carcinoma was found in 45 and pure follicular carcinoma in 4 patients. The incidence of malignancy in patient (s) with multinodular thyroids detected by palpation or on the thyroid image was not less than that in patients with solitary cold nodules.

We conclude that thyroid imaging with Tc-99m using the gamma camera and single pinhole collimator can appreciably increase the number of thyroid abnormalities detectable preoperatively but does not help differentiate benign from malignant lesions.

PINHOLE IMAGING OF HIP DISORDERS IN CHILDREN. Judith M. Ash, David L. Gilday, and Bernard J. Reilly. The Hospital for Sick Children, Toronto, Ontario.

Radiographs of the hip provide excellent morphological detail of bones, but little information about their blood supply and metabolic state, whereas the bone scan provides information about the bone's functional state. Using a fine pinhole collimator on a gamma camera, magnification images of the hip permit adequate resolution to define the femoral head, epiphyseal growth plate, femoral neck, greater and lesser trochanters.

We have examined 176 patients of whom 28 had Legg-Perthes disease, with either avascular or revascularizing femoral heads, and 47 had synovitis of the hip all showing

a diffuse increase in radioactivity involving the femoral head, epiphyseal plate, and acetabulum. Of the patients showing a focal increase in activity, 17 had osteomyelitis involving the proximal femur or adjacent iliac regions, 4 had intratrochanteric osteoid osteomas. Three patients had fractures of the femoral neck, 2 with decreased activity in the femoral head indicating avascular necrosis, a third with increased activity indicating a viable head; 4 with slipped femoral epiphyses had marked decreased radioactivity in the epiphyseal plate after pinning of whom 2 showed a viable femoral head at the same time, 3 with dislocations of the hips showed either normal, decreased or increased activity, 2 with epiphyseal dysplasia showed normal or decreased activity of the femoral head, 4 other patients had avascular necrosis of the femoral head secondary to systemic disorders. Fifty-nine patients had normal hip scans and did not have any unusual subsequent clinical diagnoses. Pinhole bone scans of the hips have proved to be extremely valuable in evaluating the blood supply of the femoral head, epiphyseal plate, and in detecting lesions in the area of the hip such as osteoid osteomas and osteomyelitis.

LESION DETECTABILITY USING THE PHOTOPEAK AND BACK-SCATTER ENERGY WINDOWS: A.B. Ashare, G. Dubuque, C.G. Rauf and J.G. Kereiakes. Radioisotope Lab., VA Hospital and University of Cincinnati Medical Center, Cincinnati, Ohio.

Lesion detectability with scintigrams using a low energy radionuclide can be enhanced by using dual energy windows encompassing the photopeak and the backscatter peak. While previous studies have used computer simulated scintigrams, this represents the initial attempt at experimental verification. Using 3 mCi of Tc-99m in a thyroid phantom, rectilinear scintigrams were obtained with a 19-hole, 3-inch focal length collimator. Various energy windows between 85 and 170 keV were used. The iodine escape peak for Tc-99m is 112 keV and the backscatter peak is 90.5 keV. All counting densities were maintained at 1000 cts/sq. cm. After the eight scintigrams were randomized, ten experienced observers ranked the scintigrams in order of their image quality. The scintigrams were then rerandomized and ranked again by the same ten observers. Analysis of variance indicated that there was a difference between the scintigrams at the .05 level; however, no significant difference was noted between observers. Duncan-Bonner statistical test showed that the dual energy window setting of 85-95 and 130-170 keV produced images ranked significantly higher when compared to all other energy window settings. The settings of 140-170, 130-170 and 120-170 keV were not significantly different in image quality; however, they were of lower quality than for the above. The dual energy window allowed scanning times or patient administered activity to be decreased by a factor of two.

GAMMA CAMERA FIELD FLOOD UNIFORMITY CORRECTION. IS IT WORTHWHILE? A.B. Ashare, T. Padikal, G. Cohen and J.G. Kereiakes. Radioisotope Lab., Univ. of Cincinnati Medical Center, Cincinnati, Ohio.

Daily field floods are used for quality control of Anger type gamma cameras. Computers are commercially available to check the uniformity of the field flood and can also provide coefficients to correct each clinical study. One of the variables is that the clinically interesting situation is not at the collimator face, but is at varying distances from the collimator with interspersed scattering media. For this reason, we investigated changes in the Co-57 field flood at distances from collimator face with interspersed scattering media. The uniformity over the entire face of the crystal was evaluated using a minicomputer with 64 x 64 matrix storage. The computer determines the number of channels within, above and below a predetermined acceptable uniformity range. The uniformity as a function of scatter thickness, energy window and uniformity limits indicates that the uniformity decreases as scattering media is increased for the first two inches. From two to three inches scatter thickness there is no significant change in uniformity with a symmetric

energy window of 20%. Uniformity, is a function of the amount and extent of scattering material present and the size of the energy window used. A field flood taken at the collimator face for the purpose of establishing normalization factors for uniformity correction will not take into consideration the scattering media. We suggest that computer uniformity correction not be done, but rather that the nonuniform field flood be corrected by retuning the photomultiplier tubes.

HEPATITIS B ANTIGEN AND ANTIBODY STUDIES
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The discovery of hepatitis B antigen HBAG in 1963 and the use of competitive binding assay for its detection made it feasible to screen out different populations and study the incidence and prevalence of the disease.

In addition to determining the incidence of Hepatitis B antigenemia by the direct solid phase radioassay, the Hepatitis B antibody HBAB was also detected and studied using a new solid phase direct radioassay in which a bead is antigen coated and immersed in test serum, after incubations and following washing, the bead is again immersed in I¹²⁵ labeled antigen for 4 hours, resulting in antigen, antibody, antigen complex, this is followed by washing and counting.

Our study of various medically related populations revealed the following results:

1. First year medical students had no detectable HBAG or ABAB.
2. Hemodialysis employees had 0.4% incidence of HBAG and 18% incidence of HBAB, while hemodialysis patients had no positive HBAG but a 17% incidence of +HBAB.
3. Blood Blank Donors had a 0.5% incidence of HBAG and 13% incidence of HBAB.
4. General hospital admissions had 3% incidence of HBAG and 18% incidence of HBAB.
5. Women in labor had a 0.4% incidence of HBAG and 16% incidence of HBAB, and 1% of them positive for HBAG and Ab at the same time.
6. Cord blood showed a 0.6% incidence of HBAG and 12% incidence of HBAB.

BIOLOGICAL BEHAVIOR AND PHYSICAL PROPERTIES OF THALLIUM-201
H.L. Atkins, A.N. Ansari, E. Lebowitz, M.W. Greene,
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Following previous studies in animals indicating Thallium-201 as thallos chloride to be a superior myocardial imaging agent, studies in man have been instituted to determine blood clearance rate, urinary excretion and whole body retention. Organ distribution and retention was also imaged in man. In addition, studies with a live phantom were performed to determine optimal imaging methods.

Blood disappearance is rapid enough (0.003%/ml at 5 minutes) that radioactivity in the heart blood pool does not interfere with myocardial imaging. Approximately 4-8% of the administered dose is excreted in the urine in the first 24 hours. No special concentrations other than in myocardium and renal medulla were noted initially. After several hours a generalized distribution of radioactivity was present.

Whole body retention was measured using 1.5 μ Ci Tl-200 because of more favorable physical parameters with the whole body counter. On a normal diet the whole body disappearance half-time was 9.8 ± 2.5 days. For Tl-201 this means a $T_{1/2}$ (eff) of 2.3 days and a whole body radiation dose of 162 mrad/mCi. The effect of a high potassium diet on whole body clearance is under evaluation.

Imaging the x-ray emission provided the highest count rates but resolution was less satisfactory using a conventional straight bore collimator compared to imaging the 167 keV gamma photons. However, the use of a small pin-hole collimator with the x-rays provided the best compromise of sensitivity and resolution.

Excellent myocardial images are obtained from 5 minutes to a few hours following intravenous administration of thallium-201.

A STUDY OF INDUCED CEREBRAL INFARCTION IN PRIMATES: XE-133 CEREBRAL BLOOD FLOW FUNCTIONAL MAPPING. Stephen Bacharach, Harry Agres, Jr., Mary K. Hammock, Michael V. Green, Apichati Pongpatirojana, Gerald S. Johnston and Giovanni Di Chiro. National Institutes of Health, Bethesda, Md.

Functional maps of regional cerebral blood flow (rCBF) were used to study a group of Rhesus monkeys before and after a transorbital occlusion of the middle cerebral artery. The maps were created with a computer-interfaced Anger camera, using a stochastic analysis of Xe-133 washout.

During each study, the monkey was viewed laterally by the camera with a converging collimator. A bolus of Xe-133 in saline was injected into a polyethylene catheter indwelling into the internal carotid artery. The computer collected one 64 by 64 picture frame each second for approximately 14 minutes. Each frame was then reduced to a 32 by 32 array (1024 points). Using the peak counts to area stochastic technique, flow per unit mass to each area in the cerebral hemisphere (about 500 points) was computed and stored in a single flow image (map).

The normal regional cerebral blood flow distribution was established by creating several, independent, pre-infarction flow maps. The middle cerebral artery was then clipped, producing a cerebral infarction. After infarction, rCBF functional maps were generated daily for the first week, and two to three times per week for the next three to four weeks.

The flow maps after infarction showed markedly reduced local flow in the appropriate areas of vascular distribution, reaching a minimum within one day after infarction. Thereafter, a gradual restoration of local flow and an increase in homogeneity of the flow maps were noted. Preliminary results suggest that this methodology may be a useful tool for the quantitative regional assessment of the natural evolution of cerebral infarction, as well as a means of evaluating various modes of therapy.

A SIMPLIFIED RADIOIMMUNOASSAY FOR TRIIODOTHYRONINE: EVALUATION OF A NEW COMMERCIAL KIT. Suppiah Balachandran, David C. Moses, James C. Sisson, and Shantilal R. Patel. University of Michigan Hospital, Ann Arbor, Mich.

We report the evaluation of a new T-3 RIA kit (Ames Company) which offers the advantages of greater simplicity of methodology and shorter incubation time while at the same time providing accuracy and reproducibility.

I-125 labeled T3 and standard or unknown serum are added to a Sephadex G-25 column; the T3 is freed of protein in alkaline pH. After washing with buffer, antiserum is added and incubation carried out at room temperature for 2 hrs. The % of free hormone remaining on the column was measured by radioactivity counting after an additional wash. Serum T-3 values were determined by a standard curve.

Sera of 15 volunteers, 41 euthyroid, 19 hyperthyroid, 25 hypothyroid patients, and 7 subjects who were pregnant or on oral contraceptives were assayed by the present method. Simultaneously 82 sera were assayed by an established method of RIA. The euthyroid, hyperthyroid & hypothyroid ranges were 72-297 ng%, 291-752 ng% and 0-121 ng% respectively. Pregnancy and treatment with oral contraceptives were associated with abnormally high serum T-3 values. The hormone levels by the present method correlated well with the clinical status of the patients & the values obtained by the other method of RIA.

Cross reactivity tested with analytical grade thyroxine was minimal (0.6%) and probably related to the T3 in the thyroxine. The recovery of T-3 added to hypothyroid serum was complete. Serial dilutions of a hyperthyroid serum established parallelism with the standard curve. Precision within run = 8% C.V. at a mean of 188 ng% and that between run = 13.6% C.V. at a mean of 127 ng%. The procedure was simple to carry out and the short incubation time allowed results to be obtained in less than 4 hrs. The kit should be valuable for use in clinical laboratories.

OPTIMUM DATA PROCESSING WITH ANNULAR CODED APERTURES H. H. Barrett and R. G. Simpson, Univ. of Arizona, Tucson, Arizona and H. D. Fisher, San Diego, California.

The use of an annulus as a coded aperture was first suggested by Walton (J. Nuc. Med. 14, 861, 1973). In common with other coded apertures such as the Fresnel zone plate, the annulus should offer advantages in collection efficiency, tomographic imaging and, frequently, dose, exposure time or resolution.

In Walton's work with the annulus and, indeed, in all coded-aperture imaging to date, the decoding operation was basically matched filtering, or cross-correlation of the coded image with a scaled replica of the aperture. In this work we have departed from strict matched filtering and investigated other filter functions that are closely related to the so-called rho-filters used in computerized axial tomography. Although fairly reasonable point images can be obtained without rho-filtering, we have shown by computer simulation that the images of larger objects are completely unreliable, with the reconstructed intensity at any point depending strongly on the object intensity at very distant points. With rho-filtering, this effect is completely eliminated and edge sharpness is greatly improved. The "DC background" is also removed. Computer simulations have produced images of points, discs and resolution test targets. The effects of focus, annulus size, detector resolution, filter function and noise have been studied. Many of these results have been verified experimentally with an Anger camera as the detector.

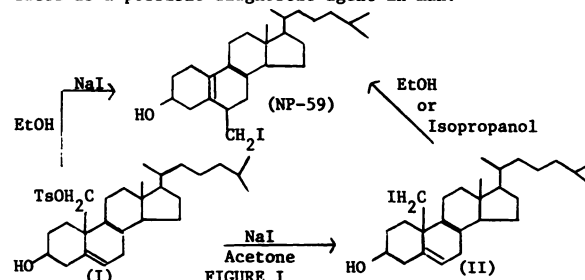
We conclude that in many respects the annulus is an excellent coded aperture. With proper filtering, the images are very clean and well-behaved and the resolution and count rate requirements on the detector are not severe. The collection efficiency of the annulus is lower than the zone plate, but fewer counts are required for the same signal-to-noise ratio.

SYNTHESIS OF A NEW ADRENAL IMAGING AGENT: 6 β -I-131-iodomethyl-19-norcholest-5(10)-en-3 β -ol (NP-59). Garabed P. Basmadjian, Kenneth R. Hetzel, Rodney D. Ice, and Wm. H. Beierwaltes. University of Michigan Hosp., Ann Arbor, Mich.

A new adrenal imaging agent, 6 β -I-131-iodomethyl-19-norcholest-5(10)-en-3 β -ol (NP-59) was synthesized from cholest-5-ene-3 β ,19-diol-19-toluene-p-sulfonate (I) via homoallylic rearrangement with the iodide ion as a nucleophile in alcohol and subsequent exchange with NaI-131. The same reaction in ketonic solvents yields exclusively 19-iodocholesterol (II). NP-59 and 19-iodocholesterol are homoallylic analogues of each other. 19-iodocholesterol can be converted in 90% yield to NP-59 in refluxing alcoholic solvents (See figure 1).

The original synthesis, purification, isotope exchange, formulation and stability of NP-59 as well as the product's specific localization in the adrenal in rats and dogs have been completed.

NP-59 administered intravenously demonstrated adrenal uptake of 10% (kgm) D/gm at 24 hrs, 5 times the concentration of 19-iodocholesterol. NP-59 is presently being evaluated as a possible diagnostic agent in man.



SALIVARY GLAND UPTAKE OF GA-67 CITRATE FOLLOWING RADIATION THERAPY. Carlos Bekerman and Paul B. Hoffer. University of Chicago, Chicago, Ill. and University of California, San Francisco Ca.

Gallium-67-citrate scanning is a useful examination in the staging and follow-up evaluation of patients with Hodgkin's Disease and other lymphomas. However, we have frequently observed salivary gland uptake in post-treatment scans in such patients which may be easily confused with cervical node uptake. The purpose of this study was to determine the association between radiation therapy and salivary gland uptake of gallium-67-citrate.

All gallium-67-citrate scans performed at the University of Chicago Clinics between January 1st, 1974 and December 31st, 1974 were reviewed. The scans were performed at 72 hours following the intravenous injection of 3 to 5 mCi of the radiopharmaceutical. All scans were performed on an Ohio Nuclear rectilinear scanner using the three independent window method. Of these 520 studies, there were 17

cases of apparent salivary gland uptake of radionuclide. Fifteen of these 17 patients had a history of radiation therapy (4,000 rad) including the cervical region within one year of the gallium scan. In none of these 15 patients was there clinical evidence of recurrent tumor in the cervical region at the time of scan. Fourteen of these 15 patients had scans prior to radiation therapy with no evidence of salivary gland uptake. No other modality of therapy was clearly associated with salivary gland uptake. Bilateral salivary gland uptake was observed in two unirradiated patients, one with chronic renal failure and one with systemic lupus erythematosus.

These findings indicate an association between salivary gland uptake of gallium-67 and recent radiation therapy. Therefore, following radiation therapy, extreme caution must be used to avoid misinterpreting salivary gland uptake of gallium-67 as recurrent cervical lesions.

CLINICAL STUDIES WITH A LIGHT-WEIGHT OVERHEAD SCANNING SCINTILLATION CAMERA. Edward G. Bell, David F. Mahon, Charles A. Henry, Michael F. Barnes, Crouse-Ingving Memorial Hospital, Syracuse, N. Y., John G. McAfee, Upstate Medical Center, Syracuse, N. Y., Ronald E. Turcotte, Jay R. Wolff, and William White, Searle Radiographics, Des Plaines, Ill.

One of the major limitations of the commercial general purpose gamma-type cameras has been a lack of mobility. This limitation is imposed by the shielding and collimation required to image distributions of gamma-emitters with energies up to 511 KEV. A camera was exclusively designed for use with low energy isotopes, in order to minimize the bulk and yet still perform the great majority of the clinical studies in current practice using Tc-99m labeled radiopharmaceuticals.

In this paper, we report on the clinical use of the experimental light-weight (approximately 200 pounds) Anger-type camera head, supported by an overhead x-ray tube conveyor and telescope of the type commonly used in radiography. Over 2,000 patients have been studied. We find that the increased mobility and freedom from floor encumbrances not only facilitates patient positioning in studies involving trauma cases and in those patients who are difficult to move but also readily adapts to a scanning mode for large area imaging, i.e., total body skeletal surveys, bone marrow distributions, abdominal imaging of genitourinary system, vascular pool imaging, radioisotopic venography of the pelvis and lower limbs, subarachnoid space, etc.

REST AND EXERCISE MYOCARDIAL IMAGING WITH Rb-81 AND THE SCINTILLATION CAMERA: IMPROVED SCREENING FOR SIGNIFICANT CORONARY STENOSIS. Daniel S. Berman, Antone F. Salel, Gerald L. DeNardo, and Dean T. Mason. University of California, School of Medicine, Davis, California

The sensitivity of rest and exercise myocardial perfusion studies using scintillation camera imaging of intravenously administered Rb-81 in the detection of myocardial ischemia was compared to that of exercise electrocardiography (ECG) by relating results in 38 patients (pts) to degree of stenosis as delineated by coronary arteriography. For each rest or exercise study, 4 mCi of Rb-81 was injected into a peripheral vein, and high resolution images were obtained with a scintillation camera equipped with a pinhole collimator and a specially constructed lead shield. Areas of myocardial ischemia were seen as regions with decreased Rb-81 uptake after exercise compared to rest.

In 32 pts with greater than 75% stenosis of at least one of the 3 major coronary vessels, rest and exercise Rb-81 imaging detected ventricular ischemia in 28 (88%), whereas simultaneous exercise ECG was positive (1 mm or more horizontal ST segment depression) in only 18 (56%) of the same pts. Importantly, 5 of the 32 pts who exhibited radio-nuclidic evidence of ischemia on exercise studies compared with rest did not develop angina and were without positive exercise ECG. In 6 additional pts with less than 50% narrowing of a major coronary vessel on coronary arteriography, the exercise Rb-81 images were negative, while the exercise ECG was positive in one of these pts. Interestingly, this one exercise ECG positive pt had normal coronary vessels documented by selective arteriography. In conclusion, high resolution images can be obtained with Rb-81 using the scintillation camera with special shielding, and rest and exercise Rb-81 myocardial imaging appears to offer enhanced sensitivity as well as specificity over exercise ECG in the noninvasive identification of significant coronary stenosis.

SPECIFICITY OF Tc-99m PERTECHNETATE IN SCINTIGRAPHIC DIAGNOSIS OF MECKEL'S DIVERTICULUM: A REVIEW OF 100 CASES. Thomas H. Berquist, N. G. Nolan, David H. Stephens, H. C. Carlson. Mayo Clinic, Rochester, Minn.

Tc-99m pertechnetate is concentrated in the surface epithelial cells of gastric mucosa and has been of value in the pre-operative diagnosis of Meckel's Diverticulum. In an attempt to evaluate the specificity of this technique, as well as possible causes of false positive and false negative scans, we reviewed 100 patients who were studied for a suspected Meckel's Diverticulum.

Seventy-eight adults and 22 children (less than 15 years of age) were studied. Seven scans were interpreted as positive and surgical confirmation of Meckel's Diverticulum was obtained in six cases. In the seventh patient, peptic ulceration in islands of ectopic gastric mucosa located in the small intestine was detected at laparotomy. Scintigrams had demonstrated two areas of abnormal uptake in the region corresponding to the areas of gastric mucosa.

Of the remaining 93 cases in whom scans were interpreted as negative, 22 underwent laparotomy. One Meckel's Diverticulum was detected at laparotomy in a patient with a negative scintigram.

The literature has suggested that certain conditions may cause false positive scintigrams. These entities include A-V malformation, hydronephrosis, inflammatory bowel disease and peptic ulceration of the small intestine. We performed scintigrams on patients in each of these categories. The scintigrams were negative in all cases except the patient with ulceration in islands of ectopic gastric mucosa in the small intestine.

Tc-99m pertechnetate is of value in pre-operative diagnosis of Meckel's Diverticulum. One false negative study occurred in 22 patients, but other abdominal pathology previously thought to cause false positive results did not demonstrate concentration of Tc-99m unless gastric tissue was present.

RADIATION DOSIMETRY OF BISMUTH-204 AND BISMUTH-206 CITRATE. Rodney E. Bigler, Gerald A. Russ and John S. Laughlin. Memorial Sloan-Kettering Cancer Center, New York, N.Y.

Recent reports have suggested that radioisotopes of bismuth salts are selectively taken up by a broad spectrum of soft tissue tumors. In order to better evaluate the relative radiation risk versus benefit of radiobismuth, the absorbed radiation dose to humans was calculated. Bismuth-204 has a half-life of 11.2 hours and decays by electron capture with a complex spectrum of 238 gamma ray emissions ranging from 79 keV to 3.06 MeV. Bismuth-206 has a half-life of 6.24 days and decays by electron capture with 68 gamma rays ranging between 39 keV and 2.76 MeV. Biological parameters were derived from theoretical least-square fits to rat data. These data clearly indicated that kidney uptake was two orders of magnitude higher than other body tissues and therefore the organs at highest risk. Calculations were performed according to methods of the MIRDO Committee. Equilibrium dose constants were provided by LT Dillman of the Health Physics Division at Oak Ridge National Laboratory by private communication. The estimated absorbed dose to a 70 kgm standard man's total body, kidneys and ovaries for Bi-204 are respectively 1.04, 1.42 and 63 mrad/ μ Ci injected. Bi-206 estimations similarly yielded 1.18, 1.84 and 75 mrad/ μ Ci. Clearly, little advantage is seen for Bi-204 compared to Bi-206 in spite of the somewhat shorter half-life of Bi-204. The minimal improvement observed in absorbed radiation dose does not at present justify the added cost of Bi-204 production, specifically the need for a high energy cyclotron and separated isotope target material. (Research supported in part by AEC(11-1)-3521 and NCI grant CA-08748-08B.)

SKELETAL MUSCLE UPTAKE OF BONE SEEKING AGENTS IN BOTH TRAUMATIC AND NON-TRAUMATIC RHABDOMYOLYSIS WITH ACUTE RENAL FAILURE. Richard J. Blair, Edward T. Schroeder, John G. McAfee and Charles E. Duxbury. The Upstate Medical Center, Syracuse, New York.

The occurrence of hypocalcemia during the oliguric phase of acute renal failure followed by hypercalcemia in the diuretic recovery phase was reported from this center in 1968. More recently in another center, this same phenomena was reported in three patients with non-traumatic rhabdomyolysis and acute renal failure.

Over the past two years, three patients with acute renal failure following acute rhabdomyolysis have been

studied with rectilinear whole body and scintillation camera imaging after prior injection with a skeletal imaging agent. Of the two cases of non-traumatic rhabdomyolysis, the first, secondary to severe exercise, received Tc-99m labeled polyphosphate, and the second, due to a prolonged episode of epileptic seizures, received Tc-99m labeled methylene diphosphonate. The traumatic case due to crush injury from a falling tree received Tc-99m labeled pyrophosphate.

Anuria, myoglobinuria and markedly elevated creatine phosphokinase values were initially noted in all three patients. The imaging study illustrates initial skeletal muscle uptake, and, in one case, lung uptake also, during the oliguric phase and later normalization during the diuretic recovery phase. Muscle uptake correlates with hypocalcemia while normalization of skeletal imaging occurs with hypercalcemia or normocalcemia. This suggests that the hypocalcemia may result from the deposition of calcium in the damaged muscle.

The pathophysiology in this study correlates with the so-called "white muscle disease" (exercise myopathy) reported by veterinarians in cattle, horses, and sheep which occasionally progresses to frank muscle calcification.

APPLICATION OF THE CERENKOV EFFECT FOR THE DETECTION OF ENDOCRINE TUMOURS. P. Blanquet*, D. Blanc**, N. Safi*, E. Thoreson**, J. Barthe**, and M.J. Lerebeller***. *Hopital Pellegrin, **Universite Paul Sabatier, and ***Hopital St-Andre, Bordeaux, France.

In its present state, the ocular scintigraphy permits only a relatively small percentage of ocular tumours to be detected (melanomas) because of the utilisation of specific radioactive vectors for this type of tumour. The metastasis and other primitive tumours cannot be detected by this method of investigation.

Phosphorus 32, which is the undisputable indicator of neoplastic processes, cannot be employed for the external detection of posterior tumours because of the short mean path length of β particles.

In order to get around this disadvantage, we have utilized the Cerenkov effect produced by β particles from ^{32}P in the vitreous humour. This allows the detection of the concentration of this isotope in the posterior half of the eye.

The detector of the Cerenkov effect is the eye itself. The β particles, in crossing the vitreous humour, produce light towards the anterior, light which is focalized by the crystalline lens. This light is transmitted by a light pipe of the cathode of a photomultiplier with high sensitivity in the spectral region of the Cerenkov effect.

In ameliorating the performances of the tube by using a cooling system and a system of thermal isolation, the theoretical evaluation of the apparatus yield permits a sufficient detection of the signal. This atraumatic method allows one to study the primitive or secondary mitotic processes of the posterior half of the eye.

ANTINEOPLASTIC ACTIVITY OF IODINE-125 LABELED IODODEOXYURIDINE. William D. Bloomer and S. James Adelstein. Departments of Radiation Therapy and Radiology, Harvard Medical School and Joint Center for Radiation Therapy, Boston, MA.

Despite early enthusiasm for 5-iododeoxyuridine as an antineoplastic agent, clinical efficacy was limited by unfavorable physicochemical properties, toxic side effects and general suppression of proliferating cell renewal systems. The exquisite radiotoxicity of iodine-125 when incorporated into DNA as the thymidine analog I-125 IuDR has been demonstrated in both microorganisms and mammalian cells and suggested that I-125 IuDR might be effective in the treatment of certain neoplastic diseases.

An experimental murine ovarian carcinoma arising spontaneously in a female C3H mouse has been maintained and utilized in its ascitic form in C3HeB/FeJ female mice. Challenge doses of 10,000 and 100,000 cells intraperitoneally (ip) were used. Carrier-free I-125 IuDR (New England Nuclear) was administered ip at levels of 300 and 500 μCi as single and fractionated doses 12 to 72 hr following tumor cell inoculation. Experiments were followed for 150 days.

Large single doses of I-125 IuDR (500 μCi) prolonged median survival with the lower (10,000) tumor cell inoculum. Fractionated doses of 300 and 500 μCi I-125 IuDR prolonged median survival and resulted in 25% and 50% long term disease-free survivors respectively. Treatment of animals with corresponding doses of NaI-125 had no effect.

Prolongation of survival in tumor bearing animals treated with I-125 IuDR suggests a promising new approach to tumor therapy and needs further investigation. (This work was supported by USPHS Grants CA-12662, CA-05237 and CA-15523.)

PROBLEMS, SOLUTIONS AND RESULTS IN COHERENT OPTICAL SCINTISCAN PROCESSING. Ioannes Bofilias, Josef Hofer, Hans W. Pabst, and Helmut Platzler. Technical University of Munich, Western Germany.

A two year co-operation between the Clinic of Nuclear Medicine and the Institute of Communication Science of the Technical University of Munich lead to a deeper understanding of the generation, the recording and the improving of the Anger camera scintiscans. The applied technique was the processing of coherent - optical spatial filtering. Considerable improvement of the evaluability could be achieved.

The problems to be solved center around two points: 1) The signal to noise ratio in the photographically taken scintiscans is far lower than given by count-statistics. Some theoretical tools had to be established to understand this effect and to fight it. A corresponding modification of the photographic registration leads to an average gain factor of 2.5 of the signal to noise ratio. Essentially, this is done by avoiding most of the cross modulation products of signal and noise.

2) The scintiscans in form of small transparencies undergo a homogenous spatial filtering. The filter function is optimised in order to approximate the ideal deconvolution as far as possible regarding the limits set by the frequency-dependent signal to noise ratio. Consequently, new methods of generating the filters had to be developed in order to achieve the necessary precision required by the theory. This was done by compensating the nonlinearities of the photographic material of the filter plate by aid of a digital computer.

Using this methods the visibility of lesions in scintiscans is evidently improved.

A NEW WHOLE-BODY UNIDIRECTIONAL MOVING SCANNER : COMPARATIVE STUDY OF PERFORMANCES. B.D.BOK, F. FONROGET, Inst. G. Roussy and Hbp. Cochin, Paris, (France).

A new whole-body unidirectional moving scanner was built using a single large bar crystal, 12 photomultipliers on its top, and a delay line system to compute the X coordinate. Motion is required in only one direction on the Y axis, and a special collimation is adapted in order to equal the X and Y performances of the detector.

The performances of this detector (C.G.R. Scanicamera) (S.C.) were compared under the same conditions with those of a moving rectilinear scanner (R.S.) (Ohio-Nuclear F 84 dual head scanner, 12.5 cm crystal) and with an Anger gammacamera equipped with its whole body attachment (W.B.C.) (Nuclear Chicago Pho Gamma III H.P.).

Several visual tests were used for resolution studies, and moreover the point spread functions were measured in water-equivalent material at different depths and M.T.F. computed. With Tc-99m the results are grossly far better than with R.S. and quite as good as with W.B.C. Using higher energy nuclides, the results are better with S.C. than with the two other devices. Detailed results will be shown. The sensitivity of the S.C. is less than the R.S. and the gammacamera for the same duration of a scan, but it is high enough to enable good statistics for a bone scan within 15 minutes.

In addition comparative clinical studies including Tc-99m pyrophosphate bone scintigraphies, Ga-67 and I-131 whole body pictures will be shown, and also some organ scintigraphies such as lung and liver scans.

The general impression obtained from these studies is that this new whole body unidirectional moving scanner is a very convenient device for whole body studies and can also be used for large organs scintigraphies.

COMPLIANCE TESTS AND RADIATION SAFETY PROCEDURES FOR BROAD AND SPECIFIC MEDICAL BYPRODUCT MATERIAL LICENSES. Suresh M. Brahmavar, Saïd M. Zu'bi and John P. Sullivan. Department of Pathology, Medical Center of Western Massachusetts, Springfield, Mass.

Broad and specific medical byproduct material licenses are granted pursuant to the Atomic Energy Act of 1954 (now, Nuclear Regulatory Agency) and Title 10 Code of Federal Regulations Chapter 1, parts 19, 20, 30, 32, 34 and 35 and in reliance on statements and representations made by the licensee. An attempt has been made to determine the types of different required tests, periodicity of these tests, record keeping and administrative procedures described in the massive volume of Title 10 Code of Federal Regulations.

A careful search has resulted in compilation of over thirty(30) different tests and administrative actions that would be necessary to be in compliance. These tests with their 10 CFR references and pertinent data are organized into an easy check list entitled Radiation Protection Officer Inspection Form (RPOIF) which keeps an up to date listing of every test performed and status of license compliance performance. The use of RPOIF on monthly basis at our medical center with broad medical license has helped to detect the deficiencies and conduct the required tests before the expiry of time period stipulated by the conditions of the license.

Further, usefulness of RPOIF is tested in an institution with specific medical license. The deficiencies pointed out by RPOIF were later confirmed during the routine inspection by the AEC compliance inspector.

It is our belief that, although this compilation of required tests and administrative actions will have to be amended to incorporate future regulations, it is useful in quality control of compliance performance for institutions with broad and specific medical byproduct material licenses.

METHODOLOGY REQUIRED TO INVESTIGATE MICROVASCULAR DYSFUNCTION IN THE EYE. J. Bronzino, J. O'Rourke, C. Miller, and D. D'Amato. University of Connecticut Health Center, Farmington, CT.

Microvascular dysfunction in the eye primarily involves the restriction of normal capillary perfusion and the formation of aqueous humor. By utilizing Iodine-125 HSA for aqueous humor flow and Xenon-133 for blood flow a quantitative study of these mechanisms of eye disease may be obtained.

This cinematic presentation will highlight the procedures and an instrumentation package ("eye physiometer") developed at the University of Connecticut Health Center to investigate these processes. The microinjection techniques and apparatus required to introduce isotopes into the eye, the arrangement of off-the-shelf instrumentation components to detect and count activity of the specific isotope, and the utilization of a PDP-8E to analyze the data and provide a visual display to the clinician, will be emphasized. Animal studies and clinical experiments will also be introduced to illustrate the nature of these displays and our results. These findings are an extension of work presented to SNM in 1973.

EARLY THYROID IODIDE AND PERTECHNETATE KINETICS: A COMPARTMENTAL MODEL DERIVED FROM SCINTILLATION CAMERA DATA. Philippe Brooke, Philippe Decostre, Francis Cantraine. Service des Radiosotopes, Hôpital St-Pierre, Bruxelles.

Scintillation camera data are processed by the SAAM 25 program and a new model of early thyroidal I^- and TcO_4^- metabolism is elaborated; unidirectional clearance C , exit rate constant k_{TB} and binding rate constant k_b are evaluated, as well as their modification by action of methimazole (MMI) and perchlorate. Data consist of two one-hour curves (one point per minute): a thyroidal curve, corrected for extrathyroidal neck activity by the choice of adequate areas of interest, and a cardiac curve, corrected for extraplasmatic cardiac activity by two blood samples (third and 40th mn). The simplest suitable model has 7 compartments for iodide, 6 for pertechnetate.

In euthyroid subjects, C ranges from 9.5 to 52 ml/mn and k_{TB} from .028/mn to .1/mn. Concerning organification (for iodide only), increa-

sing MMI doses (injected 1/2 hour before tracer injection) induce a progressive drop of k_b : .08/mn for an untreated subject, .02/mn for 1 mg of MMI, .008/mn for 2 mg, 0./mn for 40 mg.

The proposed model is used to determine:
1- the evolution of plasma concentration from external counting; 2- the parameters C , k_{TB} and k_b ; 3- the binding rate inhibition caused by MMI; 4- the variation of the trapping parameters C and k_{TB} due to perchlorate action.

ELIMINATION OF COLLIMATOR-HOLE PATTERN BY DOUBLE DISPLACEMENT OF A HEXAGONAL ARRAY. B. Brunsten, P. V. Harper, and R. N. Beck. University of Chicago, Chicago, Ill.

In gamma camera images made with parallel hole collimators, the hole pattern superimposed on the image becomes very prominent at high energies because of the thicker collimator septa required and because of the reduced loss of intrinsic resolution at high energies. With recent camera designs which have better intrinsic resolution characteristics, this phenomenon is expected to be even more marked. Random motion of the collimator eliminates this effect without loss of resolution. Random motion of a heavy collimator, however, poses awkward mechanical problems. If a hexagonal array of holes, containing a central hole is placed off-center on the collimator blank by 1/3 the distance between adjacent holes, and if it is rotated first through 120° and then through a further 120° angle, these three positions interleave to produce a hexagonal array with three times the actual number of holes spaced 1/3 of the distance apart. Thus, collecting 1/3 of the total counts in each of the three positions results in a smooth picture without sacrifice of collimation. This rotational method of displacement of the hole pattern avoids the creation of gaps in the shielding which would result from linear shifting of the collimator blank.

A DEVICE FOR THE CONTINUOUS RADIO-METRIC MEASUREMENT OF IN-VITRO METABOLISM IN A LIQUID SCINTILLATION COUNTER. Edward U. Buddemeyer. University of Maryland Hospital, Baltimore, Md.

The purpose of this study was to test a newly-developed device in which suspensions of bacteria, cells or tissues may be cultured and their metabolism measured radio-metrically in a liquid scintillation counter.

The device consists of a vial within a vial. The outer one is an ordinary scintillation vial lined with a closely fitting cylinder of paper that has been impregnated with 2, 5-diphenylloxazole and then dampened with sodium hydroxide solution. The inner vial is sterilized, charged with the specimens to be assayed and an appropriate C-14 substrate and then placed within the scintillation vial which is tightly capped. Metabolically produced C-14 labelled carbon dioxide diffuses from the inner vial and is absorbed on the treated paper where it produces scintillations. The method of sampling is cumulative, continuous and non-destructive so that active specimens can be counted as frequently as desired without interrupting experiments.

Labelled carbon dioxide was detected promptly upon release and the detected activity was linearly related ($r=.995$) to the amount present. The device has been applied to the detection of the growth of several species of bacteria (*M. lepraemurium*, *E. coli*, *salmonella E.*), to the measurement of the metabolism of resting and stimulated human leukocytes and to the assay of a decarboxylic enzyme (Glutamic acid Decarboxylase), in each case giving a sensitive and precise indication of metabolic activity.

This simple device, economically constructed from readily available materials, has proven to be a sensitive, quantitative detector of in-vitro metabolic activity. It provides the means by which the high sensitivity, large sample capacity and automatic operation of liquid scintillation counters may be applied to the radiometric measurement of metabolism.

GENERAL THEORY FOR IMPROVEMENT OF SIMPLE SUPERPOSITION TOMOGRAPHY. Thomas F. Budinger, Lawrence Berkeley Laboratory and Donner Laboratory, University of Calif., Berkeley, CA.

Both transverse section and longitudinal tomography involve the superposition of defocused data on in-focus data or planes. Starting with these blurred images, it is possible to reconstruct the true distribution using Fourier transform methods.

Transverse section blurring tomography, also known as back projection B, involves the convolution of the true distribution A with the blurring function $1/r$, where r is measured from each image point. From the convolution theorem and Bessel function relations, the true image is $\mathcal{F}^{-1}\{|\mathcal{R}|\mathcal{F}(B)\}$ where \mathcal{F} denotes the spatial Fourier transform and \mathcal{R} is the measure in frequency space. For digital implementation this ramp filter has a cut-off at $R_{max} = 1/2\Delta x$, where Δx is the sampling interval. The ramp filter must be modified to suppress lobes (ringing) in the reconstruction. Modification is done using filters such as Butterworth, Hann, Hamming, and Parzen. The composite filter can be applied to the back projection images or to the projections before back projection.

The method of improvement of longitudinal tomography involves subtraction of out-of-focus data from planes adjacent to the in-focus plane. Each tomographic image plane is related to the true distribution O_j in the other planes by $\mathcal{F}\{I_i\} = \sum_j H_{ij} \cdot \mathcal{F}\{O_j\}$ $i = 1, 2, \dots, n$

where $\{H_{ij}\}$ are the transfer functions relating each object plane to the particular image I_i . The matrix of coefficients can be determined for any given system, and a solution for the true distribution obtained by employing iterative methods or generalized inverse matrix methods. The simple direct matrix method is not possible because of limited statistics and nonlinear contribution of attenuation which must be included in the $\{H\}$ coefficients.

CLINICAL APPLICATION OF A LARGE FIELD OF VIEW SCINTILLATION CAMERA. J. A. Burdine, P. H. Murphy, T. Galen. Baylor College of Med., St. Luke's Episcopal-Texas Children's Hospitals, Houston, Texas

In contribution to the current reassessment of the future of radionuclide imaging which has been stimulated by computerized transverse axial tomography, the purpose of this study was to evaluate a new generation scintillation camera designed to provide improved sensitivity and resolution particularly at depth, and an expanded field of view.

The general performance characteristics of the camera were determined. In addition, in 636 patients clinical images of brain, liver/spleen, lung, bone, kidney, or heart were compared with those from standard commercially available cameras using established criteria.

The camera's useful field-of-view with parallel hole collimation (15.25 in) was substantially larger than standard models. With converging collimation, the image magnification significantly increased resolution and sensitivity, especially at depth, while the larger detector prevented convergence from unduly restricting field size.

Improved statistical content resulted in noticeable enhancement of image quality in dynamic images with the converging collimator and in breath-holding images (such as the lung) with the parallel hole collimator. In addition, the reduced imaging time tended to diminish motion artifact and facilitate studies such as total body scanning. In all clinical applications, the images were judged superior to those of standard cameras.

The improvement in performance observed in this study suggests that substantial potential exists for continuing advances in scintillation camera performance.

CURRENT STATUS OF RADIOMETRIC DETECTION OF M. TUBERCULOSIS AND M. LEPTAEMURIUM. Edwaldo E. Camargo, Steven M. Larson, Patricia Charache, Byron S. Tepper and Henry N. Wagner, Jr. The Johns Hopkins Medical Institutions. Baltimore, Md.

Last year we reported our early results in applying radiometric methods to the detection of $^{14}\text{CO}_2$ released from the metabolism of (U- ^{14}C) acetate and (U- ^{14}C) glycerol by *M. tuberculosis* and *M. lepraemurium*.

Since then we have evaluated different substrates, the optimum volume of the media and have documented the effectiveness of the system in the evaluation of chemotherapy. One ml of 7H9 medium (ADC) with 1 μCi of (^{14}C) formate was found to be best for the detection of the metabolism of inocula from 10^5 to 10^6 *M. tuberculosis* organisms. For *M. lepraemurium*, and animal model of human leprosy, detectable $^{14}\text{CO}_2$ levels were produced by 10^9 organisms inoculated into 10 ml of either a simple buffer (K-36) or a complex medium (NC-5) with 5 μCi of (U- ^{14}C) acetate or (U- ^{14}C) glycerol. In the past, it was impossible to detect *M. lepraemurium* because this organism cannot be grown in cell-free media.

Metabolism could be monitored easily despite no evidence of multiplication. The effect of chemotherapeutic agents in murine leprosy was also studied: out of 17 drugs tested, ethionamide and nitrofurantoin caused the most marked inhibition on the $^{14}\text{CO}_2$ production by *M. lepraemurium*. The addition of 0.05% of Tween 80 and the use of only 1 ml of K-36 buffer stimulated the substrate oxidation and led us to the study of a series of (1- ^{14}C) fatty acids. Decanoic, lauric, myristic and stearic acids were metabolized to $^{14}\text{CO}_2$ much more rapidly than (U- ^{14}C) acetate. Their use will permit us to decrease the time of detection or the number of organisms/vial. The metabolism of the same fatty acids by *M. tuberculosis* is currently under investigation. In conclusion, radiometric techniques are particularly useful for the study of the metabolic requirements and pathways of the fastidious organisms of the genus *Mycobacterium*.

ACCURACY OF TECHNETIUM-99m LABELLED PHOSPHATES FOR DETECTION OF ACUTE MYOCARDIAL INFARCTION. Richard J. Campeau, Stuart Gottlieb, S.K.C. Chandraraj, A. Mayorga-Cortes, and August Miale, Jr. Jackson Memorial Hospital and Veterans Administration Hospital, Miami, Fl.

The incidence of false positive and false negative myocardial scans obtained with two of the Tc-99m labelled phosphate bone imaging agents was investigated in patients suspected of acute myocardial infarction (AMI).

Forty-eight patients were scanned within 7 days of onset of chest pain with a gamma camera 90 minutes after intravenous administration of 15 mCi of either Tc-99m pyrophosphate (PYP) (26 patients) or Tc-99m polyphosphate (POP) (22 patients).

Each patient was examined by a cardiologist for the presence or absence of AMI. The clinical diagnosis was unknown to the nuclear physicians prior to interpretation of the scintiscans. Three experienced readers independently categorized these scintiscans with respect to presence or absence of myocardial radioactivity. There was agreement among all 3 readers with respect to a positive or negative interpretation in 90% of the scintiscans.

Of 22 patients scanned with POP, 4 (18%) had false negative findings and 2 (9%) had false positive findings, or an accuracy of 73%. In the other group of 26 patients scanned with PYP, 2 (8%) were false negatives and 2 (8%) were false positives, or an accuracy of 85%. This data suggests the possibility of a higher frequency of false negative results with POP than with PYP, and that the overall incidence of false negative and false positive studies obtained with either radiopharmaceutical may be higher than previously reported.

F-18 FLUORO-DOPA - AS A NEW BRAIN SCANNING AGENT. Peter Chan, Gunter Firnu, Edmund S. Garnett. McMaster University Medical Centre, Hamilton, Ontario, Canada,

DL 5-Fluoro-DOPA (3,4-dihydroxy-5-fluoro-DL-phenylalanine) is a unique analogue of DOPA. It was prepared to serve as a gamma emitting marker for native DOPA when labelled with the radionuclide fluorine-18. It is a radiopharmaceutical which will be used to investigate the derangement of catecholamine metabolism which are believed to categorize disorders of affect and locomotion.

The head of dogs and baboons was scanned after i.v. injection of [F-18] fluoro-DOPA. The caudate nucleus was clearly visible as an area of increased accumulation of isotope. The significance of this observation is discussed.

ABNORMAL TECHNETIUM-99m PERTECHNETATE IMAGING FOLLOWING STANNOUS PYROPHOSPHATE BONE IMAGING. William M. Chandler, and Lorri D. Shuck. Fairview Hospitals, Minneapolis, Mn.

A specifically abnormal imaging pattern has been observed consistently when technetium-99m pertechnetate brain imaging followed Tc-99m stannous pyrophosphate (Tc-99m PYP) imaging using the Mallinkrodt Technescan PYP kit. Our purpose is to evaluate this abnormal technetium distribution and propose an explanation for this abnormal isotope pattern.

Twenty consecutive patients received Tc-99m pertechnetate brain imaging one day following a Tc-99m PYP bone scan. Several patients had brain imaging before and after bone imaging; some patients had multiple sequential brain

scans in the three weeks following the bone imaging. Potassium perchlorate 250 mg. "blocking" preceded all Tc-99m pertechnetate injections and the five view brain scans were obtained with an Anger camera two hours post-injection. Sequential blood samples were obtained throughout the day of pertechnetate imaging and the plasma and cells were counted separately.

All brain imaging obtained one day following bone imaging showed an abnormal pattern demonstrating increased activity in the superior sagittal sinus, the transverse sinuses, and the region of the choroid plexi. All brain imaging obtained before bone imaging showed a normal pattern.

In vitro testing showed a thirty fold increase of activity in the erythrocytes during pertechnetate imaging that followed bone imaging. Electro-arc-spectroscopy revealed a marked increase of both tin and technetium in the red cells during pertechnetate imaging.

Analysis suggests that tin labels the erythrocytes following bone imaging and pertechnetate may undergo intracellular reduction and labeling of red cells during the pertechnetate brain imaging. Pertechnetate brain imaging should therefore precede TechneScan PYP bone imaging.

WHAT IS THE OPTIMUM GRAY SCALE FOR PHOTOSCANNERS?

Wei Chang and Monte Blau, Roswell Park Memorial Institute, Buffalo, N.Y.

The gray scale providing maximum ease of visual interpretation of photoscans has been determined by empirical studies in a series of observers. This ideal count rate vs. film density curve was compared to that provided in several commercial photoscanners.

Each of 50 subjects was asked to choose the 5 (out of 28 available) gray strips which he felt represented equal steps between two extremes, 0.15 and 3.0 optical density, representing fog level and full black. This made a series of 7 strips which divided the gray scale into steps of equal perceptible difference. Plots of differential perceptibility vs optical density were made for each individual. There was little variation in the general pattern between observers. As expected, small optical density differences could be perceived at low film densities, but on darker films large changes in O.D. were necessary.

Using a signal generator, count rate vs film density curves were measured for several commercial scanners. None of these matched the ideal curve. All provided too little differentiation in the dark end of the scale. This enhances the ability to see the changes at the light end but only at the expense of easy perception at the dark end.

One scanner was modified to provide a better gray scale. It was not possible to match the ideal curve exactly, but scans with the modified curve are definitely preferable.

The detailed studies on the commercial scanners uncovered many instances of poor calibration, non-uniform speed, change in gray scale with count rate or speed, etc.

BONE TRACER UPTAKE: EVALUATION BY A NEW MODEL.

N. David Charkes, Charles Phillips, and Leon S. Malmud, Temple Univ. Med. Sch., Phila., Penna.

Bone blood flow cannot be measured directly. Indirect estimates made from the blood disappearance rate of injected bone-seeking nuclides have given values of about 4-12% of cardiac output, much less than that of the microsphere distribution technique. To investigate this disparity, we evaluated all published data of F-18 kinetics in humans. A 4-compartment model of bone tracer uptake was developed and simulated on an EAI 580 analog computer. In this model, the extracellular fluid (ECF) compartment (C2) is interposed between blood (C1) and bone (C3); the urinary compartment (C4) feeds from blood, with rate constants $k_{21}=100, k_{12}=45.6, k_{32}=4.2, k_{23}=1.0, k_{41}=2.4, k_{14}=0.7$ (all per hr). Excellent fits to the known blood concentrations, urinary excretion rate, and total bone uptake Q_0 (estimated from animal data) were obtained. Bone tracer uptake rate at any time t , $dQ/dt = (k_{32})(Q_0 - Q)$, and is proportional to ECF tracer concentration; it does not depend upon blood flow to bone except insofar as tracer leaves blood in the first minute to enter ECF in bone. Previous determinations of "extraction ra-

tio" measured only tracer loss to ECF, not bone extraction. This model predicts that living bone exposed to a tracer in a bathing medium (such as ECF), even in a dead animal or in vitro, will continue to extract tracer at a normal rate. Bone blood flow therefore cannot be measured by skeletal tracer extraction technique. Summary: A model of bone tracer uptake has been developed which closely fits human kinetic data using F-18. This model stresses the pivotal role of ECF in skeletal tracer metabolism.

POTENTIATING EFFECT OF PARATHORMONE IN ^{32}P TREATMENT OF WIDESPREAD BONE METASTASES. Tapan K. Chaudhuri, L.G. May, Robert D. Dwyer and G. de los Santos, Nuclear Medicine, Urology and Surgery Service, Eastern Virginia Medical School and V.A. Center, Hampton, Virginia

^{32}P has long been used for palliative treatment of severe bone pain in diffuse metastatic involvement. Previously, ^{32}P alone was used. Because of high failure rate of using ^{32}P alone, therapist switched to the protocol of 'testosterone followed by ^{32}P ' in order to stimulate the metastatic areas of the bone to pick up maximum amount of ^{32}P available in the circulation thus attaining a maximum therapeutic efficacy. We are presenting here our experience in treating patients with widespread bony metastases (proven by both x-ray and scintiscan) from primary lung and prostate cancer using the regimen of 'Parathormone followed by ^{32}P .' In the patient with primary prostate cancer, measures such as orchiectomy and estrogen therapy failed to relieve bone pain. In this patient as well as in patient with primary lung cancer, external radiotherapy was not recommended because of the diffuse nature of the bony metastases. A decision to institute ^{32}P therapy was therefore made. Previous recommendation of administering testosterone prior to ^{32}P therapy was not followed because of its potential disadvantage of accelerating the metastatic growth per se. More recent idea of priming the bone with parathormone prior to ^{32}P administration was carried out. Our regimen consisted of administering to the patient 100 units of parathyroid extract I.M. T.I.D. for 6 days followed by a single intravenous dose of 10 mCi ^{32}P labeled sodium phosphate. We also gave a trial of ^{32}P alone before instituting 'Parathormone- ^{32}P ' regimen. While ^{32}P singularly did not work, parathormone in conjunction with ^{32}P was very effective in symptomatic relief of bone pain.

PREPARATION AND EVALUATION OF ^{131}I TETRACYCLINE AS A TUMOR SCANNING AGENT. PART I. PREPARATION AND STABILITY. Depew Chauncey, Samuel E. Halpern, Naomi P. Alazzaki, V.A. Hospital and University of California, San Diego, Calif.

In the past, tetracycline incorporation into tumor tissue has been studied briefly in both the non-labeled and radioiodinated forms. No conclusion as to its usefulness as a tumor scanning agent is possible on the basis of these data because of variance in production methodology. Accordingly we have studied the effect of mass, acidity and temperature on the labeling efficiency of tetracycline and on the in-vivo and in-vitro stability of the iodinated derivative. The following are the results of these studies.

^{131}I -tetracycline (^{131}I -Tet) was prepared by heating a solution containing varying quantities of tetracycline and HCl in methanol with I^{-131} in a sealed reaction vial. Under optimum conditions ($65^{\circ}C$, 2 hr., 300 ul tetracycline solution (10 mg/ml); 25 ul (I^{-131}) a labeling efficiency of 80% was consistently observed. Minimal in-vitro breakdown occurred in 96 hours. In-vivo biological distribution and stability studies were performed in Sprague-Dawley rats. Organ specific activities (counts/min/gram) and scintiphotos were obtained at 24 hours post IV injection. Very little uptake of radioiodine was noted in the thyroid gland and stomach indicating only token in vivo dehalogenation. The distribution studies indicate that ^{131}I -Tet behaves in a manner very similar to non-labeled tetracycline, with 70% of the radiopharmaceutical eliminated from the body via urine and feces within 24 hours. Disappearance of the compound from the blood and muscle tissue is also rapid. ^{131}I -Tet would appear to possess suitable in-vivo and in-vitro properties for use in Nuclear Medicine.

PREPARATION AND EVALUATION OF 131-I TETRACYCLINE AS A TUMOR SCANNING AGENT. PART II. UPTAKE IN VIABLE AND NON-VIABLE TUMOR. Depew Chauncey, Samuel E. Halpern, Philip Hagan and Naomi P. Alazraki, V.A. Hospital and University of California San Diego, Calif.

The distribution of 131-I tetracycline was studied in 100-200 gram Buffalo rats bearing transplanted hepatomas to determine the quantity of the radiopharmaceutical extracted by the viable and non-viable portions of their tumors. The effect of time, mass of tetracycline injected, and preloading of the animal with stable KI on the specific activity of these tissues was also studied. Control experiments were performed using carrier free 131 iodine.

Thirty minutes post-injection, the viable tumor contained more radiopharmaceutical than did the non-viable, however, a progressive decrease in the specific activity of viable tumor occurred with time. The highest ratios for non-viable tumor to blood, liver, kidney and muscle were obtained at 96 hours post-injection, being 103:1, 7:1, 48:1 and 386:1 respectively. The viable tumor ratios at this time were 8:1, 0.6:1, 4:1 and 30:1 for the same organ systems. In comparison, carrier free 131 iodine ratios were usually 1.0 and never rose above 2.6:1 for either viable or non-viable tumor.

Preloading the rats with stable KI had little effect on the radiopharmaceutical concentration by non-viable portions of the tumors, the ratios becoming 125:1, 4:1, 39:1 and 468:1, however, it markedly affected the viable tumor tissue (1.5:1, .05:1, .51:1, and 6:1).

Varying the mass of 131-I tetracycline induced an inverse relationship in the non-viable tumor specific activity.

In view of the above findings, 131-I tetracycline may offer advantages as a tumor scanning agent especially when the lesion contains some degree of necrosis.

TECHNETIUM-99m-Cu-HEDSPA-A NEW SKELETAL IMAGING AGENT. L. Rao Chervu, Quimat R. Goyal, and M. Donald Blaufox, Albert Einstein College of Medicine, Bronx, N.Y.

A new method of reducing Tc-99m pertechnetate with cuprous ion has been reported recently by our laboratories for the preparation of a Tc-99m-Cu-DTPA complex as a successful renal function agent. Subsequently the synthesis of Tc-99m labeled 1-hydroxy-ethylidene-1, 1-disodium phosphonate with cuprous chloride serving as a reducing agent has been investigated. Organ distribution data of the preparation in fifteen intravenous injections into mice shows very rapid uptake in bone with concurrent clearance of the remaining activity in urine. Negligible amounts remain in blood, muscle, liver, kidneys and GI tract after 1 hour. These data compare favorably with studies of the Tc-99m-Sn phosphate complexes previously reported in literature.

The blood clearance of the copper preparation is very rapid in the rabbit as well. Gamma camera studies obtained after intravenous administration of the technetium-copper-phosphonate complex in the rabbit yield excellent images within one hour post injection obviating the normal waiting period of three hours needed with most of the currently available Tc-99m-Sn-skeletal imaging agents.

The toxicity of copper in similar preparations has been evaluated. The administration of 100µg of copper chloride to an adult patient is well below established toxic limits with a safety factor of at least 10,000. Thus the new agent should prove useful as a valuable alternative to the currently used bone scanning radiopharmaceuticals.

Radiopharmaceutical agents formulated using this new reducing method employing copper in place of tin appear to show subtle differences in their pharmacodynamics. They may be physically and chemically more stable than comparable tin reduced agents. The new copper reducing method has potential for wide application in nuclear medicine.

CHEMISTRY OF LABELING SCHIFF'S BASES (PYRIDOXAL AMINO ACID COMPLEX) WITH Tc-99m AND THEIR USE IN HEPATOBIILIARY SCINTIGRAPHY. E. Chiotellis, G. Subramanian and J. G. McAfee, Nuclear Research Center "Democritos", Athens, Greece and Upstate Medical Center, Syracuse, New York

Baker et al. (J. Nucl. Med. 15:476, 1974) had reported on the preparation of Tc-99m pyridoxylidene glutamate, its rapid biliary excretion in experimental animals and man and found it to be a promising agent for this purpose.

This report summarizes our results on optimization of reaction conditions for Tc-99m Pyr-glu. and a wide variety of other Tc-99m labeled Pyridoxal-amino acid complexes.

These compounds were prepared by mixing in 3:1 ratio of pyridoxal with respective amino acids and Tc-99m pertechnetate in a volume of 5-8 ml. This mixture was autoclaved for different time intervals from 15 min. to 1 hr. and also the effect of pH was studied at these heating times.

Various analytical methods such as paper chromatography, T.L.C., I.T.L.C., electrophoresis, with different solvent systems were used for the separation and characterization of this class of compounds in comparison with free Tc-99m pertechnetate. Electrophoresis in barbitol buffer (pH 8.5) found to be the best method. Further, biological distribution studies were performed with these compounds in New Zealand albino rabbits by imaging using a scintillation camera from 5 min. to 1 hr. after injection.

The results indicate that most of the amino acid complexes of pyridoxal studied showed good biliary excretion with varying degree of kinetics. The optimum pH for most of the compounds seemed to be about 8.0. Some amino acids combined with Tc-99m and pyridoxal with considerably shorter heating time instead of 1 hr. 15' required for Tc-99m pyridoxylidene glutamate.

THE UTILITY OF BRAIN SCINTIPHOTOGRAPHY IN RECURRENT MEDULLOBLASTOMA. Edgar E. Clark and Robert S. Hattner, University of California Medical Center, San Francisco, Ca.

Twenty-three patients were evaluated for recurrent medulloblastoma with brain scans (86 total scans). Scan findings were correlated with clinical findings, other diagnostic tests, surgical and autopsy findings to determine the utility of brain scanning in detection of recurrent medulloblastoma.

In 19/23, clinical findings suggested recurrence in the posterior fossa. Only 13 of these 19 had lesions on scan. Of the other six, three had no evidence of tumor recurrence at surgery or autopsy and three had no evidence of tumor recurrence on prolonged follow-up. In addition, scans demonstrated posterior fossa recurrence in two patients without clinical findings.

Supratentorial metastases were demonstrated in 9/23. Only one of these was clinically suspected. Posterior fossa recurrence was present in 8/9 of these patients.

Correlation of scan findings with other diagnostic tests, surgical and autopsy findings shows agreement in 13/14 for posterior fossa recurrence and agreement in 7/11 for supratentorial metastases.

Other scan findings include subdural hematoma in two patients and skull metastases in one patient. The angiographic posterior flow sequence was abnormal in only 3/15 patients with posterior fossa recurrence. One patient's tumor was more distinct on immediate blood pool image than on delayed images.

Conclusions: (1) Brain scans are sensitive to recurrence of medulloblastoma in the posterior fossa and more specific than clinical findings. (2) Scans are far more sensitive than clinical findings for supratentorial metastases. (3) Scans are useful for detecting other conditions which are clinically confused with recurrent tumor. (4) Immediate post flow scintiphotos are occasionally the most useful images for detecting recurrent medulloblastoma.

AN ANALYSIS OF FACTORS WHICH INFLUENCE THE LOCAL ACCUMULATION OF BONE SEEKING RADIOPHARMACEUTICALS. Geoffrey Coates, Barry M. Bowen, Claude Nahmias, and Edmund S. Garnett, McMaster University Medical Centre, Hamilton, Ontario, Canada.

Van Dyke et al postulated that the skeletal distribution of the bone seeking radio nuclide F-18 is determined by differences in the blood flow to the various bones. This postulate was based on the assumption that F-18 was totally extracted in a single passage through bone. Wootton has recently proved that this is the case. In addition it has been shown that manoeuvres known to increase local blood flow also increase the local accumulation of F-18 and other bone-seeking radio nuclides.

A study of other factors which influence the accumulation of radiopharmaceuticals in bone is presented. The avidity with which Tc-99m-Sn-pyrophosphate and F-18 fluoride are adsorbed by bone crystals has been measured in vitro and the efficiency with which these radiopharmaceuticals are extracted by one passage through normal bone has been measured in rabbits. It is postulated that alterations in the capillary permeability in the region of a bone lesion greatly influence the target to background ratio that can be obtained with bone seeking radiopharmaceuticals. Quantitated gamma camera studies in man are presented in support of this hypothesis.

LABELLED SOLUBLE FIBRIN: RAPIDLY CLEARING THROMBUS LOCALIZING AGENT. R. Edward Coleman, Sylvia S. L. Harwig, John F. Harwig, Laurence A. Sherman, and Michael J. Welch. Washington University School of Medicine, St. Louis, Mo.

We have evaluated radioiodinated soluble fibrin as an agent which could be used to image a thrombus in a region with a large blood pool since radioiodinated fibrinogen, with a biologic half-life of 120 hours, is not suitable for imaging during the first day after injection.

Labeled soluble fibrin was prepared by clotting radioiodinated canine fibrinogen and dissolving the clot under specified conditions. Thrombi were induced by intimal injury with an electric current in the coronary arteries of 6 dogs and femoral veins of 10 dogs. Labeled soluble fibrin and fibrinogen were injected 2, 4, 8 or 24 hours after venous thrombosis and 4 hours after coronary artery thrombosis. The thrombi were removed 24 hours after injection.

Biologic clearance studies of soluble fibrin in 3 dogs revealed a half-life of 5 hours. Accumulation of labeled soluble fibrin and fibrinogen in coronary artery thrombi was the same. Tissue distribution revealed higher thrombus/blood, thrombus/infarcted myocardium and thrombus/normal myocardium ratios with soluble fibrin than with fibrinogen. In venous thrombosis, maximum thrombus/blood ratios were obtained when the labeled soluble fibrin and fibrinogen were injected 4 hours after thrombosis and the ratios were greater for soluble fibrin than for fibrinogen when these tracers were injected 4, 8, or 24 hours after thrombosis.

Labeled soluble fibrin has some advantages when compared to fibrinogen as a thrombus imaging agent, especially in a region with a large blood pool. Labeling of soluble fibrin with I-123 or Tc-99m is desirable since it is cleared so rapidly. (This work supported by NIH SCOR, Grant No. 1 P17 HL 14147-04)

APPLICATION OF COMPUTERIZED RADIONUCLIDE TRANSAXIAL TOMOGRAPHY WITH POSITRON EMITTING RADIOPHARMACEUTICALS.

R. Edward Coleman, Edward J. Hoffman, Michael E. Phelps, Michael J. Welch, and Michel M. Ter-Pogossian. Washington University School of Medicine, St. Louis, Mo.

A Positron Emission Transverse Tomograph (PETT III) has recently been developed at Mallinckrodt Institute of Radiology and we are presently evaluating it for clinical and research applications. A prototype PETT had a constant resolution with depth of 1 cm, gave a quantitative reproduction of the activity in the cross section and eliminated the problem of superimposition of activity. Several cyclotron-produced radiopharmaceuticals have been evaluated with the prototype PETT.

Normal myocardium has been imaged after the intravenous administration of N-13 ammonia. The myocardial blood pool has been determined with C-11 carbon monoxide inhalation and measurement of the C-11 carboxyhemoglobin distribution.

The PETT provides a means for simple, non-invasive studies of cerebral hemodynamics. Cerebral blood volume can be determined from a tomogram after C-11-CO inhalation if the blood activity is determined. The relative distribution of cerebral perfusion can be evaluated after the intravenous administration of N-13 ammonia. Abnormalities in the blood-brain-barrier can be detected with the use of generator-produced Ga-68-EDTA.

We have demonstrated the advantages of transaxial tomography using positron-emitting radiopharmaceuticals. The PETT offers a significant improvement in evaluating different physiologic functions of several organ systems. (Work supported by NIH grant No. 1 P01 HL 13851).

IMPROVED DETECTION OF MYOCARDIAL INFARCTION WITH Tc-99m(Sn) PYROPHOSPHATE AND SERUM MB CPK. R. Edward Coleman, Milton S. Klein, S. Aftab Ahmed, Robert Roberts, and Burton E. Sobel. Washington University School of Medicine, St. Louis, Mo.

To evaluate the relative sensitivity of Tc-99m (Sn) pyrophosphate imaging and elevated serum MB CPK (the "myocardial" isoenzyme) in the detection of acute myocardial infarction (MI), we studied 45 patients with suspected MI, 10 recovering from cardiac surgery, and 10 dogs subjected to transient coronary occlusion from 10 min to 1 hr duration.

All 5 dogs with occlusion exceeding 30 min had increased serum MB CPK. Four had abnormal images. Of 5 dogs with occlusion for less than 30 min, none exhibited either increased MB CPK or an abnormal image.

Serum MB CPK increased after cardiac surgery in all patients undergoing valve replacement (5) as well as those undergoing coronary bypass (5). No patient exhibited an abnormal image after cardiac surgery.

Confirmed acute myocardial infarction in 25 patients was invariably associated with increased MB CPK. Twenty-three (92%) of these patients had abnormal images. Abnormal images occurred in 2 of 20 patients who did not have confirmed MI. Image localization correlated well with electrocardiographic locus of infarction. However, infarct size estimated by imaging did not correlate well with estimates based on serial changes in MB CPK activity.

Results indicate: 1) false-positive images in patients without myocardial infarction can be recognized by consideration of MB CPK activity; 2) interpretation of elevated MB activity, particularly after cardiac surgery, is facilitated by evaluation with imaging; and 3) increased MB CPK associated with abnormal images occurs after transient experimental coronary occlusion of comparable duration.

CARBON-11 LABELLED PSYCHOACTIVE DRUGS. Dominique Comar, Mariannick Maziere, Christian Marazano and Claude Raynaud. C.E.A., Service F. Joliot, Hôpital d'Orsay, France.

Methylation of secondary amides and amines by methyl iodide and formaldehyde respectively are rapid processes for incorporating carbon-11, particularly in psychoactive substances. Carbon-11 produced as CO₂, by a compact cyclotron, is reduced to methanol-C11 by LiAlH₄. Methanol is converted to formaldehyde-C11 by a silver catalyst oxidation with a 50 % yield. Methanol can also be converted to methyl iodide with a 90 % yield. Chlorpromazine, thiopropazine, imipramine and nicotine were labelled by action of formaldehyde-C11 on the nor corresponding derivative. Diazepam and caffeine were labelled by action of methyl iodide-C11 on nor diazepam and theobromine. The overall time for synthesis, purification and sterilisation of these molecules is about 30 minutes with a 10 to 20 % radiochemical yield. When injected in animals these products show a high uptake in the brain and lungs for chlorpromazine and imipramine, in the brain and heart for diazepam and in the brain and kidney for nicotine.

After i.v. injection in humans, the brain uptake for chlorpromazine and imipramine was found to be 4 to 7 % of the injected dose 30 to 60 minutes after the injection for normal subjects and significantly lower in psychotic subjects under chronic administration with one or the other of these drugs.

Demethylation, which represents an important process of degradation of these drugs, is a long phenomenon compared to the 20 minutes C11 half-life, in case of chlorpromazine and imipramine. On the other hand the low uptake of diazepam in the brain and the absence of a heart image in humans may be explained by the rapid demethylation of this product. Thanks to the C11 labelling of psychoactive molecules having a high blood-brain barrier permeability, human brain imaging becomes now possible.

RADIONUCLIDE EVALUATION OF DISTAL FEMORAL METAPHYSEAL IRREGULARITIES WHICH SIMULATE NEOPLASM. James J. Conway, Nihal Gooneratne, and George Simon. The Children's Memorial Hospital, Chicago, Ill.

Benign bone defects are common in children. Most of these defects are readily diagnosed by their location and roentgenographic appearance. One such defect occurs in the distal metaphyseal region of the femur in young children and adolescents. The defect often produces consternation even to those who are familiar with the entity since its appearance, cortical disruption, periosteal irregularity, and even Codman's triangle, simulates neoplasm.

Indeed, there are reported examples wherein the patient was subjected to surgical biopsy or excision of the defect. It has been given a variety of names including: the avulsive cortical irregularity, periosteal desmoid, subperiosteal desmoid, cortical desmoid, subperiosteal abrasion, cortical abrasion, medial distal metaphyseal femoral irregularity, subperiosteal cortical defect, fibrous cortical defect, and fibrous metaphyseal defect. These names imply an etiology arising from trauma, infection, or neoplasm. It would be expected that abnormal radionuclide bone images would be found if such were the case.

Several children with this entity were studied with radionuclide bone imaging. One adolescent was referred for "amputation of an osteogenic sarcoma." The radionuclide images were normal excluding trauma, infection, or neoplasm as an etiology for the bone appearance. It, therefore, represents a normal developmental configuration in childhood of which one should be aware. Radionuclide bone imaging is strongly recommended for the evaluation of such lesions in order to alleviate concern on the part of the patient as well as the clinician regarding its origin.

A COMPARISON BETWEEN DIRECT AND INDIRECT RADIONUCLIDE CYSTOGRAPHY FOR DETECTING VESICoureTERAL REFLUX. James J. Conway and Gerald D. Kruglik. The Children's Memorial Hospital, Chicago, Illinois.

Direct radionuclide cystography has been shown to be more effective for detecting significant vesicoureteral reflux and with a marked radiation dose reduction when compared with roentgenographic cystography. Indirect radionuclide techniques have also been proposed to detect reflux but have not been evaluated in a comparative manner. The elimination of catheterization is a desired advantage of the indirect method but is of little benefit if the technique is ineffective for detecting reflux. Our initial direct technique involved the instillation of the radionuclide directly into the bladder and imaging during filling and after voiding. A modification of this method to include imaging during voiding would simulate an ideal indirect method, that is, a completely cleared radiopharmaceutical within the bladder. Thus, a comparative method was achieved without subjecting the child to additional radiation from the comparative study.

Only those patients who demonstrated reflux during the examination were evaluated in this study. 137 studies in 90 patients were evaluated. In 29 patients (21%) reflux was detected only during the filling phase of the examination. In 12 patients (9%) reflux was detected only during voiding. These results indicate that techniques which only evaluate the presence of reflux during certain phases, i.e. during voiding, such as indirect radionuclide cystography and roentgenographic cystography will miss a significant number of examples of vesicoureteral reflux. It is therefore recommended that the direct technique be used to include prefilling, voiding, and post-voiding images.

THE ROLE OF RADIONUCLIDES IN EVALUATING CENTRAL NERVOUS SYSTEM COMPLICATIONS FROM CHEMOTHERAPEUTIC AGENTS. James J. Conway, Joanna J. Seibert, Gerald P. Kuhn, and William E. Bell. The Children's Memorial Hospital, Chicago, Ill.

In the last decade, chemotherapeutic agents have become increasingly more important in the management of malignancy. Major advances have been achieved in the treatment of leukemia. Intrathecal methotrexate has been given prophylactically and for treatment of central nervous system involvement. The complications from its use are well known and include chemical meningitis, arachnoiditis, transverse myelitis, death (acute hypersensitivity reaction) and leukoencephalopathy. The syndrome of "leukoencephalopathy" includes malaise, tremors leading to seizures and in many instances coma leading to death. Recovery is often accompanied by severe neurological deficit. Etiology for the symptoms has not been established but factors such as central nervous system involvement with leukemia, radiation therapy, infection, and preservative agents within the pharmaceutical have been excluded as causal agents.

Eight patients have been collected from several institutions. Characteristic radionuclide images demonstrating ventricular or meningeal patterns of abnormal radionuclide localization herald the abnormality. Calcification within the paraventricular region of the brain occurs at a delayed interval in recovered patients.

It is proposed that toxic concentrations of methotrexate produced by altered cerebral-spinal fluid flow contribute to the histologic finding of microvascular infarction. Radionuclide imaging performed at the proper time to detect infarction may demonstrate the abnormality. Radionuclide cisternography is suggested as a means to determine abnormal cerebral-spinal fluid flow and thus prevent injections of intrathecal methotrexate which would localize in toxic concentrations.

THE SOLITARY BONE LESION: A CLINICAL DILEMMA. Robert C. Corcoran, James Thrall, Ralph Kyle, and Merrill Johnson. Walter Reed Army Medical Center, Washington, D.C.

To assess the significance of solitary lesions in bone scan interpretation and clinical patient management, 2000 consecutive whole body scans were reviewed. Either Tc-99m-Polyphosphate or Tc-99m-Diphosphonate was used as the radiopharmaceutical. 142 or 7% demonstrated solitary foci of increased tracer uptake. The overall series positivity rate was 45% and therefore 15% of all abnormal scans were in the solitary category.

23 of the 142 cases were in patients with primary bone tumors and 22 in patients with various benign conditions. In all of the former, and 18 of the latter, radiographic correlation or other data confirmed the scan findings. Therefore, as a group, these patients did not present a problem in clinical decision making.

Ninety-seven of the 142 cases were in patients with known extra-osseous neoplasms. The clinical significance in this subset was generally more difficult to establish and particularly for the 20 rib lesions which were encountered. Trauma would be an explanation but could not be implicated radiographically or by history. In 3 cases excisional biopsy after tracer localization was also negative.

32 of the 97 patients with non osseous primary malignancies had follow-up scans. In 5 patients, the repeat scan failed to reveal a lesion. In 9 patients, the scan went from a solitary positive area to multiple areas of involvement. The remainder showed no change.

Solitary lesions represent a unique interpretive and management problem. Radiographic and clinical correlation may be helpful. But, when searching for metastatic disease, the solitary lesion, particularly in the ribs, cannot be regarded as proof of skeletal involvement without other correlative data.

BONE IMAGING WITH F-18 AND Tc-99m-EHDP AFTER TOTAL HIP REPLACEMENT. Hans Creutzig. Medizinische Hochschule Hannover, Germany.

Total hip replacement has been proved to be an optimal therapy for some hip diseases. Conventional diagnosis often failed to detect complications after replacements i.e. infections early enough for a successful conservative therapy.

Bone imaging might be useful to do so. In a prospective study we examined 35 patients every 3rd month after replacement up to now for more than 12 months. F-18 and Tc-99m-EHDP were compared in their diagnostic efficiency. Simultaneous scintigraphy was done with a 5"-scanner attached to a 2x4096 core memory.

Eight patients developed clinical signs of infection one to three months after scan had become positive. The uptake ratio between infected bone and normal contralateral femur was not different for both radionuclides. In five patients with only an extraosseous infection the Tc-99m-ratio was significantly higher. In 14 patients with normal prothesis both scans had been negative. In additional four patients with normal prothesis the F-18-scan was negative but the Tc-99m-scan strongly positive. A method for early detection of complication with a false-positive rate of 4/35 and no false-negative results may be acceptable. F-18-bone-imaging without any false result in our patients will be better.

COMPARISON OF GREY SCALE ECHOGRAPHY AND Cs-131 SCANNING IN THE EVALUATION OF THE SOLITARY, NON-FUNCTIONING THYROID NODULE. - A STUDY OF 110 CASES. Ernest F. Crocker, Andrew F. McLaughlin, Roger F. Uren, John G. Morris, Department of Nuclear Medicine, Royal Prince Alfred Hospital, Sydney, Australia. Jack Jellins, George Kossoff, National Acoustic Laboratories, Sydney, Australia.

Two procedures used in the evaluation of the nature of solitary, non-functioning thyroid nodules as determined by technetium scintiscanning include radionuclide scanning with Cs-131 and grey scale echography. Whereas echography provides information regarding nodular infrastructure, the affinity of a nodule for Cs-131 reflects the cellularity and vascularity of the lesion. These investigations were performed over a 12 month period on 110 patients. Seventy four lesions were subjected to excision biopsy.

The caesium scans were performed on a Picker Magna scanner two hours after a 1.5 mCi I.V. dose of Cs-131 chloride Echography was performed by the water delay method using a medium focussing 7.5 MHz transducer.

Each nodule was classified according to its affinity for Cs-131 and subclassified according to its ultrasonic appearance as solid, solid with some degree of cystic degeneration or cystic. All lesions which accumulated caesium were echographically solid; 63% of those which did not accumulate caesium however were also solid. This latter group of "cold" caesium nodules are often mistakenly assumed to be cystic and managed conservatively. Excision biopsy confirmed that echography was 100% accurate in the differentiation of solid from cystic lesions.

The study confirms that grey scale echography is far superior to Cs-131 scanning in the identification of those solitary non-functioning nodules which are solid and should replace the latter investigation whenever ultrasound facilities are available.

A NUCLEAR MEDICINE INFORMATION NETWORK. James L. Daly, Francis K. Herbig, James W. Fletcher. St. Louis Veterans Administration Hospital and Saint Louis University School of Medicine, St. Louis, Mo.

A Nuclear Medicine Information Network has been established which links three Veterans Administration Hospitals in rural Missouri and Illinois to the Nuclear Medicine Service of the John Cochran Hospital in St. Louis, Mo.

By utilizing computer acquisition of pre-defined studies and synchronous telephone transmission of the acquired images to the central site, analysis of both static and dynamic studies is available to the remote hospitals without a nuclear medicine specialist in residence.

As images are acquired during the day at each remote site they are stored on a magnetic disk cartridge together with the patient information for the study. At the end of the day the acquisition computer at the central site contacts each remote hospital and initiates the transmission of the images and patient information collected during the day.

The transmitted images are read by a physician at the central site, and reports dictated for transmission to the remote hospitals.

An average of six studies per day from each remote hospital are presently being acquired, transmitted and interpreted at the central facility in St. Louis.

The simplicity of the technologist's interaction with the computer at each remote site, and the efficiency of telephone transmission of images have shown the Network to be a practical means of providing high level Nuclear Medicine service to hospitals which would otherwise lack this diagnostic capability.

A MINI-COMPUTER SYSTEM FOR DYNAMIC RADIOISOTOPE STUDIES IN THE EYE. D. D'Amato, J. Bronzino, C. Miller and J. O'Rourke. University of Connecticut Health Center, Farmington, CT.

A complete computerized system, both hardware and software, has been developed to automate and display various procedures in an ophthalmology clinical laboratory. Radioisotope clearance studies are greatly simplified with this system. Recorded counts are immediately logarithmically converted and displayed on a fully annotated graph. At the conclusion of the study, the clinician may choose regions of the study (with a graphics cursor) that he desires to be least squares fitted. The calculated clearance rates along with the associated standard errors and quality of fit parameters are displayed above the clearance graph.

The system is based on a PDP-8E computer with 16K of core memory and includes a dual-drive Decasette system and a Tektronix 4010-1 Interactive Display Terminal. The software controls the acquisition of data from a NIM scaler or an analog-to-digital converter, precisely (with a crystal clock) times the procedure, analyzes and simultaneously displays the data and stores the data with documentation on magnetic cassettes. The library of user-written routines is on cassettes and also includes programs for acquisition and display of tonograms of the eye, for retrieval, display and analysis of previously stored data and for paper tape to cassette transfer of data obtained outside of the clinical laboratory. The programs have been written in a Fortran specially modified for cassette usage. Fortran compatible assembly language sub-

outines for control of the 4010 plotting, the cassettes, the crystal clock, the scaler and the ADC have also been written.

ACUTE MYOCARDIAL INFARCT IMAGING AGENTS: STRUCTURE-ACTIVITY RELATIONSHIPS. Michael A. Davis and B. Leonard Holman. Harvard Medical School, Boston, Mass.

A number of radiolabeled compounds with marked variation in chemical structure were examined to determine their biologic distribution and infarct specificity. The animal model utilized for this screening and evaluation was a heat inflicted myocardial lesion in the rat. Values of absolute concentration within the infarct as well as the ratios of infarct to normal myocardium, blood and muscle were determined. Two technetium labeled skeletal imaging agents, pyrophosphate (PP_i) and 1-hydroxyethylidene-1,1-diphosphonate (HEDP) exhibited the most potential among the Tc-99m labeled compounds followed by tetracycline. The infarct to normal myocardium ratio (MI/N1) for the three agents was 26, 28 and 14, respectively. The relationship between infarct specificity and the presence of one or more sulfhydryl groups in a molecule containing additional function groups (NH₂, OH or COOH) was explored using five technetium labeled compounds, penicillamine, 2-mercaptoisobutyric acid, dihydrothioctic acid, 2,3-dimercaptosuccinic acid and 1-thio-glycerol. The two latter compounds exhibited the best infarct localization within this group, having MI/N1 ratios of 10. The radiopharmaceutical showing the most favorable concentration in the infarct and the best target to non-target ratios (MI/N1=35) was an iodinated derivative of mercurihydroxyfluorescein. Values obtained with chlormerodrin and rose bengal indicated that both covalently bound mercury and the fluorescein structure are necessary to insure high infarct specificity. From these results it is clear that certain structural configurations and functional groups are responsible for the preferential sequestration of radiopharmaceuticals in the injured myocardium. These chemical regularities have permitted us to speculate on the biologic and chemical properties most suitable for infarct imaging.

ENHANCED TUMOR DETECTION BY GALLIUM SUBTRACTION TECHNIQUES. Frank H. DeLand, Robert M. Beihn, Guy H. Simmons, and Teresa V. Hafner. University of Kentucky Medical Center and V.A. Hospital, Lexington, Ky.

Since the introduction of Gallium-67 citrate for the detection of lymphomatous neoplasms, extensive studies by the ORAU group have documented its value. However, 67-Ga citrate has undesirable depositions in several organs including bone, as well as general body retention. The purpose of this study was to determine if radionuclide subtraction techniques using different radiodiagnostic agents would enhance diagnostic detection. Twenty patients with neoplasia were examined with 67 Ga-citrate employing subtraction scans with 99mTc-sulfur colloid, 99mTc microspheres, 99mTc-diphosphonate, or in combination with the 99mTc labeled agents. Patients with primary and metastatic tumors were examined and included lymphomas and carcinomas of the lung, breast, buccal mucosa, and liver. Each suspicious area in the 67 Ga-citrate images were treated as an individual lesion and the value of the subtraction procedures was also applied to each area. The interpreted results of the subtraction technique were categorized as: 1) confirming a positive 67 Ga abnormal area, 2) confirming a suspicious region, 3) eliminating a suspicious region, or 4) identifying a previously undetected area. In the composite gallium-67 images, 34 positive or suspicious lesions were observed. The subtraction technique confirmed 7 positive lesions and eliminated 3 that were previously thought to be positive; 8 suspicious regions were confirmed and 16 were eliminated. Seven lesions not observed on the gallium scans were identified. Subtraction techniques eliminated 30% of lesions thought to be positive, 67% of suspicious lesions, and identified as many unsuspected lesions as confirmed positive lesions. The value of radionuclide subtraction has been so significant that all 67 Ga-citrate studies are routinely accompanied by appropriate subtraction.

COMPUTER CORRECTION OF IMAGE ERRORS. Frank H. DeLand, Dale Fisher, P.R. Bell, Wm. J. McClain, Robert S. Dillon and D. A. Ross. University of Kentucky, Lexington, Ky., V.A. Hospital, Gainesville, Fla., and ORNL, Oak Ridge, Tenn.

Images from scintillation cameras or rectilinear scanners contain erroneous information inherent in the method and instrumentation. Design correction of these errors are either impossible or prohibitively expensive. A computer program has been designed that removed the most prominent of these faults so that application of statistical processing has greater validity. The basis of the program is the elimination of gamma ray scattering within the patient and penetration of collimator septa. Point source response of the system provides the information for calculating and subtracting the unwanted part of the image. The correction for these two defects is applied to each specific instrument. Other data processing includes correction of crystal non-uniformity response, data bounding, gaussian smoothing and validation. The degree of improvement is more marked when the radionuclide emits more than one gamma energy, eg., gallium 67, potassium 43, etc. The program was initially applied to normal brain images to evaluate the improvement in distribution of radioactivity. The processed and unprocessed images were correlated with expected distributions of $^{99m}\text{TcO}_4$. Multicycling of the data visibly revealed the value of the correction processing. In $^{99m}\text{TcO}_4$ brain scans the most significant improvement was observed in those regions with the most intense activity. Cold mass lesions of the liver not defined by the raw data were reconstituted by the computer processing. Our results indicate that this computer program provides greater validity of radionuclide distribution.

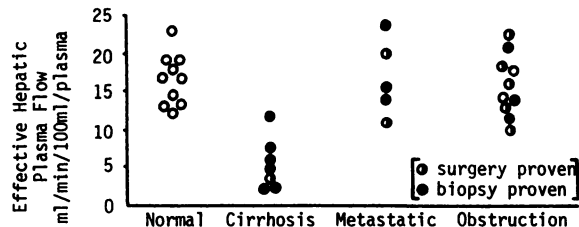
TUMOR LOCALIZATION IN ANIMALS AND PATIENTS USING RADIOIODINATED BLEOMYCIN. Gerald L. DeNardo, Sally J. DeNardo, Jeanne Meyers and Kenneth A. Krohn. University of California, Davis, Ca.

Both Ga-67-citrate and In-111-bleomycin have proved useful in the evaluation of patients with cancer, yet neither has proved entirely satisfactory. In the case of In-111-bleomycin, *in vivo* instability of the radiopharmaceutical is believed to be a basic problem so that a variety of other radionuclidic cations have been used to chelate bleomycin. None of these radiopharmaceuticals is satisfactory in all respects. We have labeled bleomycin with I-123 and I-131 and the resultant radiopharmaceuticals have been stable *in vitro* and *in vivo*. Tissue distribution of Ga-67-citrate, I-131-bleomycin, In-111-bleomycin and other radio-labeled bleomycins have been compared in tumor bearing rodents. During the first 24 hrs, tumor uptake of I-131-bleomycin was good with more favorable tumor:blood (12.1 at 6 hr) and tumor:muscle (36.8 at 6 hr) ratios than other bleomycin radiopharmaceuticals. Six hours after injection of the radiopharmaceutical the body content of I-131-bleomycin and Ga-67-citrate was $8 \pm 2\%$ and $85 \pm 5\%$ of the injected dose in the whole body and $.17 \pm .06\%$ and $9.7 \pm 1.9\%$ injected dose/gram in the blood respectively. Because of these encouraging results, whole body scintigraphy, clearance and blood clearance with I-123-bleomycin, In-111-bleomycin and Ga-67-citrate have been compared in patients with cancer. When I-123-bleomycin was used, increased radioactivity was present in the neoplastic tissue, kidneys, bladder and to a lesser extent in the thyroid, salivary glands and gut. The iodinated bleomycin was rapidly distributed and rapidly cleared from the body. These definitive animal studies and preliminary studies in patients cause us to conclude that I-123-bleomycin is chemically, biologically and physically the most suitable radiolabeled bleomycin thus far used for scintigraphic tumor localization, and warrants more extensive clinical comparison with Ga-67-citrate.

CLINICAL PATTERNS OF EFFECTIVE HEPATIC PLASMA FLOW IN DIFFERENTIATING CIRRHOSIS FROM METASTATIC OR BILIARY OBSTRUCTIVE DISEASE. Sally DeNardo, George Bell, Gerald DeNardo, Robert Carretta, Paul Scheibe, Thomas Imperato, and Peter Jackson. Univ. of Calif., School of Medicine, Davis, Calif.

The clinical usefulness of effective hepatic plasma flow derived from radioactive colloid clearance has not previously been evaluated. During the past year, 60 individuals of whom 27 were normal or had cirrhosis, hepatic metastasis, or hepatobiliary obstruction have been studied in the following manner. Gold colloid kinetics were determined by both camera areas of interest and probe detectors; using a mathematical model, the hepatic clearance rate (effective plasma flow), the ratio of hepatic to splenic clearance, and the ratio of hepatic to extrahepatosplenic clearance were derived. Useful differences in kinetic patterns were noted. Cirrhosis was characterized by a reduced effective

plasma flow, hepatic to splenic ratio, and hepatic to extra-hepatosplenic ratio; metastatic diseases, which may mimic cirrhosis on colloid scan, and hepatobiliary obstruction were not significantly abnormal with respect to the indices.



This difference in effective plasma flow appears useful, in conjunction with the static colloid liver scan, to differentiate cirrhosis from metastatic liver disease.

CLINICAL USEFULNESS OF I-123-FIBRINOGEN (I-123-F) FOR DETECTION OF THROMBOPHLEBITIS (TP). Sally J. DeNardo, Gerald L. DeNardo, Robert F. Carretta, Anne-Line Jansholt, Kenneth A. Krohn, Neal F. Peek. University of California School of Medicine, Davis, Calif.

TP is common, potentially lethal because it results in emboli in 3-10% of patients, and clinically occult in 50-75% of patients. Existing non-radioisotopic methods are either invasive, painful, insensitive or not specific. I-125-fibrinogen (I-125-F) uptake has proved sensitive in the legs, but can be falsely positive in inflammatory conditions, and is not effective for thrombotic disease of the trunk. We have evaluated the usefulness of I-123-F imaging for detection of TP in 35 patients (40 studies). These patients were selected because of: 1) abnormal perfusion lung scan without clinical TP (8 pts); 2) abnormal I-125-F uptake with or without clinical TP (7 pts); 3) nonspecific manifestations possibly due to TP (20 pts). 25 studies in 22 patients were abnormal and the remainder were normal. 18 of 19 radiopaque venograms (RV) and 18 of 21 I-125-F studies confirmed the I-123-F images. The other RV was performed after 2 weeks on heparin, and the other 3 non-confirmatory I-125-F involved one patient with pelvic thrombi and 2 on 1 week heparin prior to I-123-F. In addition, I-123-F made possible specific diagnosis of arthritis and TP in 2 patients suspected of TP and cellulitis respectively; I-125-F was not diagnostic in the 1st instance and was not performed in the 2nd instance because of its non-specificity. 5 positive studies were repeated after 8-18 days of IV heparin; 3 again demonstrated incorporation of I-123-F in thrombi.

This study suggests that I-123-F imaging is a sensitive method for: 1) detecting active thrombi, even in the pelvic area; 2) differentiating TP from inflammatory diseases; 3) determining the adequacy of heparin therapy; and 4) determining the need for surgical therapy.

OPTIMAL COLLIMATORS FOR POSITRON-EMITTING ISOTOPES. Stephen E. Derenzo, Haim Zaklad, and Thomas F. Budinger. Lawrence Berkeley Laboratory, Berkeley, Calif.

The increasing availability of positron-emitting isotopes in multi-mCi activities (especially generator produced 75 sec Rb-82 for myocardial imaging) has motivated us to design, build, and test a prototype high resolution parallel channel collimator for 511-keV gamma rays. The use of interlocking lead sheets 1.9 mm thick ("eggcrate" assembly) permitted a low cost construction of 3.2 mm square channels 11.4 cm long. The image resolution for 6 mm diam sources of F-18, Rb-81, and Rb-82 placed 13 cm from the collimator was 12 mm FWHM. The intrinsic collimator resolution is calculated to be 9 mm FWHM. For F-18 the septal leakage (i.e., septal penetration plus septal scatter integrated over all angles) was 40% of the geometrical transmission of 3.2×10^{-5} (imaging sensitivity was approximately 220 dots/sec/mCi).

Our Monte Carlo computer code accurately simulates the absorption and scattering processes that occur within the collimator septa. The code predicts resolutions, geometrical transmissions and septal leakages that are in agreement with experimental observations. Using this code it was possible for the first time to calculate designs for collimators having fixed septal leakage and maximal geometrical transmission for high energy gamma rays. For example, the optimal square channel lead collimator for

511-keV gamma rays with a resolution of 10 mm FWHM at a depth of 13 cm and a septal leakage 20% of the geometrical transmission has the following properties: channel length 17 cm, channel size, 4.9 mm, septal thickness, 1.8 mm, and geometrical transmission, 4.2×10^{-5} .

These collimator designs and fabrication techniques are being used for imaging Rb-82 in the myocardium.

A CLINICALLY PRACTICABLE PROCEDURE FOR THE QUANTITATIVE EVALUATION OF REGIONAL CEREBRAL CIRCULATION.
Arnold H. Deutchman, Lawrence R. Fulmer, Gary R. Wise, Don W. Miller, and William W. Hunter, Jr.
The Ohio State University, Columbus, Ohio.

A clinically practicable, routine procedure for the quantitative evaluation of regional cerebral circulation using a bolus of intravenously injected Tc-99m Pertechnetate has been developed and used effectively for over a year. The procedure guarantees results which are reproducible in individual patients and comparable from patient to patient through the use of new head-shielding technology and completely automatic data analysis routines. The vertex view is used which allows the separation of the regions perfused by the anterior, middle, and posterior cerebral arteries. The percentage difference in the arterial phase of the right and left hemisphere circulation curves in each of the three automatically selected regions is calculated. The quantitative presentation of the study allows detection of smaller differences in regional circulation than are apparent by visual interpretation of sequential one-second static images. Separation of normal from abnormal patients who have mild to moderate C.N.S. symptoms due to cortical ischemia can be accomplished with a low false positive rate. Thus far the method has been successful in diagnosing patients with internal capsule or vertebral-basilar ischemia. The reproducibility of the results and the safety of the procedure permit its use as a screening test for patients in whom angiography is being considered.

MECHANISM OF LOCALIZATION OF Tc-99m LABELED PYROPHOSPHATE AND TETRACYCLINE IN INFARCTED MYOCARDIUM.
Mrinal K. Dewanjee, Paul C. Kahn, Urmila Dewanjee and R.J. Connolly.
N.E. Medical Center and Tufts Medical School, Boston, Massachusetts.

To correlate the phenomenon of pathophysiology of infarcted myocardium and localization of Tc-99m-labeled pyrophosphate and tetracycline and calcium ion, double labeling, subcellular localization and autoradiographic techniques were used in this investigation. Myocardial infarct in the rabbit was induced by coronary artery ligation. The animals were then injected with mixtures of H-3 tetracycline, P-32 pyrophosphate, Ca-45, Tc-99m tetracycline or pyrophosphate. Animals were sacrificed at 3 and 18 hours after infarction and gamma and beta-ray activity in the normal, infarcted myocardium, and other tissues were determined with NaI (Tl) and liquid scintillation detector; β - and γ -ray activities in the cellular components were obtained from the homogenates of normal and infarcted myocardium. At 18 hours after injection, (infarcted vs. normal myocardium) ratio of (5:1), (8:1), and (20:1) were obtained for P-32, Ca-45, and Tc-99m pyrophosphate respectively. The differential centrifugation studies indicate that about 50% of the radioactivity is obtained in the lysosomal enzyme and 10-20% in the mitochondrial fraction. This may occur due to the enhanced affinity of denatured macromolecules for the labeled compounds. The labeled pyrophosphate activity in infarcted tissue increases with the rise of the cationic charge of the chelated metal ion. The faster uptake of Tc-pyrophosphate, Tc-tetracycline, Ca^{2+} and Sr^{2+} ions and slower uptake of pyrophosphate in infarcted lesion and biochemical analyses of labeled dead cells indicate that the apatite formation is not directly responsible for the localization of Tc-chelate. It might correspond to a process of pseudo-calcification as in other pathological mineralization and might occur due to the binding of denatured macromolecules with a Tc-chelate.

EARLY SEQUENTIAL AND DELAYED IMAGES OF TECHNETIUM-99mSn DTPA IN CHRONIC OBSTRUCTIVE RENAL DISEASE.
John E. Devenney, Jose O. Morales, and David E. Kuhl.
Hospital of the University of Pennsylvania, Philadelphia, Pa.

Seldin has shown that in the chronically obstructed kidney there is a marked depression in tubular function

with renal excretion depending primarily on glomerular filtration. Tubular agents such as orthiodhippurate and chlormerodrin are useful in documenting reduced renal function in many disease states. However, we reason that a glomerular agent might be preferred to a tubular agent in patients with far advanced chronic obstruction when there is a need to estimate residual renal function and visualization with tubular agents is poor. Because of this, we have examined the use of early sequential and delayed images of Tc-99mSnDTPA in the chronically obstructed kidneys of adults and children.

Our results suggest that in the early stages of chronic obstruction, tubular function is minimally altered and there is no advantage to a glomerular agent over a tubular agent. In the far advanced stages, where tubular function is maximally altered, the glomerular agent becomes the agent of choice in demonstration of residual function. The delayed (24 hour) Tc-99mSnDTPA images demonstrate function in the far advanced chronically obstructed kidney when the Hg-197 Chlormerodrin, I-131 Hippuran, and intravenous pyelogram were negative. In addition, early sequential images may have particular advantage over the intravenous pyelogram when there is overlying bowel gas and feces or urine reflux which can obscure the faint radiographic image of renal cortex in the radiographic procedure.

LIVER/SPLEEN SCINTISCANNING IN THE MANAGEMENT OF BLUNT ABDOMINAL TRAUMA IN CHILDREN.
Ramesh D. Dhekne, Arnold Nitishin, and John A. Burdine.
Baylor College of Med., St. Luke's Episcopal-Texas Children's Hospitals, Houston, Texas

The judicious correlation of serial liver/spleen scintiscanning with the clinical manifestations of liver/spleen injuries following blunt abdominal trauma may result in avoidance of invasive diagnostic procedures and laparotomy in the management of selected patients.

This conservative approach is illustrated by the following cases. A 3-year-old girl was admitted following an automobile accident. Initial scintiscanning following administration of Tc-99m sulfur colloid demonstrated a large, irregular area of decreased colloidal uptake in the posterior-superior aspect of the right lobe of the liver, compatible with the presence of liver injury. Surgery was deferred because of the relatively inaccessible location of the lesion. A second scan performed 3 days later showed extension of the lesion; however, subsequent scans during the next several weeks demonstrated progressive resolution, correlating well with the patient's clinical improvement. A second case is an 18-year-old boy who was injured by a blunt object in his left flank. Initial liver/spleen scan demonstrated a normal liver; however, the spleen was enlarged and contained a defect in its mid-lateral portion, compatible with the presence of splenic injury. Surgical treatment was deferred because of increased susceptibility of post-splenectomy patients to sepsis. Subsequent scans demonstrated continued resolution, paralleling the clinical improvement.

THE SYNTHESIS OF F-18-HALOPERIDOL.
George A. Digenis, C. S. Kook, and M. F. Reed.
University of Kentucky Medical Center, Lexington, Ky.

Our interest in obtaining data on tissue distribution and pharmacokinetics of the neuroleptic drug haloperidol by external scintigraphy has lead us to devise a synthetic route for its rapid preparation in the F-18-isotopically labeled form.

Treatment of acetanilide with 4-chloro-butryloylchloride and aluminum trichloride gave 4-(4-chloro-butryryl)-acetanilide. The latter was fused with 4-(p-chlorophenyl)-4-hydroxypiperidine and KI in toluene and the resulting solid subjected to alkaline hydrolysis to produce 4-[4-(p-chlorophenyl)-4-hydroxypiperidine]-4-aminobutyrophenone. Treatment of the amine with HCl, LiBF₄ and NaNO₂ gave its diazonium salt which was freeze dried and dissolved in acetone. To this an aqueous solution of F-18 (produced by the Ne-20 (d, α) F-18 nuclear reaction) was added and the mixture allowed to stand for 5 min and then dried. It was subsequently pyrolyzed in xylene-dioxane at 145 degrees for 4 min. The product was chromatographed on

neutral alumina with 2% MeOH in chloroform to produce, after further purification with ether, F-18-haloperidol. The identity of the product and its radiochemical purity was further substantiated by two dimensional TLC and autoradiography. The percent yield of incorporation of F-18 into the final product was calculated to be 35.5%. The present method permits the production of F-18-haloperidol at specific activities of about 4-5 μ Ci per mg in about 140 min.

Distribution studies were determined in two rats. Sixty μ Ci (10 mg) of the drug were administered intravenously and the animals imaged at 2, 11, 24, 60, 90, 150 and 210 minutes. It was found that activity was detected in the brain (2-60 min); urinary bladder (11-210 min); liver (2-60 min); and intestinal tract (2-210 min).

PARTICLES AND LUNG IMAGING OR HOW LOW CAN YOU GO. H.J. Dworkin, R. Gutkowski, W. Porter and M. Potter. William Beaumont Hospital, Royal Oak, Mi.

Generator systems which yield concentrated eluates and commercially available kits are capable of producing radio-labeled lung imaging particles of extremely high specific activity (100 mCi of Tc-99m per 10^6 particles). This raised concern over a new statistical variable in lung imaging. Heck and associates have claimed degradation of lung scintiphotos when less than 3×10^4 microspheres (Tc-99m labeled) were employed during routine lung imaging in patients. This prompted us to undertake a study to examine the variables associated with the number of injected particles and their effect on lung images in normal mongrel dogs.

Special stannous macroaggregated human serum albumin (MAA) kits capable of high specific activity labeling (one Ci per 10^6 particles) were prepared by modifying the method of Subramanian. Unlabeled (carrier) MAA of the same size distribution, 10 - 50 μ , was prepared employing the same technique but eliminating the stannous chloride.

Eight dogs were injected intravenously with varying numbers of Tc-99m labeled particles ranging from 250 to 40,000 particles. In four additional dogs unlabeled MAA (0.5×10^6 particles) was mixed with the radiolabeled particles prior to injection. All animals were sacrificed at 5 minutes post injection and images (with constant total counts) were obtained employing a gamma camera. The animals and their removed lungs were weighed.

Animals injected with 10^4 radioactive particles (60 particles per gm. of lung) or less showed degraded lung images. The quality of normal lung images decreases with decreasing numbers of injected radiolabeled particles (unaffected by added carrier MAA) and was found to be directly related to the number of radioactive particles injected from 10^4 down to 250 Tc-99m MAA particles.

THE CHEMICAL AND BIOLOGICAL PROPERTIES OF ISOLATED RADIOLABELED BLEOMYCIN COMPONENTS. W.C. Eckelman, W.J. Rzeszotarski, B. Siegel, H. Kubota, M. Chelliah, R.C. Reba. Washington Hospital Center, George Washington University and AFRR, Washington, D.C.

Cobalt-57 bleomycin is a diagnostically sensitive compound but little is known about the nature of the individual fractions in regard to their metal binding capacity and their in vivo distribution. Bleomycin was separated by high performance liquid chromatography (HPLC) into four major components. These components were labeled and the distribution studied in tumor bearing rats at 2 and 24 hrs. In vivo radiochemical purity was also determined. Of the 9 HPLC systems studied Porasil A eluted with a 0.3% $\text{NH}_4\text{OOCCH}_3$: CH_3OH mobile phase gave the best separation of the fractions and these fractions were copper free and retained their biological activity and purity. An in vitro competitive binding study of Co-57 bleomycin with either Co-57 HSA or Co-57 EDTA showed the labeled bleomycin to be a strong chelate. The biological distribution in tumor bearing rats showed significantly higher concentration in tumors at 2 hr. for fractions A_2 and B_2 . The other fractions A_1 and demethyl A_2 did not reach as high a concentration in the tumor. The tumor to blood ratio for A_2 and B_2 was not significantly different from the bleomycin mixture suggesting that the concentration of the bleomycin in the tumor was related to blood concentration. Tumor to blood ratios of greater than 11:1 at 2 hr. were achieved for the mixture, A_2 and B_2 and ratios of greater than 31:1 at 24 hrs. From this data it appears that the major components A_2 and B_2 are the most useful for diagnostic tumor imaging at 2 hours. (Supported by USPHS Contract CM 43710)

COMPARATIVE STUDY OF Tc-99m-CITRATE, Tc-99m-DIPHOSPHONATE, AND Tc-99m-PERTECHNETATE IN BRAIN SCINTIGRAPHY. M. Ectors, J. Abramovici, and M.H. Jonckheer. St. Pieter Hospital, Free Universities of Brussels, Brussels, Belgium.

The investigation was undertaken to compare the diagnostic usefulness of the newly introduced Tc-99m-citrate to more classical tracers in brain lesions.

20 Patients with histologically proved intracranial neoplasms or cerebrovascular accidents were investigated. Each patient was injected with the same dose of each of the three Tc-99m-complexes, at intervals of 48 hours. The instrumentation used was a high performance γ -camera with a high sensitivity parallel-hole collimator (Pho-Gamma III, Nuclear Chicago), a minicomputer (Varian 620L,16K) and an electrostatic printer/plotter (Statos).

Dynamic studies were recorded during the first minute. Static views were obtained and recorded at the fifth minute and at 3 hours. Zones of interest (lesions and an equal area of normal brain tissue) were chosen on the electrostatic documents, and target to non-target ratios were obtained at 5 minutes and 3 hours.

Tc-99m-citrate was found to be superior in regard to both detection and image qualities for the neoplasms but of equal diagnostic usefulness for the cerebrovascular accidents. It is our feeling that a differential diagnosis between intracerebral neoplasms and vascular lesions is possible by comparing the scintigraphies obtained with Tc-99m-citrate to those obtained with one of the other tracers.

INTERNAL MAMMARY LYMPHOSCINTIGRAPHY: RATIONALE, INTERPRETATION AND CLINICAL APPLICATION. Günes N. Ege. The Princess Margaret Hospital, Toronto, Ont., Canada.

Internal mammary lymphoscintigraphy utilizes Tc-99m antimony colloid injected subcostally into the origins from the posterior rectus sheath of the parasternal lymphatics. Since interstitially introduced radiocolloids gain rapid access to drainage lymphatics, a scintigraphic image of regional lymph nodes can yield physiologic and morphologic information relevant to such anatomic sites not suitable for contrast lymphography. The small particle size of the colloid (4-12 μ) and the accurate injection are critical factors for the success of the procedure.

Individual variability in number, size and location of parasternal lymph nodes, as documented by anatomic series, can be confirmed by lymphoscintigraphy. Normal asymmetry between right and left lymphatic chains, frequent cross communication, and other anatomic variations have been demonstrated. Criteria for interpretation of the lymphoscintigram have been defined on the basis of 969 studies carried out on 645 patients with malignant disease seen at The Princess Margaret Hospital.

This simple and reliable technique has proven valuable for assessing the integrity of parasternal lymphatics and establishing the baseline pattern for each individual patient, in demonstrating disparity between parasternal nodes and conventional radiation fields, as well as in detecting cross drainage between potentially involved nodes and contralateral lymphatics. Reproducibility of the scintigraphic image and correlation with clinical status further fulfil criteria required in a diagnostic discipline.

F-18-21-FLUOROPREGNENOLONE-3-ACETATE AS AN ADRENAL SCANNING AGENT. R. Eng, G. Hinn, and L. Spitznagle. Department of Pharmaceutical Sciences, University of Washington, Seattle, Wash.

The synthesis and biological distribution of 21-fluoropregnenolone-3-acetate labeled with F-18, a radiopharmaceutical potentially useful for adrenal gland visualization will be described. With the use of F-18 obtained from the O-16(He-3,n)F-18 reaction in a water target and 21-iodopregnenolone-3-acetate, F-18-21-fluoropregnenolone-3-acetate has been prepared in amounts up to 5 millicuries.

Rats given intravenous injections of the radiopharmaceutical were sacrificed in groups of three at 1, 5, 10,

and 30 minutes after administration. The highest tissue concentration of radioactivity was found in the adrenal glands five minutes after administration. The adrenal-kidney ratios at 1, 5, 10, 15 and 30 minutes were 5.1, 10.9, 9.3, 10.6 and 6.6 respectively, while the adrenal-liver ratios were 12, 19.6, 4.6, 4.9 and 2.9.

In summary, F-18-21-fluoropregnenolone-3-acetate has been prepared in an overall radiochemical yield of 15% from KF-18. Initial distribution studies in rats indicate that the compound may be useful as an adrenal scanning agent.

Tc-99m SULFUR COLLOID LABELED LEUKOCYTES FOR DELINEATION OF ABSCESSSES AND INFLAMMATORY PROCESSES. Denis K. English, Burton R. Andersen and Hakki E. Akalin. West Side VA Hospital, Chicago, Ill.

The purpose of this study was to determine the potential clinical usefulness of Tc-99m labeled phagocytic cells for delineation of abscesses and inflammatory lesions. Labeling of phagocytic cells was accomplished by in vitro incubation (30 min, 37°C) of buffy coat cells from 100 ml of canine blood with 20-40 mCi of Tc-99m sulfur colloid (TcSC). The colloid is phagocytized by blood granulocytes and monocytes with little resultant alteration of the cells chemotactic function. The cells were washed to remove unphagocytized colloid and returned intravenously to donor animals. Three to 8 mCi of radioactivity remained cell associated. Scanning of normal dogs 4-24 hours after leukocyte infusion showed uniform uptake in liver, lungs and spleen. The label localized in sterile and infected intramuscular abscesses in amounts sufficient for imaging four hours after leukocyte infusion. Accumulation of the label into abscess fluid was maximal 3-4 hours after infusion of labeled cells. Experimental staphylococcal, right-sided endocarditis was induced in dogs in order to produce multiple areas of septic embolization in the lungs. Such dogs showed multiple, clearly defined areas of increased pulmonary uptake of the label when scanned 4-24 hours after leukocyte infusion. Radioactivity levels of inflamed lung tissue taken at autopsy were approximately twice the levels of normal lung tissue. Eight normal dogs scanned after infusion of labeled white cells demonstrated no such foci of increased uptake. Over 60 dogs have received autologous TcSC labeled leukocytes and none have shown any adverse reaction which could be attributed to infusion of the labeled cells. These results suggest that TcSC labeled leukocytes will be a useful diagnostic tool for localizing abscesses and inflammatory lesions in humans.

DOSIMETRIC EVALUATION OF THE HEART-IMAGING RADIONUCLIDES: Cs-129, K-43, Rb-81, and Tl-201. Paul A. Feller and Vincent J. Sodd. Nuclear Medicine Laboratory, BRH, FDA, Cincinnati General Hospital, Cincinnati, Ohio.

In conjunction with research into the relative clinical suitability of Cs-129, K-43, Rb-81, and Tl-201 for heart imaging, a study of their comparative dosimetry was made. Literature searches revealed a total lack of human organ distribution data, and limited data for animals. From one animal study enough information was obtained to determine approximate expressions for curves of uptake and retention of cesium in the heart, kidneys, liver, lung, and testes of the rat. Using these expressions and assuming the concentration of cesium in each specific type of organ tissue per mean concentration in the total body is the same in humans as in rats, cumulated activities were determined for these organs. Estimates of radiation dose to each of the above organs from activity in all of these organs and from activity in the remainder of the body were obtained using a computer code for detailed organ dose computations by the MIRD method. Since biological data for the other three elements were not found in sufficient detail, and since the biological actions of these four monovalent cations have been found to be similar, though not identical, dosimetry estimates based on cesium distribution data were made for K-43, Tl-201 and Rb-81 (including its radioactive daughter, Kr-81m).

The results indicate significantly lower doses from Cs-129 in the kidneys and testes than previously stated in the literature. Total body absorbed radiation doses from Rb-81, Cs-129, Tl-201 and K-43 were found to be 0.08-, 0.17-, 0.26-, and 0.60-rads per millicurie administered, respectively. In addition, doses to the heart, kidneys, liver, lungs, and testes were found to be similarly ordered for the four nuclides.

USE OF COMPUTER GENERATED "PULSE MODE DISPLAY" TO PROVIDE DIGITAL COLOR CODE SCINTIPHOTOS. Charles E. Finney, Donald D. Larson, Ernest J. Braun and David Lieberman. White Memorial Medical Center, Los Angeles, Calif.

New methods of computer processing of digitized scintigraphic data reported here permit multi-image color scintiphotos to be produced in a rapid, convenient and flexible manner.

A series of color filters mounted in front of a camera lens attached to a cathode-ray tube is driven by a mechanism controlled by the computer. During the time that a particular color filter is interposed between camera and cathode-ray tube, a "pulse mode" display is generated and photographed. "Pulse mode" display of digitized scintillation image data is achieved by sequentially pulsing, on the cathode-ray tube, elements of the image matrix. The number of pulses per element is related by a color parameter table to the number of counts in that element.

The authors will show examples of four on one color scintiphotos demonstrating the enhanced contrast, extended dynamic range and versatility of this display format.

Currently we are generating four 128 x 128 matrix images on one film with up to 50 or more separate hues available and suggest that it is feasible to include this attractive, inexpensive and diagnostically useful series on a final report to the referring physician.

LEUKOCYTE TAGGING BY PHAGOCYTOSIS OF Tc-99m HUMAN SERUM ALBUMIN MICROSOPHERES...USE IN LOCALIZATION OF EXPERIMENTAL ABSCESSSES BY EXTERNAL SCANNING. Charles H. Fisher, Ursula Scheffel, Min-Fu Tsan, Buck A. Rhodes and Henry N. Wagner, Jr. The Johns Hopkins Hospital, Baltimore, Md.

The purpose of this investigation was to develop a simple method of tagging leukocytes with Tc-99m so that the labeled cells could be used to detect areas of inflammation by external scanning. Six rabbits were injected in the thigh muscle with 0.2 cc turpentine to produce sterile abscesses 24-48 hours of age. Peripheral blood leukocytes were tagged by phagocytosis of Tc-99m labeled human serum albumin microspheres (0.1-1 micron diameter) during incubation with the buffy coat. Autoradiography indicated predominant tagging of the polymorphonuclear leukocyte. The entire process of obtaining blood, tagging the leukocytes and returning the cells to the circulation required less than one hour. Labeled cells were demonstrated to accumulate in experimental abscesses, and abscess wall to normal muscle activity ratios ranging from 29:1 to 70:1 were achieved by four hours. Obvious scan abnormalities were present at one hour in all animals and progressive accumulation of tagged cells was demonstrated by computer analysis of serial images. Activity was also present in: (a) lungs due to margined and embolized clumped leukocytes (b) reticuloendothelial organs due to contaminating free unphagocytized microspheres and (c) kidneys and bladder due to excretion of free pertechnetate released from metabolized microspheres. Control rabbits with abscesses given In-113m transferrin, Tc-99m microspheres or Tc-99m pertechnetate showed no increase in the blood pool and only minimal increased phagocytic activity and extracellular fluid in the region of the abscess. We believe this method can be applied to clinical abscess and inflammation detection.

COMPARISON OF LEFT VENTRICULAR EJECTION FRACTION (LVEF) IN MAN AND DOGS USING FIRST TRANSIT AND ECG-GATED SCINTIANGIOGRAPHY. James W. Fletcher, Francis K. Herbig, James L. Daly, Robert M. Donati, Kenneth E. Walter. St. Louis VA Hospital and St. Louis University School of Medicine, St. Louis, Mo.

Paired serial determinations of LVEF were obtained in humans or open chest dogs utilizing both first transit (high frequency) data analysis and ECG-gated scintiphography. Dogs were subjected to right heart bypass and single or paired electrical pacing techniques in order to obtain constant cardiac output and varying ventricular rates. Serial determination of LVEF were made over a wide range of heart rates and stroke volumes after the left atrial injection of 5.0 mCi of 99m-Tc human serum albumin. All data were acquired on a pho/gamma HP Anger camera with converging collimator interfaced to a small (32K) digital computer. The detector was placed in the left anterior oblique position and first transit data acquired at 10

frames/sec for 30 seconds. Integrated end-systolic and end-diastolic ECG-gated images were obtained 10 min after each bolus injection for 300 seconds. Human patients were investigated at cardiac catheterization, and paired determinations of LVEF were made after the pulmonary artery injection of 10.0 mCi of ^{99m}Tc human serum albumin. In this group the results of paired radioisotope determinations of LVEF were compared to standard angiographic techniques. Paired determinations of LVEF obtained by first transit analysis and ECG-gated scintiphotography showed no statistical differences over a wide range of heart rate and stroke volume, and correlated well with angiographic determinations. These results demonstrate the feasibility of rapid serial determinations of LVEF in both experimental animals and man over a wide range of ventricular function utilizing either method of data acquisition and data analysis.

MOSSBAUER SPECTROSCOPIC AND AUTORADIOGRAPHIC STUDIES OF THE LOCALIZATION AND CHEMICAL BINDING OF Sm-153 IN TUMORS. A.M. Friedman, J.C. Sullivan, S.L. Ruby, A. Lindebaum, J.J. Russell, B.J. Zabransky, and G.V.S. Rayudu. Argonne National Laboratory, Argonne, Ill. Rush University Medical Center, Chicago, Ill.

Several authors have recently noted that a variety of metallic tracers, especially rare earth and actinide ions (J. Nucl. Med. 14:615, 1973 and Int. J. Nucl. Med. and Biology 2:44, 1975) concentrate in soft tissue tumors with tumor/tissue ratios as high as 100/1. This work was performed in an attempt to understand the bonding of a typical rare earth ion. One of the parameters obtained by Mossbauer Spectroscopy (MBS) is the isomer shift which can be directly related to the type of chemical bond of the radioactive species. The MBS spectra of over 30 samples of 14 compounds of Sm-153 were obtained at 4°K. Samples of Sm-153(III) citrate were then given IV to a group of normal and tumor bearing ICR white mice. After 24 and 48 hours the mice were sacrificed and the MBS spectra of various excised tissues were observed at 4°K. In addition, autoradiographs were made of thin sections of tumor and normal tissue. The results of these experiments show that the Sm-153 is present in all tissue as a Sm-153(III) hydrated species, ionically bound to a protein. There is no observable difference in the bonds in the tumor and other tissues, therefore the concentration factors observed for these ions may be due to other than chemical effects. The autoradiographic studies show that the Sm is concentrated in the outer layer of the tumor.

SERUM INHIBITION OF Ga-67 BINDING BY L-1210 LEUKEMIC CELLS. Richard A. Gams and Jerry D. Glickson. University of Alabama School of Medicine, Birmingham, Alabama.

An *in vitro* test system employing L-1210 murine leukemic lymphoblasts has been used to study the influence of human serum on cellular uptake of Ga-67. Whole serum markedly inhibits uptake of the isotope by these cells. Dialysis of serum to remove low molecular weight components eliminates approximately half the inhibitory capacity. Serum ultrafiltrate containing components with molecular weights less than 10,000 is about equal in inhibitory capacity to dialyzed serum containing the high molecular weight fraction. Inhibition by high molecular weight components correlates closely with the extent of binding of Ga-67 as measured by gel filtration on Sephadex G-25. Purified apotransferrin (iron-free) in a concentration equivalent to that found in serum also inhibits uptake of Ga-67, but to a lesser degree than dialyzed serum. Saturation of apotransferrin with iron (III) reduces this inhibition by 82%, whereas, the inhibitory capacity of dialyzed serum is reduced only 16% by iron (III) saturation. Furthermore, serial dilution of dialyzed serum and apotransferrin indicates that purified apotransferrin is only about 1/10 as effective as dialyzed whole serum in binding Ga-67 or inhibiting the uptake of the isotope. Transferrin, thus, participates in high molecular weight inhibition, but it accounts for 10% or less of the inhibitory and binding capacity. Similarly, low molecular weight components including citrate, phosphate, glutamate, lactate, and others were found to contribute to inhibition. Consequently, in-

hibition of cellular uptake of Ga-67 by serum results from the presence of several, perhaps many, high and low molecular weight inhibitory components, and appears to be a potentially important factor in *in vivo* tumor scanning with this radionuclide.

Tc-99m-POLYPHOSPHATE UPTAKE BY RESORBING BONE. Daniel A. Garcia, Donald E. Tow, Krishan K. Kapur and Herbert Wells. Veterans Administration Hospital, West Roxbury, Harvard School of Dental Medicine and Boston University School of Graduate Dentistry, Boston, Massachusetts.

Chronic alveolar bone disease of the oral cavity is primarily a resorbing process yet often produces positive images with bone-seekers. It was important to know whether resorbing bone of itself can accumulate sufficient amounts of bone-seekers to produce hot spots on images. We examined Tc-PP uptake in an animal model such that bone resorption was independent of formation.

The leg muscles of 10 rats received 2 types of implants: demineralized allogeneic bone matrix (DM), a bone forming system, and devitalized autogenous bone (DV), a resorbing system. Radiographs and bone images of the implant sites were made weekly. Tetracycline injections of 10 mg/kg were given each week to label newly formed bone. The rats were killed at 6 weeks and implants and specimens of normal bone were excised, weighed, counted for Tc-99m and prepared for cellular and fluorescence microscopy.

Hot spots were produced by all DM and 6 of 10 DV implants. Radiographs showed DM mineralization. There was little evidence of gross radiographic DV resorption. H-E stained sections, however, confirmed giant cell resorption of DV. Tetracycline fluorescence was seen in DM and normal bone but not in DV, indicating no new bone formation in DV. Tc-99m cpm/gram of DM and DV were, respectively, 177% and 76% of normal bone.

The results indicate that resorbing bone by itself does not accumulate bone-seekers such as Tc-PP in sufficient quantities to produce a positive image. Positive radionuclide detection of osteolytic disease appears to require reparative bone-forming responses in adjacent tissues since only the process of mineralization can accumulate bone-seekers in amounts greater than normal bone uptake.

SUITABILITY OF RADIOPHARMACEUTICALS FOR DETERMINING CARDIAC SHUNTING. Gary F. Gates and Michael L. Goris. Stanford University, Stanford, Calif.

Quantitation of right-to-left shunting following injection of 10-50 micron sized radioparticles depends upon determining the nuclide fraction which bypasses the pulmonary capillaries to enter the systemic circulation. However, this value will be falsely elevated if small particles and/or unbound nuclides enter the systemic circulation due to either a suboptimal radiopharmaceutical preparation or delay in onset of scintigraphy during which time pulmonary particles fragment and pass systemically. These variables were studied as part of an ongoing quality control program in 23 non-cyanotic patients referred for lung scanning. Shunting was determined at various intervals following injection of either Tc-99m microspheres, Tc-99m macroaggregated albumin (MAA), or In-113m Fe(OH)₃ particles. If the calculated shunt did not approximate the expected 4% physiologic transpulmonary shunt, the disparity could be due to the radiopharmaceutical and/or delay before scintigraphy.

Following nuclide injection, total-body imaging was performed via moving table and a scintillation camera interfaced with a digital computer. After isolating the lungs as areas of interest, total-body and pulmonary "counts" were separately determined, and the percentage of nuclide shunted systemically was calculated. When studied immediately after injection, average systemic shunting was: 8.6% with In-113m Fe(OH)₃ (range = 5-14%), 5.8% with Tc-99m microspheres (range = 4-8%) and 5.2% with Tc-99m-MAA (range = 3-6%). If scintigraphy was delayed for 15 minutes following injection, the calculated shunt could more than double. Both Tc-99m microspheres and MAA resulted in a calculated shunt appropriate for a non-cyanotic person, whereas variability occurred with the In-113m Fe(OH)₃ preparation. Thus proper radiopharmaceutical selection and prompt scintigraphy are crucial for accurate calculation of cardiac shunts.

SURGICAL SYSTEMIC-PULMONIC SHUNTS ASSESSED BY RADIONUCLIDE SCINTISCANNING. Gary F. Gates, Harry W. Orme, and Earl K. Dore. Stanford University, Stanford, Calif. and Memorial Hospital, Long Beach, Calif.

Surgically created systemic-pulmonic shunts are used as palliative treatment for children with cyanotic heart disease. As shunt function may be difficult to assess, a method was devised to make this determination without cardiac catheterization. Following intravenous injection of Tc-99m macroaggregated albumin (MAA), whole body scintiscanning is performed. MAA deposition within each lung is calculated and is proportional to pulmonary blood flow to each side. The fraction of MAA bypassing the lungs to enter the systemic circulation is determined and indicates the magnitude of right-to-left shunting. A series of children with surgical shunts (7 Waterston, 4 Blalock-Taussig, 2 Potts) were studied by this method. Seven faulty shunts were detected (5 Waterston, 2 Blalock-Taussig) resulting in persistent elevation of right-to-left shunting and often hyperperfusion of one lung. Well-functioning anastomoses reduce right-to-left shunting by increasing pulmonary blood flow to each lung but sometimes unequally. Malfunctioning anastomoses do not significantly reduce right-to-left shunting and may cause unilateral pulmonary hyperperfusion. Non-functioning shunts do not decrease right-to-left shunting but may alter distribution of pulmonary flow. Perfusion lung scans alone are inadequate for evaluating shunt function. Other investigators report preferential nuclide accumulation in the lung opposite a well-functioning shunt. However, this study shows preferential nuclide accumulation may occur in either lung, regardless of shunt function, depending upon magnitude of right-to-left shunting, degree of pulmonary outflow obstruction, variability of intercommunication between right and left pulmonary arteries, and the anatomic configuration peculiar to each anastomosis.

SPECIES DIFFERENCES IN MYOCARDIAL LOCALIZATION OF N-13-LABELED AMINO ACIDS. Alan S. Gelbard, Joseph M. McDonald, Robert E. Reiman and John S. Laughlin. Memorial Sloan-Kettering Cancer Center, New York, N.Y.

The selection of an animal model for evaluating organ scanning agents is usually based on the size and availability of the animal. Attention is often not paid to physiological or biochemical species differences. We have compared the uptake of N-13-labeled amino acids in organs of the dog and rhesus monkey and have found quantitative differences in organ distribution between the two species.

The compounds evaluated were N-13-ammonia and enzymatically prepared N-13-L-glutamine, L-glutamic acid and L-valine. 5-10 mCi of labeled compound were injected intravenously. *In vivo* distributions of radioactivity were determined using our high energy gamma-ray scanning system. Whole body quantitative scans of the animals were carried out 5-60 min after injection.

Ammonia was incorporated in the myocardium of the monkey and the dog. In the monkey all of the amino acids were taken up in the heart to a significant degree. In contrast to these results there was little or no myocardial uptake of the labeled amino acids in the dog. In both species glutamine uptake in the liver was much greater than noted for the other amino acids or for NH₃ although all these compounds concentrated in the liver to a significant degree. The species difference in myocardial uptake may reflect variations in amino acid metabolism or transport.

EMISSION AND TRANSMISSION NOISE PROPAGATION IN 3-D FOURIER CONVOLUTION RECONSTRUCTION. Sebastian Genna and Sing C. Pang. Boston V.A. Hospital and Boston University Medical Center, Boston, Mass.

Noise propagation limits the fidelity of three-dimensional images which are reconstructed from transversely projected data. This paper is concerned with the noise propagated by Fourier convolution reconstruction of data from parallel and fan projection geometries. Through computer simulation each of the two reconstruction techniques is applied to X-ray transmission and gamma-ray emission measurements.

The test objects are computer simulated phantoms each of which is composed of many discs of different size and composition (absorption coefficient or radioactivity). The counts projected by an X-ray beam or emission sources are

calculated and noise is simulated by adding pseudo-random numbers such that the standard deviations of the simulated data are made equal to the square root of the projected cell counts.

A number of X-ray beams and emission strengths are simulated and their corresponding images are reconstructed. Along with each reconstruction, the population of image cells as a function of their deviation from the true values is also derived. From this population-deviation data one can estimate, for example, the X-ray or gamma-ray source strengths required to prevent errors from clustering so as to form artifacts.

Quantitatively, the uncertainty in the projected cell count is higher in the emission case. Noise propagation is also higher because of the absence of the logarithmic term deriving from exponential X-ray attenuation. On the other hand, a much higher reconstruction uncertainty can be tolerated in emission as compared to transmission diagnostic applications.

MONITORING OF RENAL ALLOGRAFT FUNCTION BY TRIPLE RADIOAGENT STUDIES. E.A. George, R.E. Henry, H. Halbach, J.E. Codd, W.T. Newton, and R.M. Donati. St. Louis VA Hospital and St. Louis and Washington Universities Schools of Medicine, St. Louis, Missouri.

A total of 184 triple examinations were performed in 54 cadaver kidney transplant recipients. Studies were performed on an Anger camera. The 3 studies performed in each patient included: sodium I-131 iodohippurate (HIPP) renography, Tc-99m pertechnetate (PERT) rapid vascular scintigraphy, and static images of the renal transplant following Tc-99m sulfur colloid (TSC) administration. The parenchymal transit, clearance, and excretory pattern of HIPP and the transplant size was assessed on HIPP renography. Transplant vascularity and perfusion patterns were evaluated with the dynamic PERT study. Transplant accumulation of TSC was evaluated on a static image as either absent, about equal or greater than marrow activity. Normal functioning renal transplants presented normal HIPP and PERT kinetic patterns, and failed to accumulate TSC. Transplants with acute tubular necrosis demonstrated abnormal HIPP patterns, a normal sized transplant, and non-specific vascular transit abnormalities. TSC accumulation was absent. Varying degrees of acute rejection were characterized by transplant enlargement, slight to marked HIPP abnormalities and an altered transplant distribution of PERT. TSC transplant accumulation was seen. Different patterns were characteristic of stages of acute rejection and chronic rejection. The triple radioagent evaluation agreed with the clinical diagnosis of acute rejection in 103 of 106 studies, although there was greater disagreement as to the stage of the acute rejection. In chronic rejection, there was agreement with the clinical diagnosis in 23 of 32 instances. These data suggest that the triple radioagent evaluation of renal transplant function is a powerful diagnostic tool.

Tc-99m-EHDP BONE SCANNING IN BREAST CARCINOMA Frederic H. Gerber, James J. Goodreau, and Peter T. Kirchner. National Naval Medical Center, Bethesda, Md.

A prospective study was undertaken to evaluate the value of pre- and post-operative bone scans performed with the new Tc-99m compounds in the management of breast carcinoma patients. 115 patients with biopsy proven carcinoma had pre-operative bone scans. 63 of the 115 were serially scanned 3 to 36 months post-operatively. 61/115 patients were post-menopausal. 109/115 were operative stage I or II.

Whole body dual-probe rectilinear scans taken 3-5 hours after a 15 mCi dose of Tc-99m-polyphosphate or Tc-99m-EHDP were supplemented as needed with gamma camera images. Of 115 pre-operative scans 15 were abnormal. 8 of the 15 were read as benign disease after correlation with X-rays. Biopsy proved 2 of the remaining 7 to be benign. Of the 5 patients with positive scans, 4 were post-menopausal.

Serial post-operative scans (101 studies) were done in 63 of the 115 patients over a 3 to 36 month period. Of 59 patients with a negative pre-operative scan 11 developed positive scans within 3 to 24 months. 8 of these 11 patients were post-menopausal. In 6 of the 11 the new lesion was solitary. Only 3 patients developed non-bony metastases in the face of a normal bone scan.

The low incidence (5%) of positive pre-operative bone scans in this series may be related to early diagnosis: 109/115 patients were operative stage I or II. The high

incidence of negative to positive conversions post-operatively (23%) indicates the value of serial post-operative scanning and underscores the importance of a pre-operative baseline scan, especially since 6 of 11 new lesions were solitary. The incidence of bone metastases is much higher in post-menopausal patients with breast carcinoma both pre-operatively and post-operatively.

A NEW RADIOLABELED QUINOLINE ANALOG IN MICE WITH MALIGNANT MELANOMA. Satinder P. Gill, William H. Beierwaltes, Rodney D. Ice, and Stephen T. Mosley. University of Michigan Hospital, Ann Arbor, Mich.

The relative tissue distribution of four quinoline analogs in mice with malignant melanotic melanoma was compared with that of C-14 chloroquine. Fifteen black mice (C67Bl/6) with subcutaneously implanted B-16 melanoma were given 10 μ Ci of each compound, by oral gavage. A new radiolabeled chloroquine analog 4-amino (benzo-4-methylpiperazine)-7-trifluoro-methylquinoline H-3 (compound I) had specific activity of 153.8 μ Ci/mg. Three mice in each group were sacrificed at five different time intervals at 6, 24, 48, 72 and 96 hours. Radioactivity assay of 14 different tissues were done at all time intervals. Compound I concentrated in the melanoma of mice four times greater than C-14 chloroquine and three times greater than the iodinated analog of chloroquine, 4-(3-dimethylaminopropylamino) 7-iodoquinoline (NM 113-I-125) even when the I-125 NM 113 had three times greater specific activity than the new radiolabeled compound I. NM 113 had specific activity of 514 μ Ci/mg.

The I-125 labeled analog of our new compound (Compound II) concentrated in the malignant melanoma twice greater than I-125 NM 113. Demethylated H-3 compound I (compound III) concentrated least. Previously radiiodinated NM 113 has been used successfully in the diagnosis of dermal and ocular melanoma in the human. In therapeutic doses in dogs, with malignant melanoma, iodinated NM 113 delivered 3500-5000 rads of irradiation to melanoma metastases. The new iodinated quinoline analog deserves further evaluation.

THYROID FLUORESCENT SCANNING SYSTEM. Michael Gillin, James Thrall, and Merrill Johnson. Walter Reed Army Medical Center, Washington, D.C.

A thyroid fluorescent scanning system has been commercially obtained and interfaced to a Picker Magnascanner V. This system contains twenty 1.0 Curie sources of Americium-241 arranged in a circular fashion about a 500 mm² Si (Li) detector. The pulse analysis electronics includes DC coupled SCA's. A logic signal is then fed into the Magnascanner and the image forming capabilities of the Magnascanner are used.

Two main clinical objectives have been achieved with the system. The first was to obtain technically and diagnostically adequate fluorescent scans of the thyroid. This objective was accomplished once the detector was adequately collimated. Constant scanning factors have been used so that film density is a qualitative indicator of thyroidal iodine content. If a repeat scan is desired for more anatomic detail, the scan factors may be optimized in the usual fashion.

The second objective was to quantify thyroidal iodine content without the use of a computer to an accuracy of $\pm 15\%$. This has been accomplished using SCA's and digital counters. The region just below the iodine characteristic X-ray peak is counted for background correction of the peak itself. Calibration of net counts in the iodine peak versus milligrams of iodine has been made for the range of 0 to 25 mgm using a modified Picker phantom.

This work indicates that a Thyroid Fluorescent Scanning System can be successfully introduced into the Nuclear Medicine Clinic for scanning and quantification purposes without a large amount of technical support. The principle problems involved have been identified and practical solutions achieved.

LEUKOCYTE LABELING WITH TECHNETIUM-99m. Howard J. Glenn, Nisarut Ruksawin, Tad Konikowski, and Thomas P. Haynie. M. D. Anderson Hospital and Tumor Institute, Houston, TX.

The purpose of this study was to investigate various parameters associated with the Tc-99m labeling of leukocytes.

Leukocytes from normal donors and from donors with chronic myelocytic leukemia (CML) obtained from an IBM blood cell separator were incubated with microgram quantities of stannous chloride. A second incubation with Tc-99m pertechnetate labeled the leukocytes. Yields were determined by electrophoresis. Other reducing agents such as ferrous ion or penicillamine were not effective. Pertechnetate itself was only loosely bound to the leukocyte.

Differences in labeling efficiencies between cells from normal donors and CML cells have been detected. In 16 out of 20 (80%) labeling experiments with normal cells, the cell uptake was 1 μ Ci/10⁶ cells or greater. For CML cells, 28 out of 40 (70%) gave cell uptakes of less than 1 μ Ci/10⁶ cells. All normal cells labeling in the CML range were in the younger age group. There is little change in percent labeling yield with increased amounts of activity, but it is possible to incorporate an adequate quantity of activity in the labeled cells. Normal cells showed increasing yields with increasing total number of cells. Yield was also shown to be a function of cell concentration and was not affected by the amount of stannous chloride used or time incubated. Leukocytes label to about the same degree as erythrocytes under the same conditions. The labeled leukocytes maintained their viability (about 95%) and their phagocytic activity. The labeling procedure is being adapted to aseptic techniques.

A procedure for labeling leukocytes with Tc-99m has been developed which gives acceptable yields of labeled cells of good viability and phagocytic activity. When adapted to aseptic technique, the labeled cells will be useful in a variety of in-vivo scanning and dynamic studies in humans.

ORGAN DISTRIBUTION OF TECHNETIUM-99m LABELED AUTOLOGOUS RABBIT LYMPHOCYTES. Allan H. Gobuty, Rolf F. Barth and Ralph G. Robinson. Kansas University Medical Center, Kansas City, KS.

Recent investigations have shown Tc-99m to be useful as a label to study the organ distribution of normal and neoplastic cells in mice. Our work has evaluated the applicability of Tc-99m to study organ distribution of autologous rabbit lymphocytes by gamma imaging and organ counting.

After isolation by Ficoll-Hypaque density gradient, lymphocytes from one group of rabbits were labeled by adding 10-20 mCi Tc-99m pertechnetate to 5 million cells suspended in Hank's Balanced Salt Solution containing 100 μ g sodium chromate. Following a 10 minute incubation at 37°C, 300 μ g stannous chloride was added and the preparation incubated an additional 5 minutes at 37°C. Cells from another group of rabbits were labeled without reduction. Controls consisted of the organ distribution of Tc-99m pertechnetate.

Compartmentalization of Tc-99m labeled unreduced lymphocyte preparations two hours after administration was quite different from both reduced preparations and from Tc-99m pertechnetate. 5.7% of the administered radioactivity was in the lungs, 0.9% in the spleen, 21.7% in the liver and 30.1% in the blood. Of the reduced preparation, 12.5% was in the lungs, 2.7% in the spleen, 36.6% in the liver and 13% in the blood. Organ uptake of Tc-99m pertechnetate was 1.0%, 0.1%, 13.2% and 37.9% respectively for the same organs. Gamma camera imaging indicated that the lungs, liver, spleen, kidneys and bladder retained essentially all of the radioactivity.

The data obtained indicates that Tc-99m can be used as a label to follow lymphocyte distribution both by radionuclide imaging and by organ counting. This suggests that Tc-99m has applicability in experimental and clinical studies of lymphocyte migration in man.

THE EVALUATION OF PULMONARY SEQUESTRATION WITH RADIONUCLIDE ANGIOGRAPHY. Nihal Gooneratne and James J. Conway. The Children's Memorial Hospital, Chicago, ILL.

Chest masses in children have a greater histologic variation than that encountered in adults due to the multiplicity of congenital abnormalities which are present in childhood. One such congenital anomaly, pulmonary sequestration, is especially difficult to diagnose since selective catheterization of an aberrant systemic blood supply is required for a definitive preoperative diagnosis.

Radionuclide angiography of the chest, a much less hazardous procedure, assists in the differentiation between pulmonary and systemic blood supply and thus would be useful in the evaluation of pulmonary sequestration.

Five children with pulmonary sequestration were evaluated from 1970 through 1974. In each instance, the systemic origin of the vascular supply was indicated. In those sequestrations where the artery originated below the hemidiaphragm, the aberrant source was identified as such, providing a characteristic radionuclide appearance diagnostic of pulmonary sequestration. In three patients, selective arterial catheterization and contrast angiography were not performed.

The safety and simplicity of radionuclide angiography enforces the recommendation that the technique be used when one wishes to evaluate a chest mass in a child and especially if one suspects pulmonary sequestration.

A MOBILE DUAL SCINTILLATION PROBE SYSTEM FOR THE RAPID BEDSIDE ASSESSMENT OF LEFT VENTRICULAR PERFORMANCE. Stuart Gottlieb, Mark Groch, Nilza Kallos, and August Miale, Jr. University of Miami, Miami, Fl., and Searle Radiographics, Inc., Des Plaines, Ill.

A new probe system to record both radionuclide bolus transit through the left ventricle (LV) and simultaneous background monitoring has been developed and tested in patients undergoing cardiac catheterization. The accurate determination of left ventricular ejection fraction (LVEF) requires quantitation of the crosstalk from surrounding tissues. This mobile probe system utilizes a central collimated LV probe surrounded by an annular detector which is collimated in such a manner as to provide a simultaneous real time background record. As a bolus of radioactivity passes through the heart, dual tracings (LV and background) are generated simultaneously and read directly into a two channel, high frequency, optical strip chart recorder. LVEF, end diastolic volume, cardiac output, as well as pulmonary transit time and pulmonary blood volume, are derived easily with rapid and simple calculations. The EFs correlate well with data derived from conventional contrast angiography in a series of 25 patients. Positioning over the midpoint of the LV was performed by echocardiography. This appeared to be as accurate a method of determining the midpoint of the LV as the radiographic methods. No significant difference in calculated EF could be found utilizing a standard injection technique when the radioactive tracer was administered into an external jugular vein or through catheters in the superior vena cava, right ventricle or pulmonary artery. The entire procedure can be performed in 10 minutes at bedside, thus facilitating clinical utility.

COLLIMATORS FOR MYOCARDIAL IMAGING. L. Stephen Graham and Norman D. Poe. University of California School of Medicine and Laboratory of Nuclear Medicine, Los Angeles, Calif.

The purpose of this investigation was to measure the spatial resolution obtainable with four radionuclides which have recently been proposed for imaging the myocardium: Tl-201, Tc-99m, I-123, and K-43. In the actual experiments Xe-133 was used as a substitute for Tl-201. Ninety cm line sources embedded in lucite were used to obtain line spread functions (LSF) for an Anger camera with pinhole (10 mm aperture), low energy converging, and high energy converging collimators. From those data modulation transfer functions (MTF) were calculated. When the pinhole collimator was used the order of decreasing MTF values was I-123, Tl-201, and K-43. The MTF for Tc-99m was virtually identical to that of I-123. At a spatial frequency of 0.5 cm⁻¹ the loss of contrast between I-123 and K-43 was ~20%. For the low energy converging collimator the order of decreasing spatial resolution was Tc-99m, Tl-201, and I-123. The poor response of I-123 was due to the presence of contaminants emitting high energy photons. At a spatial frequency of 0.5 cm⁻¹ the contrast for Tl-201 was ~15% less than for Tc-99m. When the high energy converging collimator was used the order of decreasing spatial resolution was Tc-99m, I-123, Tl-201, and K-43. The difference between the MTFs of I-123 and Tc-99m was very small. At a spatial frequency of 0.5 cm⁻¹ the contrast for Tl-201 was ~15% less than the value for Tc-99m. Under the experimental conditions used in this study the MTFs for Tc-99m were essentially the same for all three collimators. For I-123 the pinhole collimator gave the best results although the high energy converging collimator was not markedly inferior. The MTF for Tl-201 and the pinhole collimator was better than for the low or high energy converging collimators. For K-43 only the pinhole collimator gave satisfactory results.

NON-INVASIVE ASSESSMENT OF THE RATE OF LEFT VENTRICULAR VOLUME CHANGE USING ECG-GATED SCINTIGRAPHIC ANGIOCARDIOGRAPHY. Michael V. Green, William R. Brody, Alan S. Pearlman, Harry Agress, Jr., Margaret A. Douglas, David R. Redwood, Samuel B. Itscoitz, James J. Bailey and Gerald S. Johnston. National Institutes of Health, Bethesda, Maryland.

ECG-gated scintigraphic angiocardiology is a non-invasive technique to measure changes in left ventricular (LV) volume throughout the cardiac cycle. To assess the accuracy of the scintigraphic method in detecting abnormal ventricular ejection and filling patterns, 14 patients with catheterization documented asymmetric septal hypertrophy (ASH), mitral regurgitation (MR) or aortic regurgitation (AR) underwent the scintigraphic procedure. One patient from each diagnostic category was selected and a complete LV volume curve was generated frame-by-frame from planimetry of the LV cineangiogram for comparison with the analogous scintigraphic curve. In each case good agreement was obtained.

In ASH, a high rate of ejection early in systole was observed. MR was associated with a high filling rate in early diastole while AR showed continuous filling throughout diastole. These findings suggest that ECG-gated scintigraphic angiocardiology can accurately resolve changes in LV volume during systole and diastole in selected disease states.

A RATIONALE FOR CHOOSING A BAR PHANTOM FOR ROUTINE PERFORMANCE MONITORING OF ANGER CAMERAS. Laurence W. Grossman, Richard J. Van Tuinen, Richard G. Hoops, and Jeannine T. Lewis. Nuclear Medicine Laboratory, FDA, Cincinnati, Ohio.

Bar phantom images have been found to be a useful part of a daily quality assurance routine for Anger cameras. These images provide linearity and resolution information that could not be determined from a field flood alone. There are a number of commercially available resolution/linearity phantoms as well as a host of experimental designs. Therefore, the question of which phantom provides the best test arises. The underlying philosophy of the majority of these phantoms has been to develop a single design that is useful for several scintillation cameras. However, a conceptual argument has been developed that indicates a simple parallel-lines-equally-spaced transmission phantom (dubbed PLES) specific for each camera is most suitable for daily performance monitoring. The lines of such a phantom should fill the entire useful field and have a center-to-center spacing that approaches the resolving power of the camera. Phantoms of this type were constructed for each of seven cameras located in collaborating nuclear medicine laboratories. These phantoms are used daily and provide a sensitive test of degradations in resolution or linearity. PLES phantoms are not commercially available but are simple and inexpensive to construct. However, they are of sufficient utility that they should be commercially available. Furthermore, it would be desirable if such phantoms were supplied by the camera manufacturer at the time of purchase.

TECHNETIUM-99m THIOALIC ACID (TMA): A NEW NON-STANNOUS RENAL SCANNING AGENT. PREPARATION AND EVALUATION. Phillip L. Hagan, Philip R. Ayres, Samuel E. Halpern and Depew M. Chauncey. Veterans Administration Hospital, San Diego, Ca.

Several radiopharmaceuticals are commercially available for renal scanning and all but one of these contains Sn⁺⁺. Recent evidence suggests that the Sn⁺⁺ ion may interfere with subsequent nuclear medicine studies in which Tc-99m Perchnetate is used as the diagnostic agent. Furthermore, the possibility of oxidation or breakdown of the Tc-99m-Sn-complex tends to impair the stability of these compounds. We have prepared a new non-stannous containing radiopharmaceutical that shows promising renal scanning properties.

The optimal conditions for labeling are as follows: to 1cc Thiomalic Acid (100mg) add 2cc Tc-99m Perchnetate eluate, giving a solution of pH 2. Heat at 100°C for 10 minutes. Chromatography on ITLC-SG media/100% n-Butanol shows less than 5% free Tc-99m Perchnetate with no observed breakdown over a 4 hour period.

Biological distribution studies were performed in 300-400 gm. Sprague-Dawley rats at 0.5, 1 and 2 hours following the injection of Thiomalic Acid (5mg/kg.). At one hour, the percent of dose remaining in the blood, liver, one kidney and muscle was 12, 7.2, 20 and 6% respectively. Scintigraphy of kidney slices revealed the radioactivity to be confined to the cortex.

Comparison studies were undertaken with Tc-99m labeled Sn-DMSA, Penicillamine, Sn-Glucoheptonate, and Sn-DTPA. The renal uptake (l kidney) of these compounds at one hour post-injection were 21, 16, 9.1 and 0.66% respectively.

Of interest was the one hour liver concentrations being highest for DMSA (43%), 7.2% for TMA and lowest for DTPA (0.57%) among all of the agents studied.

It is concluded that TMA, a non-stannous containing compound, compares favorably with available kidney scanning agents and deserves further investigation.

VIALABLE AND NON-VIALABLE TUMOR INCORPORATION OF Pb-203 AND 75-SELENOMETHIONINE. Philip Hagan, Depew Chauncey, Philip Ayres and Samuel Halpern. V.A. Hospital and University of California, San Diego, Calif.

The purpose of this study was to ascertain if differences existed in the tumor incorporation of an ionic heavy metal (Pb-203) and a labeled amino acid, 75-selenomethionine (SM-75). The tumor model used was the Buffalo rat bearing a thigh implanted hepatoma. Pb-203 studies were performed 4, 24, 48, 72 and 96 hours and SM-75 24 and 72 hrs. post-injection. Liver, muscle, blood, viable and non-viable tumor tissues were studied and ratios of their specific activities (72 hours) are shown below: (B) = blood, (L) = liver, (M) = muscle. Ga-67 was used as a comparison radio-pharmaceutical.

	Viable			Non-Viable		
	B	L	M	B	L	M
SM-75	4.2	1.9	16	1.6	.7	5.4
Pb-203	1.3	.7	51	11	6	390

As can be seen, more Sm-75 is concentrated by the viable tumor than by non-viable, while the reverse is true for Pb-203. The poor target to background ratios for SM-75 is partially due to the very slow disappearance of the amino acid from the blood, this being nearly flat from the 24-hr. time period. In contrast the Pb-203 shows a tumor and whole body distribution and time effect that is very similar to Ga-67.

It is suggested from this data that the incorporation of heavy metals by tumors may have certain similarities not shared by at least one amino acid.

PREPARATION AND EVALUATION OF 131-I TETRACYCLINE AS A TUMOR SCANNING AGENT. PART III COMPARISON WITH Ga-67 AND VARIOUS Tc-99m LABELED AGENTS. Philip Hagan, Samuel Halpern, Depew Chauncey and Naomi Alazraki. V.A. Hospital and the University of California, San Diego, Calif.

The purpose of this study is to compare the viable and non-viable tumor incorporation of 131-I tetracycline (131-I Tet), 99m-TcO₄⁻, and Tc-99m labeled tetracycline, glucoheptonate, and poly and pyro phosphate, using 67-Ga as the established benchmark. The tumor model used was the Buffalo rat bearing a thigh implanted hepatoma. Studies were conducted at intervals from 0.5-96 hours for Ga-67 and 131-I Tet and at 4 or 18 hours for all other compounds. 131-I Tet and Ga-67 achieved high specific activities (SA) in viable portions of the tumor in the first few hrs. post injection following which a progressive decrease occurred in the viable SA with very little change in the non-viable SA. Comparison ratios for 131-I Tet and Ga-67 at 96 hours post-injection are as follows: (B = blood, L = liver, K = kidney, M = muscle).

	Non-Viable Tumor To:				Viable Tumor To:			
	B	L	K	M	B	L	K	M
131-I Tet	103	7	48	386	8	0.6	3.8	30
Ga-67	93	3	4	25	33	1	1.5	9

Of the 99m-Tc compounds, the highest viable and non-viable tumor to blood and muscle were attained by the phosphates, but in general all were markedly inferior to the values achieved by Ga-67 and 131-I Tet.

It is concluded that 131-I Tet compares very favorably with Ga-67 as a tumor scanning agent under the conditions imposed by this study and that Tc-99m labeled compounds compare less favorably.

DIFFERING MECHANISMS OF Tc-99m SULFUR COLLOID (TSC) AND AU-198 COLLOID (AuC) UPTAKE. Helmut Haibach, Erica S. George, Lynn R. Hendershott and Robert M. Donati. Nuclear Medicine Services, St. Louis VA Hospital and St. Louis University, St. Louis, Missouri.

Hepatic colloid phagocytosis of TSC and AuC was studied with a single pass *in situ* perfusion model in the rat liver and by radioautography of liver from rats injected *in vivo*, to elucidate differences in their uptake. Single pass perfusion was employed to control the influence of opsonization and hepatic blood flow. The liver was isolated *in situ*, perfused at 20-25 cm hydrostatic pressure via the portal vein and the effluent collected via the inferior vena cava after a single pass. The initial perfusate consisted of radiocolloid incubated 1 hr + 30 min at 37 C in heparinized blood, followed by a saline wash. The liver was excised for radioassay. Hepatic colloid uptake expressed as % of total activity administered was greater for TSC than for AuC (72 ± 5% vs 52 ± 5%). Uptake of TSC was constant over a 4 log concentration and not altered by the addition of gelatin or gelatin-stabilized AuC to the perfusate. However, similar concentration of gelatin and/or AuC decreased the hepatic uptake of AuC by 66%. This diminution in hepatic uptake was not repaired by the addition of excess serum factors. Since the hepatic uptake of TSC was not blocked by gelatin or AuC, whereas that of AuC was, differing sites of cellular attachment are suggested. Further evidence in support of this hypothesis was provided by histologic radioautographic studies which demonstrated grains produced from TSC distributed apparently overlying the entire Kupffer cell, whereas the grains produced by AuC were localized in the cytoplasm surrounding the Kupffer cell nucleus. The study indicates differing mechanisms of TSC and AuC uptake by liver tissue.

P-32 DIPHOSPHONATE: A POTENTIAL THERAPEUTIC AGENT. Jack N. Hall, Roger P. Tokars, and Robert E. O'Mara. Arizona Medical Center, Tucson, Az.

Various phosphates labeled with P-32 have been used in nuclear medicine as radiotherapeutic agents for approximately 25 years with minimal success. P-32 labeled Orthophosphate, Pyrophosphate, and Polyphosphate are inorganic phosphates and their effect is limited because of hydrolysis, enzymatic action of phosphatases or radiosensitive tissue. In contrast, Diphosphonate is an organic phosphorus compound that concentrates in bone metastases but is not hydrolyzed by phosphatases. Consequently, a comparative study of the *in vivo* distribution of P-32 Orthophosphate and P-32 Diphosphonate in animals was performed.

P-32 Phosphorus Trichloride was obtained from Amersham/Searle and the P-32 Diphosphonate was synthesized using a modified method of Albright and Wilson. Radiochemical purity was checked by radiochromatography and *in vivo* distribution studies were performed in Fisher-344 rats. Groups of animals were sacrificed at 24 hours, 3 days, 5 days, and 7 days post-injection.

The descending order of tissue distribution with respect to the P-32 Diphosphonate concentration was bone, adrenal, liver, kidney, spleen, heart, lung, blood, and muscle. The P-32 Orthophosphate distribution was similar to that of Anghileri in white mice. The bone to marrow ratio for P-32 Diphosphonate was similar to P-32 Orthophosphate at 24 hours post-injection, but was approximately double that of P-32 Orthophosphate at 7 days.

P-32 Diphosphonate appears to be an improved radiotherapeutic agent over P-32 Orthophosphate in this biological distribution study because of the increased bone to marrow ratio. Thus, further work comparing the therapeutic effect of these two agents is in progress in Fisher-344 rats bearing a mammary adenocarcinoma and results of this study will be reported.

USEFULNESS OF BONE SCINTIGRAPHY WITH 99mTc-PHOSPHOROUS COMPOUNDS IN STAGING OF BREAST CANCER. Ken Hamamoto, Rikushi Morita, Itsuo Yamamoto, Masao Fukunaga, Toru Mori, Kanji Torizuka, and Hiroshi Kodama, Kyoto University, Kyoto, Japan.

It is well known that the bone scintigraphy with 99mTc-phosphorous compounds is the most sensitive method of detecting metastatic bone lesions. We have performed bone scintigraphy in 86 patients with breast cancer at various period

of time after surgery to investigate its usefulness in managing breast cancer. A peak prevalence of bone metastasis occurred in the 41 to 50 age group, while relatively few were in the elder groups. Fifty three percent of the cases with no positive bone lesions underwent surgery within half year after the onset of symptoms; however, 38% of the cases were revealed already to have had bone involvement by scintigraphy. No metastatic lesions were detected in 60% and 57% of the cases scanned within half year and one year after surgery, respectively. However, it should be noted that 40% of the patients were revealed to have bone lesions two or three months after the surgery. This indicated they might have had bone metastasis already at the time of surgery. It is noteworthy that about 30% of the cases classified into stage I or II developed bone metastasis within a short period of time. This suggests that bone lesions were present at the time of surgery and that they should have been classified into stage IV instead of stage I or II. As for the TNM classification there was essentially no difference among all groups. It is suggested that bone scintigraphy should always be performed in stage-making before surgery to facilitate selecting of the most appropriate treatment.

GALLIUM IMAGING IN PEDIATRICS. Hirsch Handmaker, and Robert E. O'Mara, Children's Hospital of San Francisco, San Francisco, CA and University of Arizona College of Medicine Tucson, Ariz.

The Gallium-67 citrate scan has been used to identify a variety of neoplastic and benign conditions in adults. The use of this material in pediatrics has been limited due to questions of dosimetry, material cost and availability, and limited clinical experience. A review of our experiences was undertaken to evaluate the role of this study in pediatrics.

We have studied over 30 patients in the pediatric age group, for both tumor identification and staging, and in search of inflammatory foci. Our data indicates that Gallium-67 dosimetry is comparable to other routine nuclear medicine procedures.

Commercial sources now make "standing orders" possible, permitting reduced cost (\$15 to 20 per study) and constant on-hand availability.

Clinical experience indicates that reactive thymic enlargement may produce "false positive" studies, as will epiphyseal uptake due to increased bone blood flow. Bowel activity is generally less than in older patients, but cleansing is still advisable to avoid confusing patterns. Lymphomas, Wilm's tumors, sacral teratomas, and lipomas have all shown good uptake of Gallium. Neuroblastomas and rhabdomyosarcomas have had variable uptake of the material, but generally less than Indium-111 Bleomycin. Sensitivity and specificity data appear comparable to similar tumor types in adults. Abscesses, osteomyelitis and inflammatory nodes in bacterial septicemia demonstrate avid uptake of the material while viral inflammatory abnormalities did not. A sterile hydrops due to Echo 19 virus produced a "negative" defect.

Gallium-67 citrate imaging appears to be a useful tool for pediatric patients with a wide range of benign and malignant diseases, especially when used in combination with other nuclear, sonographic, and radiographic examinations.

HEPATIC HEMODYNAMICS IN METASTATIC LESIONS: STANDARDIZATION OF METHOD. Laurence G. Hanelin, Ismael Mena. UCLA Harbor General Campus, Torrance, Ca.

This is a study of quantitative evaluation of arterial and portal contributions of hepatic blood flow. Eighteen control subjects were studied in the ant. (6), RAO (6), or rt. lat. (6) positions. ^{99m}Tc S.C. was used for positioning and 10-20 millicuries of ^{113m}In chloride was injected rapidly intravenously. Hepatic activity was recorded for 2 minutes. A time activity curve from the abdominal aorta served for quality control and also as a marker of maximum hepatic artery activity. Five areas of interest within the right lobe were monitored. From the resultant time activity curve, the time from onset to peak portal activity, arteriportal circ. time (APCT) was determined. Percent arterialization was defined as a ratio of maximum hepatic counts at peak aortic time/maximum counts at the portal peak of hepatic curve. Mean percent arterialization of control subjects and APCT in the ant., RAO and rt. lat.

projections were uniform; i.e., $30\% \pm 3$ (SEM), $31\% \pm .4$, $34\% \pm 3$ and 28 sec. $\pm .4$, 30 sec. $\pm .4$ and 26 sec. ± 1 respectively. No differences between projections and adjacent areas of interest were identified. Aorta and kidney were sources of false arterialization. Twenty-four patients with primary CA lesions and with focal (14) or irregular liver perfusion (10) were studied. 8/14 focal lesions were arterialized $75\% \pm 6$, $p < 0.001$. 4/10 patients with irregular perfusion had prolonged APCT 42 sec. ± 2 , suggestive of portal hypertension (1). 8/30 cirrhotic patients had prolonged APCT 47 sec. ± 5 , $p < 0.005$, 13/30 severe cirrhotics had APCT of 11 sec. ± 1 , $p < 0.001$ with arterialization of $70\% \pm 6$, $p < 0.001$, and markedly diminished portal flow. There were 9/30 cirrhotics with normal measurements. APCT provided useful evaluation of arterialization of hepatic focal lesion and portal hypertension. (1) Mena et al. New Eng. J. of Med. 263:940, 1960.

^{57}Co -BLEOMYCIN IN THE DETECTION OF PANCREATIC CARCINOMA. John C. Harbert, William C. Eckelman, Richard C. Reba, and Philip S. Schein. Georgetown University Hospital and Washington Hospital Center, Washington, D.C.

Preliminary studies suggest that ^{57}Co -Bleomycin prepared and administered in the manner described by Nouel and colleagues successfully identifies the presence and extent of pancreatic carcinoma. Six patients have been scanned sequentially with 500 uCi ^{57}Co Bleomycin and 250 uCi ^{75}Se Selenomethionine. Two patients with surgically and histologically proved carcinoma of the pancreas had markedly positive ^{57}Co -Bleomycin localization in the expected region of the tumor and abnormal ^{75}Se Selenomethionine scans demonstrating pancreatic defects consistent with tumor. Four other patients, two with abnormal ^{75}Se Selenomethionine scans without further evidence of pancreatic carcinoma had no abnormal ^{57}Co -Bleomycin localization. Expansion of this series of patients is expected to define the value of ^{57}Co -Bleomycin in the detection of pancreatic carcinoma.

Tc-99m - HIDA: A NEW RADIOPHARMACEUTICAL FOR HEPATO-BILIARY IMAGING. E. Harvey, M. Loberg, M. Cooper University of Maryland Hospital, Baltimore, Md. 21201

Tc-99m HIDA, an N-substituted iminodiacetic acid, has been developed as a hepato-biliary imaging agent and compared with I-131 Rose Bengal. Plasma clearance and tissue distribution studies were performed in mice. Clearance and imaging studies in dogs were compared with I-131 Rose Bengal before and after plasma loading with bromosulphthalein (BSP).

Studies in mice showed rapid blood clearance with less than 2% of the injected dose remaining by 5 mins. There was no evidence of activity accumulating in the stomach, spleen, thyroid, or kidneys and 10% of the injected dose appeared in the urine. Greater than 85% of the administered dose was cleared by the liver and excreted via the biliary system. Samples of Tc-99m HIDA were withdrawn from the gallbladder, chromatographed in saline, and reinjected into other animals. Subsequent tissue distribution and chromatographic results confirmed that after excretion by the liver, the radiopharmaceutical remained in chelated form. In dogs <10% and <3% of injected dose remained in the blood at 10 and 60 mins., respectively. The liver fully visualized at 5 mins. with the gallbladder appearing as a coldspot. Activity appeared in the gallbladder within 15 mins., and by 45 mins. all activity had left the liver. Following injection of cholecystokinin, the gallbladder emptied and sequential studies revealed activity progressing through the small intestines. BSP levels of 4-7mg%, which simulated hyperbilirubinemia, did not substantially alter the plasma clearance or imaging characteristics of Tc-99m HIDA. These images were of much better quality when compared to those obtained subsequently in the same dog using I-131 Rose Bengal.

The kinetic and imaging properties of Tc-99m HIDA appear superior to those of I-131 Rose Bengal and demonstrate the merit of this new radiopharmaceutical as an hepato-biliary imaging agent.

A SIMPLE AND RAPID ELECTROLYTIC METHOD FOR PREPARING Tc-99m RED BLOOD CELLS. J.F. Harwig, P.O. Alderson, J.L. Primeau, S. Boonvisut, and M.J. Welch. Mallinckrodt Institute of Radiology, St. Louis, Mo.

Although several reports have appeared in recent years on labeling red blood cells with Tc-99m, these methods are generally rather complicated and require manipulation of minute quantities of unstable stannous ion. We have developed a new method for preparing Tc-RBC which is simple, highly efficient, and readily reproducible. The key feature of our method is the electrolytic generation of accurate microgram amounts of fresh stannous ion at the time it is to be used. The electrolysis cell is assembled from readily available components and can be easily sterilized. A current of 1 milliampere is passed for 10 seconds between two high purity tin wires immersed in 5 ml of normal saline, pH 6.0, in a 10 ml vial. A 1 ml aliquot (1 µg stannous ion) is then withdrawn and added to the packed RBC in a sterile, evacuated blood collection vial. All further operations (washing with saline, incubating with pertechnetate, washing again with saline) are performed in this vial. The entire procedure, including incubation, requires 45 minutes. Labeling efficiencies are typically greater than 90% with human, rabbit, or rat RBC.

The labeled RBC prepared in this manner are highly stable. Only 1-2% of the initial activity is released from the RBC over a 2 hour period in vitro in air or whole blood at room temperature or 37°C. Similarly, 96-98% of the initial activity remains bound to the RBC over a 2 hour period in vivo. The Tc-RBC produce blood pool images in rabbits, while Tc-RBC which have been heat damaged at 49°C for 15 minutes produce spleen images of diagnostic quality, with no interference from liver accumulation.

The preparative ease and excellent properties of electrolytically labeled Tc-RBC should allow more widespread and routine use of this radiopharmaceutical.

IN VITRO STUDIES OF Tc-99m LABELED PROTEINS. J.F. Harwig, S.L. Harwig, L.D. Wells, and M.J. Welch. Washington University School of Medicine, St. Louis, Mo.

The chemistry of protein labeling with Tc remains complex and little understood. To elucidate some fundamental chemical considerations, we have investigated Tc labeling of fibrinogen and albumin. Fibrinogen was chosen because of its importance in the development of thrombus imaging agents. Albumin was chosen for comparison because Tc-albumin preparations are used routinely in clinical imaging.

A simple electrolytic reaction system employing tin electrodes and phosphate buffer at pH 6 was developed. In this procedure, stannous ion is generated as the intermediate reducing agent for the TcO_4^- . A charge of 0.05 coulomb produced 75-85% labeling of fibrinogen as analyzed by the ammonium sulfate precipitation technique, while albumin showed less than 5% labeling. Analysis of both proteins by the routine technique of TCA precipitation was found to be totally unreliable, and purification by dialysis lead to loss of most of the protein bound activity. Increasing the charge by a factor of ten had no effect on albumin labeling. With the more common zirconium electrode reaction system at low pH, a 45% efficiency was obtained for albumin.

Sephacrose 4B gel column chromatography revealed that the non-fibrinogen bound activity consisted of a phosphate chelate, with no free TcO_4^- . The non-albumin bound activity was entirely TcO_4^- in the Sn preparation and entirely phosphate chelate in the Zr preparation. The albumin bound activity in the latter case was in an aggregated form at the void volume. Reports of >90% Tc labeling for albumin are often based on chromatographic methods which cannot separate protein bound from reduced, non-protein bound Tc.

Clearly, study of Tc-labeling of proteins requires individual evaluation of each system by analytical methods which preserve the label and differentiate among the chemical species formed. (N.I.H. Grant No. 1 P17 HL 14147-04).

EFFECT OF IODINATION LEVEL ON THE PROPERTIES OF RADIOIODINATED FIBRINOGEN. S.S.L. Harwig, J.F. Harwig, R.E. Coleman and M.J. Welch. The Edward Mallinckrodt Institute of Radiology, St. Louis, Mo.

The widespread use of iodinated proteins in various tracer studies requires an understanding of the effect of iodination level on the properties of the labeled protein. This consideration is especially important for radiiodinated fibrinogen, in view of its increasingly frequent use in the detection of deep vein thrombosis. Previous studies in rabbits suggested that iodination of fibrinogen with >0.5 I atom/molecule results in significant denaturation, as indicated by a much lower intra-/extra-vascular pool

ratio. Other studies suggested that there is variation of this intra-/extra-vascular pool ratio of fibrinogen among animals. To further investigate these observations, we have studied changes in both physicochemical properties and biological behavior of human, canine, and rabbit fibrinogen iodinated with 0.5-9 I atoms/molecule (IC1 method). In all clearance studies we applied a double iodine isotope technique to directly compare the clearance behavior of fibrinogen at higher levels with the 0.5 I atom/molecule preparations in the same animals. SDS gel electrophoresis was employed to determine changes in molecular size. Our results suggest that iodination of fibrinogen at higher levels results in no essential change in isotopic clottability or molecular size. The biological clearance behavior of human and canine fibrinogen with 3-5 I atoms/molecule is very similar to the respective type of fibrinogen with 0.5 I atom/molecule. A slightly greater difference is observed with rabbit fibrinogen at similar levels, but with essentially no change in intra-/extra-vascular pool ratio when the clearance curves are analyzed by curve peeling techniques. Thus, human and canine fibrinogen can be safely iodinated with up to 4 I atoms/molecule, while rabbit fibrinogen is somewhat more sensitive to this iodination level. (N.I.H. Grant No. 1 P17 HL 14147-04).

AN ALGORITHM FOR MAPPING AND QUANTITATING THE UNIFORMITY OF A RADIONUCLIDE DISTRIBUTION USING A SCINTILLATION CAMERA AND A SMALL DIGITAL COMPUTER. R.S. Hattner and Leon Kaufman. University of California, San Francisco, Calif.

Uniformity of a flood field image is an accepted parameter of scintiscamera quality and performance. In the past spatial distribution phenomena have been evaluated primarily by subjective inspection, and comparisons estimated by ranking. To quantitate and map the uniformity of radionuclide distribution in camera images an algorithm, implemented in a small digital computer, has been developed.

A square matrix operator of adjustable odd dimension scans the image from point to point integrating the activity in the operators domain. At each point the summed activity minus the central value is divided by one less than the number of elements contained in the operator, resulting in the mean value of the central elements cohorts. This value is compared to the central value and the fractional difference obtained. If the difference exceeds adjustable statistical limits, it is saved with its X-Y coordinates for displaying a mapping of image uniformity. A running sum of differences is tabulated for determination of the mean difference, a quantitative estimate of image uniformity. By appropriately matching the operator size to the matrix dimensions, nonuniformities involving different spatial frequency ranges can be evaluated.

The difference images enhance visual appreciation of image heterogeneity and can also be used to find edges of organs or lesions to predefined statistical limits, objectively defining the edge of an organ (e.g. left ventricular blood pool) reproducibly.

Quantitative improvement in flood field uniformity has been documented following camera tuning. This algorithm promises to be useful for objective and precise estimation of radionuclide image uniformity.

A CRITICAL EVALUATION OF Tc-99m STANNOUS CITRATE TUMOR UPTAKE IN MICE. Thomas P. Haynie, Tad Konikowski, and Howard J. Glenn. M. D. Anderson Hospital and Tumor Institute, Houston, TX.

The purpose of this study was to compare the tumor and tissue concentrations of a recently introduced commercially available tumor scanning agent, Tc-99m stannous citrate [Solcicitran(R)], with other tumor localizing radiopharmaceuticals in an in-situ, sarcoma-like mouse brain tumor. Standardized methods for the determination of tumor and tissue concentrations were used.

The tumor content of Tc-99m stannous citrate varied from about 1.9% dose per gram tumor at 10 min to 0.31% dose per gram tumor at 2 hr. The following values are the maximum values obtained during the 10-120 min period after injection compared with those previously obtained in this system with pertechnetate:

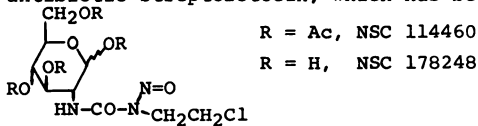
Compound	Max % dose/gm tumor	Max Ratio Tumor:Brain	Max Ratio Tumor:Blood	Max Ratio Tumor:Skin
Pertechnetate	3.93	7.30	0.38	0.58
Sn-citrate	1.88	5.64	1.47	1.26

Using a radiopharmaceutical rating system of biologic characteristics interrelating tumor uptake, tumor-to-brain, tumor-to-blood, and tumor-to-skin ratios, Tc-99m-Sn-citrate was compared with other technetium labeled brain scanning agents. In the first hour after injection the agents were rated in the following order of effectiveness: Tc-99m iron-ascorbic acid, -iron-ascorbic acid-DTPA, -Sn-DTPA, -per-technetate (perchlorate predose), -stannous citrate, and -pertechnetate. At 2 hr, the sequential rankings were: Tc-99m iron-ascorbic acid, -iron-ascorbic acid-DTPA, -per-technetate (perchlorate predose), -Sn-DTPA, -pertechnetate, and -stannous citrate.

In this mouse brain tumor model, Tc-99m stannous citrate appears to have no advantages over other technetium brain tumor scanning agents currently in use.

I-131 STREPTOZOTOCIN ANALOGS: TISSUE AND TUMOR DISTRIBUTION STUDIES. Ned D. Heindel, H. Donald Burns, Victor R. Risch, Takashi Honda, Luther W. Brady and Marlynn Micalizzi. Hahnemann Medical College and Hospital, Philadelphia, Pa.

Two of the most promising current antitumor agents are chlorozotocin, NSC 178248 and its tetra-O-acetylated analog NSC 114460. Because of a close structural similarity to the diabetogenic antibiotic streptozotocin, which has been



employed to treat islet cell tumors, these synthetic derivatives were selected for labeling and tissue distribution studies in hamsters bearing the Kirkman islet cell tumor #2309V. An improved preparation was developed from glucosamine to NSC 178248 in 37% yield and to NSC 114460 in 13% yield. Both compounds induced transient hyperglycemia and both could be readily labeled by nucleophilic displacement of the chloride by I-131 iodide. Tissue and tumor distributions were performed at regular intervals from 0.5 to 7 hours. Pancreas/liver ratios in excess of 2 were observed, with a maximum of 2.7 at 1 hour postdosing with NSC 114460 labeled with I-131. Blood levels of the radiopharmaceutical dropped more slowly with the less soluble acetylated NSC 114460 than with NSC 178248 but tumor/blood & tumor/pancreas ratios were always less than unity. (Supported by American Cancer Society Grant DT-53)

MARROW SCANNING WITH TC-99m SULFUR COLLOID IN NON-HEMATOLOGIC DISEASES. R.E. Henry, E.A. George, J.L. Daly and R.M. Donati. St. Louis VA Hospital and St. Louis University, St. Louis, Missouri.

Marrow distribution patterns have been described frequently in patients with primary hematologic diseases. In this report, the reticuloendothelial marrow distribution in 196 patients with cancer, alcoholic liver disease (ALD) or other non-hematologic diseases was determined and correlated with focal liver or spleen abnormalities, liver or spleen size, and peripheral blood counts. Patients with lymphoproliferative or myeloproliferative disorders, hemolytic anemia, hemoglobinopathy or myeloma were excluded from consideration. Extension of the marrow beyond the proximal 1/3 of the humerus or femur was present in 31 of 62 patients with ALD, 19 of 68 patients with cancer and 17 of 66 patients with other diseases. Marrow extension was more frequent among patients with cirrhosis (61%) than among patients with alcoholic hepatitis (33%). Metastatic disease or therapy was not associated with marrow extension in patients with cancer. Marrow extension was associated with leukemoid response or leukopenia (WBC \geq 20,000 or $<$ 3800) in patients with ALD, and with anemia (Hct. $<$ 39 vol %) in patients in the group of other diseases. In each disease group marrow extension was associated with splenomegaly (\geq 12 cm) but not liver size or focal liver lesions. Marrow extension, therefore, is a frequent occurrence in patients with ALD, cancer and other diseases. These data suggest that marrow extension, as determined by marrow scan, may indicate concomitant clinically-unappreciated hematopoietic or reticuloendothelial abnormalities.

BONE MARROW CELLULARITY AND MARROW TC-99m SULFUR COLLOID DISTRIBUTION. R.E. Henry, E.A. George, R.M. Donati. St. Louis VA Hospital and St. Louis University, St. Louis, Mo.

In order to determine the relationship between bone marrow distribution as imaged with Tc-99m sulfur colloid and marrow cellularity, these parameters were compared in 101 adult patients with a variety of hematologic and non-hematologic diseases. Marrow cellularity was estimated from sections of clotted aspirate or biopsy specimens. The patients were divided into 3 groups according to marrow cellularity: normocellular, hypercellular or hypocellular marrow. The marrow distribution of these patients was graded as not extended (limited to axial skeleton and proximal 1/3 of femur and humerus), extended (beyond proximal 1/3 of femur or humerus), or not visualized. A general association between marrow cellularity and distribution was found. Thirty of 39 patients with normocellular marrow had limitation of marrow within normal adult sites and 24 of 31 patients with reactive hypercellular marrow had marrow extension. Marrow extension was also present in 13 of 26 additional patients in whom the marrow was hypercellular and infiltrated with abnormal cells or tissue. In 9 other patients in this group, the marrow was not visualized with radiocolloid. All 5 patients with hypocellular marrow had marrow visualization and 3 of these had marrow extension. These results indicate that stimulation of hematopoiesis may result in marrow hypercellularity without marrow extension beyond the usual adult sites. Stimulation of one or more hematopoietic cell lines may result in marrow extension without marrow hypercellularity suggesting an impairment of hematopoietic cell response in these patients. Peripheral marrow extension as observed with radiocolloid, therefore, is not simply a reflection of marrow hypercellularity but probably represents a response of the bone marrow stroma to situations in which one or more hematopoietic cell lines is stimulated.

MEASUREMENT OF SCATTER FRACTION IN LIVER AND BRAIN SCANS MEASURED WITH A GAMMA CAMERA. Paul Hoffer, Robert Beck, Violet Stark, and Carlos Bekerman. University of California, San Francisco, Ca. and University of Chicago, Chicago, Ill.

Determination of optimum window settings for imaging *in vivo* radionuclide distributions is predicated in part on knowledge of the ratio of counts due to scattered and primary radiation in the photopeak window. All such estimates of scatter fraction to date are based on models as opposed to clinical data. The purpose of this study was to measure the scatter fraction for Tc-99m in patient studies.

Spectral analysis was performed on the energy proportional output ("Z pulses") of a scintillation camera during 10 liver and 10 brain scans. In each case the spectral distribution was determined for the entire image and also for a "Region of Interest" in the organ. The energy resolution of the camera was determined to be approximately 15%. The scatter fraction, fs (scatter/photopeak) was determined by measuring the height of the scatter peak at 112 keV (where all observed pulses are due to scattered photons) and extrapolating the scatter spectrum within the photopeak, based on the smoothed Klein-Nishina distribution equation. Scatter fraction measurements were made for a base line window setting of 126 keV (.9 of photopeak) which has been determined as the optimum setting for imaging a uniform volume distribution, if scatter is assumed to be like background; in that case, fs = 0.38.

The mean scatter fraction for the brain scans was $fs \pm \sigma = .46 \pm .02$ and $.48 \pm .03$ for total AP image and cerebral region of interest, respectively. The scatter fraction for the liver scans was $fs \pm \sigma = .62 \pm .10$ and $.60 \pm .09$ for total AP view and region of interest respectively.

Preliminary results suggest that the uniform volume distribution is a fairly satisfactory model for brain but not for liver imaging. The larger value of fs for liver scans suggests that the optimum base line is somewhat higher than 126 keV for this procedure.

PENTAGASTRIN: A NEW DRUG FOR STIMULATING GASTRIC SECRETION OF PERTECHNETATE. Lawrence E. Holder, Alan B. Ashare, Wilbur Smith, and Eugene Saenger. Radioisotope Laboratory, Cincinnati General Hospital, Cincinnati, Ohio.

Pentagastrin, the n-terminal pentapeptide of gastrin has been used in Canada and Europe for some time as a safer, more rapidly acting gastric acid stimulant in place of histamine or histalog. We performed animal

studies to investigate the ability of the drug to increase the secretion of pertechnetate by gastric mucosa.

Using three dogs who acted as their own controls, Tc-99m pertechnetate in doses of 100 uCi/kg was administered intravenously both with and without the prior stimulation by 6 ug/kg subcutaneously administered pentagastrin. Sequential upper abdominal scintiscans were obtained, demonstrating gastric secretion and accumulation while the data was being stored on video tape for later quantitative analysis. Six pairs of scintiscans were obtained and then interpreted by 5 observers without knowledge of which scan was obtained after the pentagastrin stimulation. Pentagastrin was found to be effective in increasing the rapidity of gastric appearance of pertechnetate, the absolute intensity of the gastric image, and the relative intensity of the gastric image compared to background.

These results have been sufficiently encouraging to suggest the desirability of using this drug in children in whom bleeding from a Meckel's diverticulum is a consideration.

A SIMPLE METHOD FOR QUANTITATING ANGER CAMERA RESOLUTION AND FIELD UNIFORMITY. F. Eugene Holly. University of California, Center for Health Sciences, Los Angeles, Calif.

Resolution and field uniformity measurements are of paramount importance in the assessment of Anger camera performance and are, generally, the basis of routine testing by field service personnel and institutional quality control programs. The usual approach relies on subjective judgements of visual presentations of flood fields and bar phantom patterns and is rapidly being rendered inadequate by the present generation of ultra-high resolution cameras. A more quantitative approach is necessary. A simple, inexpensive and totally portable system has been devised for this purpose.

The system is assembled from modules normally found in larger Nuclear Medicine Departments and has as a basis an easily assembled "signal conditioning" module. Either vertical or horizontal "slices" across the field of view are acquired by means of readily available x and y positioning signals from the camera. The slice width is variable down to a lower limit of 1 cm. Readout is accomplished with either a multichannel analyzer, x-y plotter or a simple line printer. The number of actual events occurring linearly along the slice are read out. It therefore has not only the capability of measuring field uniformity, but it also has a line spread function for resolution assessment.

MEASUREMENT OF REGIONAL MYOCARDIAL BLOOD FLOW WITH Xe-133 BOTH AT REST AND AFTER CONTRAST HYPEREMIA. B. Leonard Holman, Peter F. Cohn, Jackie R. See, John Idoine, and Douglass F. Adams. Harvard Medical School and Peter Bent Brigham Hospital, Boston, MA.

Regional myocardial blood flow (RMBF) (ml/min/100 gm± S.E.M.) was measured using intracoronary Xe-133 both at rest and after the intracoronary injection of contrast media (CM) in 9 patients with normal coronary arteriograms (NCA) and in 18 patients with angiographic evidence of coronary artery disease (CAD). Flow to tissue perfused by the proximal and distal left anterior descending and left circumflex arteries was calculated. There was no significant difference between RMBF at rest in NCA and CAD. After CM, the washout curve in NCA was biphasic with an initial increase in flow followed by a return to the resting clearance rate. In most CAD patients, flow was triphasic with an initial fall followed by an increase in xenon clearance, and then a return to resting levels. The duration of the initial decrease in clearance rate was 6.7±4.8 (sec±S.E.M.), 7.1±1.3, and 9.0±1.8 in patients with 80%, 90%, and 100% stenosis, respectively. After CM, RMBF in NCA was 146±7 ml/min/100 gm. In patients with one or two vessel disease, flow to tissue perfused by an angiographically normal vessel was 93±4 ml/min/100 gm. RMBF in tissue supplied by a vessel with a 70-100% stenosis was 88±6 ml/min/100 gm; the correlation between the degree of stenosis and RMBF was poor. Although the xenon washout technique after CM injection clearly differentiated patients with and without morphologic evidence of CAD, the percent of stenosis as defined by the coronary arteriogram did not predict RMBF. The decreased response of nonstenotic vessels in CAD relative to that in NCA indicates that factors in addition to vessel patency are critical for the determination of RMBF.

Tc-99m-DTPA: THE OPTIMUM RADIOPHARMACEUTICAL FOR BRAIN IMAGING. Richard A. Holmes and Ali T. Isitman. The Medical College of Wisconsin, Milwaukee, Wisconsin.

Variations in the rate of pertechnetate equilibration in brain lesions has made 2 to 4 hour delayed brain imaging routine in many nuclear medicine laboratories. To eliminate the need for delayed brain imaging without sacrificing diagnostic accuracy, we substituted Tc-99m-DTPA for the pertechnetate because it has been shown to equilibrate more rapidly in brain lesions. Measurement of blood clearance and the relative quality of sequential brain images in several patients established 30 minutes post-injection as the minimum optimum time to begin the imaging. During an 8 month period 904 patients referred for routine brain images were imaged using 250-300 uCi/kg of Tc-99m-DTPA. Abnormal images were found in 143 (15.8%) patients. Their pathology included 37 primary and secondary brain tumors, 63 spontaneous and traumatic vascular lesions, 6 acute and chronic infectious processes, a single cortical cyst and 36 extracortical lesions. All were documented at surgery or autopsy or were corroborated by their clinical course and/or radiocontrast cerebral angiogram.

Four hour delayed pertechnetate brain images were repeated within 48 hours of the Tc-99m-DTPA images on 35 of the positive cases (including infarcts, brain tumors, and abscesses). In none of these positive cases did the 4 hour delayed pertechnetate images delineate abnormalities that were not demonstrable on the Tc-99m-DTPA images, although aesthetically the images were more pleasing in 2 patients.

Since the cost of preparing Tc-99m-DTPA is more than offset by the savings realized from the elimination of oral perchlorate and the waiting or transporting time of patients, we conclude that Tc-99m-DTPA is the most efficient radiopharmaceutical for brain imaging today.

Tc-99m LABELED PHOSPHATES AS AN INDICATOR OF BREAST PATHOLOGY. Richard A. Holmes, Rajashri S. Manoli, and Ali T. Isitman. The Medical College of Wisconsin, Milwaukee, Wisconsin.

The Tc-99m stannous phosphates (diphosphonate and pyrophosphate) have been observed to concentrate in breast tissue during skeletal imaging. In our assessment of 271 female patients referred for whole body skeletal images, 97 (36%) showed variable breast uptake of the radiopharmaceuticals. Analysis of the breast uptake relative to its intensity and histology revealed several primary breast and extra-mammary lesions. The benign lesions include mammary dysplasia, fibroadenomatosis, cystic mastitis, fat necrosis, mazoplasia and intraductal papilloma and those lesions associated with inflammation showed the most intense breast uptake. Over 95% of the benign lesions showed bilateral breast uptake. Of forty breast cancer patients showing breast uptake, ten had bilateral uptake and in each case cancer was found in both breasts. Uptake was also seen in the contralateral breast of 16 post-radical mastectomy cancer patients but to date none have demonstrated cancer in the remaining breast. Sixteen patients in the series (6%) with documented breast cancer showed no breast uptake. Twenty-seven patients showing breast uptake had gynecologic cancers of the ovary (5), endometrium (16) and cervix (6).

The mechanism of Tc-99m phosphates uptake by breast tissue is unknown, and the frequent absence of demonstrable calcification in the lesions tends to support the hypothesis that tissue receptors such as enzymes and/or hormones binds the radiopharmaceuticals. Our findings suggest that Tc-99m stannous phosphate imaging may be a sensitive and early technique to detect breast pathology and the intensity of breast uptake appears to relate to the inflammatory or neoplastic nature of the lesions.

THERMOGRAPHY IN THE EVALUATION OF COLD THYROID NODULES. J. Homesley, B. Kovaleski, K. Vanags, M. Schreyer, J.Franco Department of Nuclear Medicine, O'Connor Hospital, San Jose, California.

Approximately 15% of isotopically cold thyroid nodules are malignant. However, preoperative identification of such cases is difficult. As thermography has been used successfully to detect breast cancer, we asked ourselves whether it would be of value in the preoperative identification of malignant thyroid nodules.

For the study we exposed the area of the neck and had the patient wait for about 10 minutes in an air-conditioned

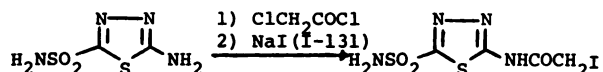
room at 76°F. Pictures then are exposed with an AGA thermovision unit 680. The skin is then cooled with alcohol and observed as it rewarms. A normal thermogram is simply no evidence of increased temperature in the region of the thyroid. An abnormal thermogram would be an area of increased temperature close to the nodule in question and in the same side as the nodule.

In our study we had 78 adult patients with isotopically cold thyroid nodules who eventually came to surgery. Thermography was abnormal in 20 of 39 patients with benign adenomas, in 5 of 17 patients with adenomatous nodules, in 4 of 11 patients with Hashimoto's lymphocytic thyroiditis, and in 10 of 11 patients with papillary or follicular carcinoma. Two patients with cystic benign lesions had negative thermogram.

In this limited series, a positive thyroid thermogram was found in approximately half the patients with a variety of benign conditions, so by itself, it would not be an indicator of malignancy. However, as a negative thermogram was found in only 1 of 11 carcinomas, it might have diagnostic significance. In other words, while a positive thermogram is not indicative of malignancy, a negative thermogram almost tends to exclude the diagnosis of malignancy.

A NEW RADIOPHARMACEUTICAL: RADIOIODINATED ACETAZOLAMIDE. Takashi Honda, Victor R. Risch, H.D. Burns, Marlynne Micalizzi, Luther W. Brady and Ned D. Heindel. Hahnemann Medical College and Hospital, Philadelphia, Pa.

Acetazolamide, an inhibitor of carbonic anhydrase, effects diuresis and suppresses pancreatic secretion of bicarbonate and total fluid. Its action on the kidney prompted its inclusion in a mixed complex of penicillamine-acetazolamide-Tc-99m which proved a useful renal radiopharmaceutical (J Nucl Med 13: 45-50, 1972). But many complexes are concentrated by the kidney independently of ligand structure and no simple labeled acetazolamide has been studied. We therefore prepared and evaluated the tissue distribution of an I-131 acetazolamide obtained by halogen interchange with NaI (I-131) on a chloroacetyl acetazolamide. The latter was obtained in 35% yield from an aminosulfonamide. Tissue distributions from 0.25 to 24 hours revealed a slow



blood clearance due perhaps to high carbonic anhydrase levels in RBC. The lung uptake was rapid, greatly exceeded that found in the kidney, and did not parallel the known organ concentrations of the enzyme, i.e., kidney >> lung > liver. Pancreatic uptake was the least of the tabulated organs and was not affected by predosing with morphine or Lugol's solution. Moreover, even slower blood clearance was observed in the Lugol-dosed animals. (This work was supported by grant DT-53 from the American Cancer Society.)

POSITRON SCINTIGRAPHY OF CEREBRAL FUNCTION IN MAN B. Hoop, Jr., D.J. Hnatowich, D.A. Chesler, K.A. McKusick, J.A. Parker, R. Subramanyam, G.L. Brownell, R.G. Ojemann and J.M. Taveras. Massachusetts General Hospital, Boston, MA

Among the advantages of positron scintigraphic techniques for visualization of cerebral function are the availability of short-lived radiopharmaceuticals for assessment of cerebral function (blood flow and metabolism), and the possibility of obtaining true three-dimensional scintigraphic information by means of focussing or by tomographic reconstruction. These advantages are being explored clinically with a multicrystal positron camera. Radiolabeled compounds currently being used are $^{13}\text{NH}_3$ (T 1/2 = 10 min) and ^{68}Ga -labeled chelating agents (T 1/2 = 68 min) given intravenously, and $^{15}\text{O}_2$ (T 1/2 = 2 min) given by inhalation.

Preliminary scintigraphic data obtained in twenty patients with a variety of intracranial abnormalities, including cerebral vascular dis-

ease and neoplasms, reveal that these agents have differing fates in the brain. Gallium-68 accumulated in two acoustic neuromas, three meningiomas, but not in some other primary and metastatic tumors. $^{13}\text{NH}_3$ and $^{15}\text{O}_2$ accumulated in a meningioma but not in other tumors examined. None of the agents accumulated in regions of cerebral infarction. However, since $^{13}\text{NH}_3$ and $^{15}\text{O}_2$ readily cross the blood-brain barrier, their distribution is such that ventricles, scalp and skull are distinguishable from the brain. This feature may provide added accuracy in the localization and differential diagnosis of intracranial abnormalities.

INDIUM-111 BLEOMYCIN SCANNING IN THE EVALUATION OF MALIGNANT MELANOMA. Neal L. Horn, Ramesh C. Verma, and Leslie R. Bennett. University of California, Center for the Health Sciences, Los Angeles, California

Malignant melanomas are well known to produce distant metastases. The present study was conducted to evaluate the effectiveness of Indium-111 bleomycin (InBLM) scanning in the detection of metastatic melanoma.

Fifty-one adult patients with malignant melanoma were referred from the Surgical Oncology Clinic of the UCLA Center for Health Sciences for total body InBLM scans. All scans were reviewed by two observers who had no prior knowledge of the physical and laboratory findings or case histories. A site-by-site analysis of the head, thorax, liver, spleen, kidneys, abdomen and pelvis, and major lymph node bearing regions was made. Scintigraphic findings were correlated with histopathologic data, roentgenographic studies, conventional liver/spleen, brain and bone scans as well as the physical and laboratory findings.

A total of 699 sites were analyzed. The overall true sensitivity (percentage of proven melanomas demonstrated by the scans) was 64% (27/42). The specificity of the scintigraphic procedure was 97% (635/657) with 22 sites showing accumulation which, on follow-up, did not reveal a malignant focus. We feel that the high degree of specificity coupled with a 64% sensitivity makes scanning with InBLM a useful procedure for the evaluation of metastatic disease in malignant melanoma. (Supported by USPHS Grant GM01920-06.)

SYSTEMATIC IN-DEPTH ANALYSIS OF NORMAL INDIUM-111 BLEOMYCIN SCANS. Neal L. Horn, Ramesh C. Verma, and Leslie R. Bennett. University of California, Center for the Health Sciences, Los Angeles, Calif.

The present study was designed to critically evaluate the pattern of distribution of Indium-111 bleomycin (InBLM) in apparently normal subjects. Careful analysis was made of 111 consecutive total body, 48-hr. scans. Of these, 16 patients (mean age 39.3 years) were without evidence of disease at the time of the scintigraphic study with a mean tumor-free interval of 14.2 mos. The relative concentrations in various organ systems were graded on a scale of 0-2+ with five subdivisions.

Bone Marrow: Half the cases had a 1+ accumulation in the spinal marrow, inferior scapular tips, and sacral wings. Kidneys and Liver: 44% of the kidneys showed a 2+ and 31% showed a 1+ accumulation. The liver activity was equal to or greater than the renal activity in all cases.

Spleen: Splenic concentrations showed a wide variation with a majority (56%) having a 1+ accumulation.

Cardiac: The activity in the region of the heart had a variable distribution with 44% having a 1+ accumulation and 25% with no cardiac activity.

Thorax: Lung areas showed a variable pattern with a 0-1+ bilateral uptake on both anterior and posterior views in 50% of the cases.

Abdomen: 56% showed no unusual accumulation in the abdomen. 31% had a 1+ focal accumulation in parts of the large colon.

Pelvis: 13 patients (81%) had no significant accumulation in the pelvic region while 3 showed focal left lower quadrant activity conforming to the sigmoid colon.

The highest concentration of InBLM is found in the liver and kidneys. A majority of the patients had no activity in the abdomen and pelvis. (Supported by USPHS Grant GM01920-06.)

COMBINED EXAMINATION OF BRAIN CIRCULATION AND KIDNEYS OF DONORS BY Tc-99m DTPA. W. Hupe, R. Montz, M. Doehn, H. F. Otto, K. H. Höhne, G. Pfeiffer. Universitätsklinik Hamburg Eppendorf / Deutsches Elektronen Synchrotron, DESY, Hamburg, Germany.

Before removing kidneys from potential donors rapid determination of brain death, control of actual renal function and exclusion of gross lesions of kidneys to be transplanted are necessary. An examination procedure of an hour's duration has been developed.

After i. v. injection of 10-15 mCi of Tc-99m DTPA the cerebral passage of the radionuclide is sequentially registered and evaluated by a γ -camera-computer system. 30-60 min p.i. a kidney scintigraphy is performed. By measuring blood samples 15, 60 and 90 min p.i. the decrease of serum activity is determined as expression of the renal clearance.

15 patients suspected of brain death have been examined. In concordance with the results of bilateral angiography we found a stop of cerebral circulation on cranium base level. One case of strangulation showed a delayed and reduced intracerebral passage. Pathological findings of kidney examinations corresponded in one case to a haemorrhage from a suprarenal rupture, in a second to parenchymal lesions, a third showed multiple renal infarctions and reduced Tc-99m DTPA clearance indicating limited renal function.

This method seems to fulfill the demand for rapid diagnosis of brain death on potential kidney donors and permits at the same time the elimination of organs with severe damage as rupture, infarction or parenchymal lesion.

EVALUATION OF A RADIONUCLIDE STAGING PROTOCOL FOR BRONCHOGENIC CARCINOMA. Sheldon Hurwitz, Naomi Alazraki, Joseph Ramsdell, Richard Peters, Andrew Taylor, Gennaro Iasi. VA Hospital, San Diego, California

Bronchogenic carcinoma is the leading cause of cancer deaths in men. Since mean survival after diagnosis is less than six months, prompt and efficient staging is essential to define those patients with resectable lesions. This study was designed to evaluate the yield of various radionuclide procedures in detecting clinically silent metastases in patients with lung cancer who are considered operable candidates.

The radionuclide search for metastases includes liver, brain, and bone scans using technetium-99m labeled radiopharmaceuticals, and gallium-67 citrate imaging, performed in that order. Concurrently, direct study of the pulmonary lesion includes spirometry, bronchoscopy and then mediastinoscopy. The initial evaluation is frequently completed so that patients reach surgery within seven days.

Our preliminary review of the first 30 protocol patients studied preoperatively shows that of 10 patients who went to surgery, 100% were resectable at thoracotomy. This is in contrast to previous surgical experience where only 60% of patients undergoing thoracotomy had resectable lesions.

Our preliminary results also suggest that only the cost-benefit of brain scanning in neurologically asymptomatic patients is doubtful; a large study population will be necessary, however, before discarding this as one of the screening procedures. Regardless of resectability, the initial battery of scans serves as a baseline for any further scans showing focal symptoms ultimately develop.

Finally, gallium-67 imaging of the chest confirms previous reports of nearly 100% positive uptake in bronchogenic carcinoma.

TECHNETIUM-99m PYROPHOSPHATE BONE SCANNING IN EVALUATION OF TRAUMA. Mataro Iimori, Kinichi Hisada, and Yutaka Suzuki. Hakusan Hospital, Ishikawa-ken and Kanazawa University Hospital, Kanazawa, Japan.

There has been increasing recognition of the usefulness of radionuclide studies in evaluating of injuries. The purpose of this paper is to compare the diagnostic usefulness of bone scanning to standard radiographic methods in evaluation of osseous trauma. Two hundred and forty two Tc-99m pyrophosphate bone scannings of 182 patients with trauma were reviewed in comparison with the bone x-ray

films taken in the same day. Bone scannings were obtained 3 to 4 hours after injection of 10 mCi of Tc-99m pyrophosphate with a scintillation camera.

Forty eight of 50 fractures determined by x-ray study were detected by bone scanning. Initial radiographic studies missed 13 fractures, — 5 in the rib, 5 in the foot and 3 in other portions, however, bone scanning detected correctly all of these fractures. Forty four cases of positive bone scanning with the negative x-ray films were found in this series. Although precise site of the increased activity were not fully understood, positive bone scanning seemed to reflect the evidence of the trauma accurately. Soft tissue injuries may show abnormalities on the bone scanning, but far often positive bone scannings could be produced by periosteal and bone injuries which are not discernible by radiographic study.

Bone scanning was very sensitive for picking up fractures in almost all portions of the body and especially useful for detection of the fractures in such areas as chest, feet, hands and skull which were frequently difficult to define by routine radiography. Whenever bone scanning demonstrates abnormal activity in the areas of the body where fractures are clinically suspected, these areas should be studied further by special radiographic techniques. Bone scanning can eliminate false negative of the radiographic study.

STUDIES ON SERUM TSH RESPONSE TO TRH IN PATIENTS WITH GRAVES' DISEASE AND WITH PRIMARY HYPOTHYROIDISM, BEFORE AND DURING THE MEDICAL TREATMENT. Minoru Irie, Kazuko Enomoto, Hitoshi Enomoto, and Kazuko Inoue. The First Dept. of Medicine, Toho Univ., School of Medicine, Tokyo, Japan.

76 cases with Graves' disease were tested on the response of serum TSH following 500 μ g TRH injection, in total 224 occasions before and following the treatment by antithyroid drug, and the results were compared with the values of serum T₄, T₃, T₃-RSU and I-131 thyroidal uptake suppression test. There was much individual difference to become the TSH response to normal, and there was no clear relation between the peak value of TSH and serum T₄ and T₃ levels. The manner of serum TSH response was not directly correlated with the I-131-uptake suppressibility by 7 days administration of T₃. The evaluation of TRH test as the prediction test for the permanent remission of the patients with Graves' disease needs further observations.

25 cases with primary hypothyroidism were tested on the response of serum TSH after TRH administration, in total 89 occasions during the treatment by thyroid hormone medication. As the treatment, T₄ alone, T₄ and T₃ combination, and T₃ alone was attempted. Normal response was observed by the administration of T₄ 60 - 150 μ g/day (1.18 - 3.31 μ g/kg/day) or 110.1 \pm 25.4 μ g/day (2.24 \pm 0.53 μ g/day). During T₃ administration, either hyper-response by 15 - 60 μ g/day (0.37 - 0.93 μ g/kg/day) or hypo-response by 50 - 75 μ g/day (0.93 - 1.39 μ g/kg/day) was observed. When TSH value was not detectable or in normal range in the serum before test in 67 occasions, hyper-response was observed in 6 cases. It is suggested that TRH test is a better aid for the determination of appropriate maintenance dose of thyroid hormone medication than single measurement of serum T₄, T₃ or TSH, by observing the normalization of feed-back mechanism.

EARLY DIAGNOSIS OF ASEPTIC NECROSIS OF THE BONE AFTER RENAL TRANSPLANTATION. Akira Ishibashi, Katsumi Ishii, Shozo Hashimoto and Shogo Masumi. Kitasato University, School of Medicine, Sagami-hara, Japan.

Bone scan with Tc-99m diphosphonate was employed for the early diagnosis of aseptic necrosis of the bone which may be considered one of the complications following renal transplantation, and its diagnostic value was studied. In our department, renal transplantation has been performed in 32 cases in the past two years, and manifestations suggestive of aseptic necrosis such as pain of the hip joint have been observed in nine of them. Scintiphotos taken by use of scintiscamera one hour after an intravenous injection of 10 mCi of Tc-99m diphosphonate revealed abnormal accumulation of the radioactivity in the parts where there appeared to be lesions. In six of these nine cases, roentgenography disclosed pathologic changes, and in four of the six, lesions were surgically demonstrated. It was in two of the six cases that bone scan led to earlier discovery of lesions than roentgenography. In two cases in

which the hip prosthesis were performed, Tc-99m diphosphate was infused preoperatively by intravenous route, and the resected heads were examined histopathologically, and at the same time, were subjected to macroautoradiographic examinations. In the result, it was revealed that the marked uptake of the scanning agent would occur in areas where proliferative changes, such as vascular fibrosis, were observed adjacent to the necrotic tissues in the early stage of aseptic necrosis. We believe that if this test is periodically made from about six months after renal transplantation whence aseptic necrosis is liable to occur, it will be possible to arrest the progress of this disease before it is too far advanced for surgery.

KR-85m VENTILATORY SCAN AGENT. G.L. Jackson, W.A. Jester, and K.N. Prasad. Harrisburg Hospital and Pennsylvania State University, Harrisburg, Penna.

Kr-85m is produced by neutron irradiation of naturally occurring Kr-84 (56.9% abundance). Kr-85m decays with a half-life of 4.4 hours and emits a 150 KEV photon (74%) and a 305 KEV photon (13%).

Irradiation of quantities of gas in the gaseous form can produce containment difficulties. A novel approach is reported here - neutron irradiation of Kr-84 in a hydroquinone clathrate. The clathrate effectively traps the noble gas in molecular "cages". At room temperature the clathrate has a crystalline form and theoretically can contain approximately 20% by weight Kr. The gas is released from the solid by melting crystals at a temperature of 170° C.

Comparison studies of the dose rate administered from irradiated krypton gas and commercially available Xe-133 were performed. An ionization chamber coupled to a vibrating reed electrometer was used. The comparison was made in terms of output voltage in the electrometer/unit of photon activity of interest expressed as uCi. Thus, 1 uCi photon activity with reference to Xe-133 would represent that quantity of the isotope which would yield 3.7×10^4 photons/second of energy 80 KEV. A similar definition applied to the 150 KEV photons of Kr-85m. The dose rate from isotopically extremely pure Xe-133 is constant. That from Kr-85m is lower for a period of approximately 40 hours after irradiation.

Use of the clathrate for containment and shipment has been studied. The Kr-85m thus delivered was used in comparison with Xe-133 as a ventilatory scanning agent in an experimental animal. The scans were all of diagnostic quality. The more penetrating Kr-85m photon appears to improve the quality of the scan. Additional study of this agent is warranted.

IMPROVED SCINTIPHOTOGRAPHY OF THE HEART USING THALLIUM-201. George Jambroes, Peter P. v. Rijk, Cees J.M. v.d. Berg, Cees N. d. Graaf, Ariaen N.E. Zimmerman. State University Hospital, Utrecht, Holland.

This study was undertaken to standardize the method of scintigraphy of the heart and to investigate the clinical usefulness of Tl-201 as a myocardial imaging agent after registration with a gammacamera and image-enhancement (IE). We tested and consequently used a modified Linum iteration technique to enhance image resolution. To investigate the required position and number of photoscans needed to portray the left ventricular wall entirely we carried out model studies. By simulating differently sized and located myocardial infarctions (MI) in the model, we could estimate the minimal size of an MI that could still be seen. In animal experiments (dogs) we extended these findings to the beating heart. By means of coronary artery ligations we induced MI of different sizes and locations. Scintigrams were made following intracoronary injections of Tc-99m microspheres. At a later stage the animals were sacrificed and the size of the MI measured. In 30 patients Tl-201 was used for myocardial imaging. Ten minutes later scintigrams were made in five projections. At least five projections were needed to get an accurate impression of the left ventricular wall of the model. In this way images could be obtained to locate MI as small as 5% accurately. In the beating heart it seems that a myocardial infarction should imply about 10% to be visualized. Human studies showed good contrast and ease of interpretation after IE. We found a good correlation between ECG and coronary angiography (CA) versus scintigraphy

although it occurred that scintigraphic abnormalities seemed to be more extended than ECG or CA would suggest. Scintiphography of the heart using Tl-201 in this way appears to be a valuable adjunct in clinical investigation.

EVALUATION OF EFFECTIVE SIZE OF PATHWAYS OF CSF DRAINAGE USING RADIOACTIVE LABELS. A. Everette James, Jr., J. Gordon McComb, Jillian Christensen, and Hugh Davson. The Johns Hopkins Medical Institutions, Baltimore, Md., and University College, London, London England

The effective pathway size through which CSF and its constituents pass from the subarachnoid space are not known. Electron microscopic, structural and histochemical label studies have yielded conflicting results. This study was designed to evaluate the size of these pathways in-vivo in rabbits by CSF perfusion with graduated sizes of radioactive labels and serial blood radioactivity determinations.

After placement of cannulae in the lateral ventricles and constant perfusion of a CSF equivalent containing multiple radioactive labels of different energies, blood samples were obtained at 15 minute time intervals from 2 to 4 hours. These blood, as well as appropriate tissue, samples were counted to measure the time course of movement across the CSF-blood interface. Radiopharmaceuticals employed were:

- 1) ^{99m}Tc pertechnetate (after perchlorate and surgical block).
- 2) ^{99m}Tc or ^{113}I DTPA (800 mol. wt.)
- 3) ^{14}C and ^3H labeled dextran (15,000 and 75,000 mol. wt.)
- 4) ^{99m}Tc albumin mini-microspheres (less than 0.1 μ)
- 5) ^{99m}Tc sulfur colloid (less than 1.0 μ)
- 6) ^{99m}Tc labeled albumin microspheres (15-30 μ)

Preliminary data shows that the ionic labels and dextran molecules entered the blood in the time period studied. Larger molecules such as mini-microspheres, colloidal particles, and albumin microspheres did not appear to pass into the blood in this time period to yield counts significantly greater than background. Appropriate organ (liver, spleen, and lung) and tissue specimen counts confirmed the blood findings. These data suggest that pathways described as being 8-12 μ in size at electron microscopy are effectively much smaller.

DETERMINATION OF RELATIVE BLOOD FLOW TO THE PLACENTA IN RHESUS MONKEYS AND HUMANS USING LABELLED MICROSPHERES. A. Everette James, Jr., Maurice Panigel, T.K. Natarajan, Michael Siegel, and Martin Donner. The Johns Hopkins Hospital, Baltimore, Md., and the University of Paris, Paris, France.

The relative distribution (uniformity) of placental blood flow and whether or not large arteriovenous communicating pathways are present in this organ have been subjects of controversy. In five rhesus monkeys (at approximately 110 days gestation) labelled ^{99m}Tc albumin microspheres were injected into the placental circulation and dynamic and static images obtained. At the same time, shunt determinations were made using the methodology described by Rhodes and Wagner. Five human placentas, immediately following delivery, were placed in the physiologic perfusion apparatus designed by Panigel to simulate intrauterine life. Labelled microspheres (albumin and carbonized) were added to the perfusate and dynamic and static images obtained. The venous return from the placenta was sampled for the presence of radioactivity. During the injection of labelled microspheres in both preparations, the counts were recorded on magnetic tape for computer analysis.

Comparison of the static and dynamic image of the radio-nuclide and contrast angiograms demonstrate significant non-uniformity of perfusion with marked increase of blood flow in the area of the spiral arteries. Quantification studies demonstrate that these areas receive 6-10 times as much blood as the remainder of the placenta. No significant arteriovenous shunts were demonstrated in-vivo in the monkey and no significant radioactivity was present in the placental venous return in the human in-vitro preparation.

ANGER CAMERA DEADTIME: MARKER SOURCE CORRECTION AND TWO PARAMETER MODEL: A. Sidney Johnston, John E. Arnold, Steven Pinsky, Michael Reese Hospital & Medical Center, Chicago, Ill.

Two approaches have been taken to quantify Anger Camera deadtime at high count rate with the goal being to develop an accurate means of computing the true counting rate from the observed rate.

In the first method a marker source using approximately 1mCi of the Tc-99m solution on an absorber in a 1/4" hole countersunk 3/8" in a 2"x2" Pb block 3/4" thick taped to the face of the collimator, was used. The fall in counts from a region of interest set on the marker source was used to correct the counting rate as activity of up to a total of 20mCi of Tc-99m was added stepwise to a 10cm diameter cylindrical source containing 10cm of water and sitting on a 1" thick lucite sheet. The decrease in camera counting rate was adequately corrected for by the decrease in counting rate from the marker source.

The second method was to fit the equation:
 $R = N / (\exp(N + T1/F) + N + T2)$, to data of several different photofractions F. T1 is the pulse pair resolving time of a paralyzable front end and T2 is the deadtime of a non-paralyzable second section model. This model, with one set of values for T1 and T2, fit data for window settings of 10%, 20% and 35% on the Pho-Gamma.

In conclusion the marker source method works well to correct the observed counting rate for deadtime losses and the equation gives a good representation of the observed vs. true counting rate data. We feel that so many variables affect the validity of any equation for any particular camera that before using analytical methods of dead-time correction for their convenience they must first be proved against a marker source or stepwise increment in source strength.

RADIONUCLIDIC IMPURITIES IN COMMERCIAL I-123 AND THEIR INFLUENCE ON THE DOSE CALIBRATOR ASSAY OF I-123. A. Sidney Johnston, S.I. Baker*, John E. Arnold, Lelio G. Colombetti, Steven Pinsky, Michael Reese Hospital & Medical Center and *Fermi National Accelerator Laboratory, Chicago, Ill.

The influence of impurities in commercially available I-123 on the reading of the sample in a dose calibrator at sample calibration time has been measured. The impurities present in the commercial I-123 were identified and quantified by use of a Ge(Li) detector spectroscopy. Activities found in the 9 samples tested are, corrected to manufacturer's calibration time:

	ACTIVITY IN MICROCURIES					
	I-123	I-124	I-126	I-130	I-131	Na-24
MAX:	100	.72	.62	2.5	.54	.03
MIN:	86	.63	.52	1.7	.46	.00
AVG:	96	.66	.55	2.2	.49	.007
MFG.						
LIMITS:	105-94	1.0	1.0	3.0	.75	.5

The response of a commercial dose calibrator for each impurity was determined. The contribution to the sample reading of the impurities was then determined for each sample studied. Impurities were found to contribute 20% to 25% of the reading at calibration time. As most impurities have longer half-lives than I-123, the impurity contribution to any dose calibrator reading will increase with time. Therefore a dose calibrator cannot be used to measure absolute I-123 activity in presently available commercial I-123 because of possible variations in impurity content. 0.1 microcurie of I-125 were found in several samples studied for I-125.

MULTIDENTATE PHOSPHONATES AS SKELETAL AND MYOCARDIAL INFARCT IMAGING AGENTS. Alun G. Jones and Michael A. Davis, Harvard Medical School, Boston, Mass.

The *in vivo* behavior of several Tc-99m labeled polyfunctional phosphonates have been examined as skeletal and myocardial infarct imaging agents. Two of the compounds, ethylenediamine tetra(methylene phosphonic acid) (ENTMP) and triethylenediamine tetra(methylene phosphonic acid) (TENTMP), are analogs of EDTA; a third material, diethylenetriamine penta(methylene phosphonic acid) (DTPMP), is the analog of DTPA; the fourth is nitrilotri(methylene phosphonic acid) (NTMP), which possesses an ammonia-like structure. Their pharmacokinetics have been compared with methylene diphosphonic acid (MDP), now routinely being used in our clinic for bone scanning, 1-hydroxyethylidene-1, 1-diphosphonic acid (HEDP) and pyrophosphate (PP_i). Organ distributions performed in rats at 0.5, 1.0 and 2.0 hours

after injection show DTPMP, ENTMP and MDP to have the highest bone/blood and bone/muscle ratios. For example, at 2 hours, the bone/blood ratios were 158, 94 and 60, and the bone/muscle ratios 432, 308 and 222, respectively. The corresponding values for HEDP were 48 and 102. No significant difference in bone uptake (% i.d./gm tissue) was noted among all the materials tested, except for NTMP, which was one-third of the others. Further studies demonstrated that the bone/blood ratios obtained in rats correlated with blood clearance rates in dogs. These agents were also administered in a rat model of damaged myocardial tissue. A hyperbolic relationship between the ratio of uptake in damaged to normal myocardium and bone activity was found. At the limiting bone value of 2.4% i.d./gm, ratios of approximately 30:1 were obtained with MDP, ENTMP, TENTMP, HEDP and PP_i. There appears to be a number of phosphonates which, because of more rapid blood clearance, promise to replace the current skeletal and myocardial infarct imaging agents.

PREPARATION OF IODINE-123 ROSE BENGAL USING COMMERCIALLY AVAILABLE IODINE-123. Michael P. Kavula, James D. Rogge, Robert T. Anger, Jr., Henry N. Wellman, and Joseph S. Fitzgerald, Indiana University Medical Center, Indianapolis, Ind.

This study was undertaken to develop a technique for the preparation of Iodine-123 Rose Bengal for the study of biliary tree patency in infants.

Iodine-123 as obtained from Medi-Physics, Inc. is transferred to a 10 ml. vial, the pH is adjusted and the solution is dried on an oil bath under a stream of nitrogen. To 0.1 ml. of a Rose Bengal stock solution is added 4.9 ml. of Sodium Acetate Buffer and 0.05 ml. of 30% hydrogen peroxide. This reaction mixture is heated for 5 minutes and then transferred to the Iodine-123 vial. The reaction vial is then heated for 20 minutes, allowed to cool, and the pH is adjusted to 7.0-7.5 with IN Sodium Hydroxide.

Labelling efficiencies have ranged from 94.46% to 99.21% Iodine-123 Rose Bengal and .16% to 4.84% Iodide. Average values were 96.48% for the Iodine-123 Rose Bengal and 2.67% for the Iodide-123.

The radiopharmaceutical was tested in nine adult albino rabbits and demonstrated good visualization of the liver and gallbladder with excretion into the intestinal tract.

FIRST ORDER CORRECTIONS FOR ABSORPTION AND RESOLUTION COMPENSATION IN RADIONUCLIDE FOURIER TOMOGRAPHY. David B. Kay and John W. Keyes, Jr., University of Rochester, Rochester, N.Y. and University of Michigan, Ann Arbor, Mich.

Radionuclide transverse tomography presents special problems due to the data losses caused by internal absorption. To compensate for this in tomograms done by a non-iterative method a correction factor is needed which can be applied directly to the original projection data. Two approximate corrections were derived to do this:

I. Linear Correction

$$g_{\text{corr}}(x') = \frac{g_{\theta}(x') + g_{\theta+180}(x')}{(2-\alpha L)}$$

II. Mean Exponential Correction

$$g_{\text{corr}}(x') = \frac{2[g_{\theta}(x') + g_{\theta+180}(x')]}{(1+e^{-\alpha L} + 2e^{-\alpha L/2})}$$

where L is the thickness of the object, g(x) is a projection and the absorption coefficient α is assumed to be constant. Note that both techniques use complementary, opposed views; a technique which was also shown to largely compensate for the resolution variation of a gamma camera parallel hole collimator. The linear correction was found to give accurate results in the special case of a uniform disk source and to a lesser degree with elliptical sources, with large total absorptions. The linear correction should thus be useful for cases such as brain imaging. The exponential correction was shown to give a correction accuracy of $\pm 5\%$ to the projection data with total absorptions as high as 60%. Both of these methods were tested experimentally on phantoms and found to give a significant improvement in image accuracy. These techniques are readily adaptable to

the Fourier reconstruction algorithms while retaining the high computational speed inherent in these algorithms. Thus significant improvement of quantitative errors is possible in radionuclide tomograms produced by noniterative methods.

IMPROVEMENT OF DIGITIZED IMAGE DISPLAYS. John W. Keyes Jr. and W. Leslie Rogers. University Hospital, Ann Arbor, Mich.

There are many advantages to be gained by using a digital data processing system in nuclear medicine. However, the poor "viewability" of the images from most digital systems makes them difficult to accept as a substitute for conventional scintigrams. Four areas in which improvements could be made with refreshed CRT type displays were identified: 1) Matching brightness scaling of the display to the sensitivity characteristics of the human eye. 2) Matching the output characteristics of the CRT to the recording medium being used. 3) Minimizing the obtrusiveness of the digital matrix lines in the image. 4) Improving image reproducibility.

These areas were studied using a commercially available computer system which allowed accurate control of the display input. Gain and intensity settings were determined which gave a phosphor brightness that was a linear function of the input signal. Within this range the display output was then matched to the exposure characteristics of several standard film types with additional corrections for secondary effects such as dot "blooming" which occurs at high CRT intensities. Matrix line visibility was minimized by interpolating to give a larger matrix and by reducing the separation between individual pixels.

These techniques permit the consistent, reproducible production of digital images at least equal in visual quality to conventional scintigrams, matched optimally to the film being used and independent of operator judgement. As these techniques permit completely digital control over the characteristics of the final image, it should be possible to predetermine display parameters for each individual study type and film type and have the image processing system generate a final, optimum image under full software control.

EFFECT OF PRIOR ADMINISTRATION OF Sn(II) COMPLEXES USED IN NUCLEAR MEDICINE ON IN VIVO DISTRIBUTION OF SUBSEQUENTLY ADMINISTERED Tc-99m PERTECHNETATE AND Tc-99m COMPOUNDS. A. Khentigan, M. Garrett, D. Lum, and H. S. Winchell. Medi-Physics, Inc., Emeryville, CA.

The present work was undertaken to evaluate the effects of prior administration of various clinically used Sn(II) complexes on subsequent in vivo distribution of Tc-99m as pertechnetate and labeled Sn(II) complexes. Various quantities of commercial preparations of SnCl₂, Sn(II) ethane-1, -hydroxy, -1, 1-diphosphonate (EHDP), Sn(II) dimercaptosuccinate (DMSA), and Sn(II) mercaptisobutyrate (MIBA) were administered intravenously to 175-gram rats, and 24 hours later Tc-99m-pertechnetate was given intravenously and the in vivo distribution of activity was compared to control rats given Tc-99m-pertechnetate alone. A typical human dose of Sn(II) DMSA [0.06 mg Sn(II)] administered to each rat failed to produce dramatic changes in Tc-99m distribution, although some increase in kidney activity was seen. A similar dose of Sn(II) MIBA given to each rat markedly increased Tc-99m accumulation in RBC (~20-fold increase over control) while producing modest increases in liver and kidney activity. Decreasing the dose by a factor of 10 almost obliterated the effects noted. Administration of 0.006 mg of Sn(II) to each rat as SnCl₂ or Sn(II) EHDP resulted in marked increased accumulation of Tc-99m in RBC and moderate increase of accumulation of activity in liver and kidneys. Effects of prior administration of Sn(II) complexes on in vivo distribution of other subsequently administered materials is presently under study and such results will be presented.

BINDING OF VITAMIN B-12 BY SERUM OF THE OYSTER TOAD FISH AS THE BASIS FOR A NEW RADIOASSAY. Hyung-Rho Kim, Richard D'Antonio, Steven M. Larson, Jan I. Thorell, J. Buchanan, Ray D. Morgan, and Henry N. Wagner, Jr. The Johns Hopkins Medical Institutions. Baltimore, Md.

We undertook a detailed study of the B-12 binding protein of toadfish (*Opsanus Tau*) serum because of preliminary observations which suggested it might provide an improved binder for use in a competitive binding assay of serum vitamin B-12. This B-12 binding protein with an electrophoretic mobility similar to human alpha-globulins was present in high titer, approximately 1000 times that of human serum. The affinity of the protein for B-12 was high with an association constant of $2 \times 10^{12} \text{M}^{-1}$. This protein was stable when stored frozen or at 4°C in the presence of bovine serum albumin. Based on these findings toadfish serum diluted 1:3500 was used as a new binding reagent in competitive radioassay for B-12. Samples were pretreated by boiling acidified serum to disrupt the binding of endogenous B-12 to naturally occurring serum binders. Albumin coated charcoal was used to separate bound from free radioactive B-12. Under assay conditions this protein was almost saturated with a trace amount of radioactive B-12 (30 pg) which permitted measurement of small amounts of B-12 present in serum. The recovery of a known amount of B-12 added to human serum measured by this method was $101 \pm 15.2\%$ (n=7) and the reproducibility was good with a mean variance of 6.3%. The results indicate the potential usefulness of this protein in a simplified, readily available serum B-12 assay.

OPERATING CHARACTERISTICS OF A COMPUTERIZED HIGH COUNT-RATE RADIONUCLIDE IMAGING SYSTEM. Dennis L. Kirch, Peter P. Steele, Michael T. LeFree and Philip L. Evans. The Denver VA Hospital and The Univ. of Colo. Medical Center.

The spatial and temporal operating characteristics of an image intensifier camera (IIC) have been measured and compared with those of an Anger camera (AC) for performing high count-rate dynamic studies. The configuration of the IIC imaging system has been described previously (*J Nuc Med* 15:506, 1974). Both the IIC and AC are interfaced to the same computer system to permit direct quantitative comparison of the two cameras. Intrinsic resolution measurements were made in the presence of scattering material and the data was digitized into a 32 by 32 array for determination of the Full Width at Half-Maximum (FWHM). The IIC (which has a mosaic crystal, but no electronic pulse-height discrimination) was found to have a constant FWHM of 1.45 cm over the range of energies from 81 keV to 662 keV. The FWHM of the AC was found to range from 1.35 cm at 81 keV to 0.97 cm at 662 keV. Count-rate linearity measurements were made using an 8 cm diameter Tc-99m source positioned 8 cm from the face of the low-energy high-sensitivity collimators. The parallel gamma ray detection capability of the IIC eliminates dead-time losses and results in linear count-rate operation within 1% for up to 50 mCi of Tc-99m (equivalent to 600,000 cps detected by the IIC). The CsI detector of the IIC has a higher detection efficiency than the NaI detector of the AC. The relative efficiency of the IIC was found to be equal to the AC at 140 keV and twice that of the AC at 662 keV. The silicon diode array which digitizes the light output from the IIC has no measurable spatial distortion and uniform response within ±5%. In spite of the somewhat superior spatial resolution of the AC, the higher sensitivity and count-rate linearity of the IIC system make it superior for high count-rate bolus studies of the heart and great vessels.

THE EFFECT OF SPECIFIC ACTIVITY ON TISSUE LOCALIZATION AND RADIATION DOSIMETRY. Alan S. Kirschner and Rodney D. Ice College of Pharmacy, University of Michigan, Ann Arbor, MI

The tissue distribution of six different specific activities each of labeled estradiol, dihydrotestosterone and selenomethionine were evaluated in rats. Utilizing a digital computer and the dosimetry scheme of the Medical Internal Radiation Dose Committee, the animal tissue distribution data of tritiated estradiol was extended to iodine-123 estradiol distribution in man.

As the specific activity of dihydrotestosterone increased from 0.057 mCi/mg to 146 mCi/mg, the concentration of radioactivity in the prostate increased while the liver, kidney and testes concentrations remained the same. As the specific activity of selenomethionine was increased from 0.018 mCi/mg to 7.14 mCi/mg, target-to-nontarget (T/NT) ratios of pancreas to liver increased from a minimum of 0.64 up to 1.83. As the total administered radioactivity of labeled estradiol was increased, the uterus to liver ratios decreased.

Using the pharmacokinetic model resulting from the estradiol tissue localization studies and by varying the administered dose of iodine-123 estradiol in man from 0.26 mCi to 20.9 mCi indicated 1) a decreased uterine concentration from 1.67% to 0.13% of the total dose, 2) that the absorbed radiation dose to the uterus increased from 19 mrad to 176 mrad, 3) that the total body absorbed dose increased from 10 mrad to 820 mrad and 4) that the maximum uptake time decreased from 30 to 5 minutes.

Thus with some radiopharmaceuticals there is a relationship between the administered mass and resultant target concentrations. The law of mass action dictates that as binding sites are saturated, maximum uptake occurs and excess is spilled over to nontarget tissues. In nuclear medicine the optimum time for patient scanning, resultant target-to-nontarget ratios and the patient's absorbed radiation dose are a function of radiopharmaceutical specific activity.

ABNORMALITIES OF REGIONAL RETICULOENDOTHELIAL CELL FUNCTION IN PATIENTS WITH MUCOPOLYSACCHARIDOSSES. William C. Klingensmith, III, Edward A. Eikman, Irene Maumenee, and Henry N. Wagner, Jr. The Johns Hopkins Medical Institutions Baltimore, Md.

Mucopolysaccharidoses (MPS) are inherited disorders of lysosomal enzymes. We have examined the sites of accumulation of intravenously injected technetium-99m sulfur colloid in order to assess the regional distribution of phagocytic function in ten patients: three with MPS type I (Hurler's), five with MPS type II (Hunter's), one with MPS type III (Sanfilippo), and one with MPS type VI (Maroteaux-Lamy). Increased lung uptake was observed in 22 of 40 studies (55%) on the five patients with MPS type II, but in none of the 38 studies on patients with other MPS types. With the technetium-99m sulfur colloid preparations employed, lung uptake was observed in 8% of 273 patients with other diseases. The incidence of lung uptake among patients studied on days when the MPS type II patients had lung uptake was significantly greater than among patients studied on days when MPS type II patients did not have lung uptake. This finding indicates that lung uptake is determined by colloid factors as well as patient factors, but this finding could not account for the increased incidence of lung uptake in MPS type II patients. All MPS patients had diffuse RE marrow hypoplasia despite nearly normal hematocrits and hemoglobin levels. The eight patients with MPS types I and II all had hepatomegaly and increased splenic uptake. Seven of these patients also had splenomegaly. The two patients with MPS type III and MPS type VI did not have hepatosplenomegaly although increased splenic uptake was present in the former. These studies indicate that the lysosomal enzymic defect of MPS results in widespread abnormalities of the distribution of phagocytic function in liver, spleen, bone marrow, and probably the lung as well.

HALOGEN-SHPP LABELING OF FIBRINOGEN, A COMPARISON OF THE I-131 AND Br-77 LABELED RADIOPHARMACEUTICALS WITH I-125 FIBRINOGEN PREPARED BY THE IODINE MONOCHLORIDE METHOD. L.C. Knight, S.L. Harwig, and M.J. Welch. Mallinckrodt Institute of Radiology, St. Louis, Missouri.

Conventional protein iodination involves addition of an oxidizing agent to the protein solution. Using the acylating agent N-succinimidyl-3-(4-hydroxyphenyl) propionate (SHPP) labeling can be carried out without subjecting the protein to oxidizing conditions. Fibrinogen was labeled with both I-131 and Br-77 by this technique and the characteristics compared to ICl labeled I-125 protein. Iodinated fibrinogen has two drawbacks which can be overcome by using 56-hr half-lived Br-77: high radiation dose accompanying the use of I-125 and I-131 and ease of hydrolysis of the weak carbon-iodine bond. Br-77 delivers 1/10 the radiation dose of either iodine isotope and can still be counted for several days. Bromine forms a stronger bond with carbon and free bromide is not concentrated by any organ. SHPP was first labeled with Br-77 at pH 2.8 using the enzyme chloroperoxidase and with I-131 using chloramine-T. Labeled SHPP was then purified and allowed to conjugate with fibrinogen at pH 8, giving a product with >90% isotopic clottability. In vitro hydrolysis studies on brominated proteins showed them to be 100% stable for over 7 days. Clearance studies of iodinated fibrinogen in rabbits showed a very similar clearance behavior for the SHPP and directly iodinated fibrinogen. Brominated SHPP-fibrinogen in dogs cleared at a rate comparable to that of ICl-iodinated fibrinogen, but a greater fraction cleared with the half-life of fibrinogen. Clot uptake studies in dogs

showed clot-to-blood ratios which were identical for I-SHPP-fibrinogen vs. I-fibrinogen, while the clot-to-blood ratio for the brominated protein was 40% greater than that for the iodinated protein. (Supported by NIH Grants #1 P17 HL14147 and 1 P01 HL13851)

A NEW ADRENAL SCANNING AGENT--6 α -IODOMETHYL-19-NOR-CHOLEST-5(10)-EN-3 β -OL-I-131. Masaharu Kojima*, Minoru Maeda*, Hiroshi Ogawa*, Kazuo Nitta*, and Takayuki Ito* Faculty of Pharmaceutical Sciences, Kyushu University, Fukuoka*, and Daiichi Radioisotope Laboratories, Ltd., Tokyo,**, Japan.

The radioiodinated analogue of 19-iodocholesterol (CL-19-I-131) has been widely recognized as a clinically useful diagnostic agent for scintiscanning of the adrenal gland. We followed up its synthesis, and unexpectedly have found the formation of 6 α -iodomethyl-19-nor-cholest-5(10)-en-3 β -ol-I-131 (NCL-6-I-131).

After isolating CL-19-I-131 according to the Counsell's procedure, its purity was checked by thin-layer chromatography using a radio-chromatogram scanner. A radioactive spot from NCL-6-I-131, with an Rf value slightly higher (Rf 0.27) than that of CL-19-I-131 (Rf 0.20) was found using CHCl₃ as eluent. The ratio of NCL-6-I-131 to CL-19-I-131 was 0.3 determined by radioactivity counting. The structure of NCL-6-I-131 was confirmed on the basis of its elemental analysis and spectral evidence.

It is evident that the preparation of CL-19-I-131 according to the Counsell's procedure always contains as a by-product a considerable amount of NCL-6-I-131. Therefore, the accumulation of very pure CL-19-I-131 and NCL-6-I-131 in the rat adrenal gland was compared. NCL-6-I-131 is scarcely excreted after accumulation in the adrenal gland and remains at a higher concentration than CL-19-I-131. The average accumulation in the adrenal gland of CL-19-I-131-dosed rats was 9.7%/g at seven days, while that of NCL-6-I-131-dosed rats was 136%/g. This means that the rat adrenal gland accumulates ten times more NCL-6-I-131 than CL-19-I-131.

We can say that NCL-6-I-131 is by far a more effective adrenal scanning agent than CL-19-I-131. Furthermore, the high selective concentration of CL-19-I-131 in the adrenal cortex previously reported should be corrected since it was not known that CL-19-I-131 usually includes NCL-6-I-131.

AN APPROACH FOR STANDARDIZATION OF SCAN TRANSMISSION VIA TELEPHONE. Jack S. Krause, William S. Maxfield, August Miale. Medical Evaluation Laboratory, Inc., Bradenton, Fl.

Optimal images of nuclear scans can be transmitted via telephone by controlling certain variables at the transmitting station. A transmitting camera (Omnimedical Tel-Image model P-256) was used to send images of nuclear scans to one of two consultants with a receiving station (Omnimedical Receiving Camera model R-256). Optimum transmission was obtained in reduced room light. Masking the view box to the size of the image for transmission also improved the quality of the image received. A light exposure meter (Weston Master II model 735) was used to measure brightness on the monitor scope of the transmitting unit. Line noise was reduced by use of a direct line (Bell System model 30A Voice Coupler). It was concluded that optimal pictures of nuclear scans could be obtained via telephone transmission by controlling the variables noted at the transmitting station and by using the light meter to set the brightness level for transmission.

TECHNETIUM-99m MINIMICROSPHERE LABELING KIT. Gary E. Krejcarek, Karen L. Tucker, James C. Nora, Paul Heerwald, 3M Company, St. Paul, Mn.

A simple kit has been developed for labeling Human Serum Albumin Minimicrospheres with Tc-99m. The kit includes 2 mg of tin containing minimicrospheres, 100 mg of carbohydrate, 0.07 millimoles of glycine-HCl buffer pH 2.4, and 5 mg of a non-ionic detergent. Size distribution studies give a mean diameter of one micron for the minimicrospheres. Ninety eight percent by weight are less than three microns.

To prevent aggregates from forming, the minimicrospheres are lyophilized in a carbohydrate and buffer suspending medium. Carbohydrates which have been successfully used

are inulin, glucose, raffinose, mannitol and inositol. Zeta potential studies have shown that the isoelectric point of the tin-minimicrospheres is near pH 4. By maintaining the pH of the reconstituted at pH 2.4 with glycine-HCl buffer, the spheres are positively charged and thus repel each other.

Five minutes in a boiling water bath is all that is needed for quantitative labeling. Technetium uptake, determined by TLC on silica gel plates with acetone as developing solvent, was consistently in excess of 99%.

An extremely stable complex of Tc-99m is formed with the tin-minimicrospheres. Eight hours after labeling less than 2% free technetium-99m is found. Organ distribution studies of the Tc-99m labeled minimicrospheres in rats sacrificed ten minutes after injection gave 88.8% in the liver, 1.8% in the lungs, 1.8% in the spleen and 4.8% in the carcass. The half-life of Tc-99m in the liver is approximately 72 hours.

The minimicrosphere labeling kit offers several advantages over other RES colloid kits including known and reproducible size distribution of the particles and quick and easy labeling with technetium-99m.

Tc-99m PYROPHOSPHATE KINETICS AND IMAGING IN PSEUDOHYPOPARATHYROIDISM. G. T. Krishnamurthy, A. S. Brickman, R. J. Huebotter, R. C. Cullison, and W. H. Bland. VA Wadsworth Hospital Center and UCLA, Los Angeles, Calif.

Tc-99m-labeled-Sn-pyrophosphate (Tc-pyro) kinetics and bone images were obtained in (1) three siblings with pseudohypoparathyroidism (PSHT) and (2) four patients with metastatic bone disease, and compared with similar data obtained in (3) six control subjects with known primary tumor without involvement of bone or kidney. Six serial blood samples were obtained for 4 hr, and the urine was collected hourly for 4 hr. Blood and urine samples were counted with the standard and the results were expressed as the percent dose/liter of blood and percent dose excreted in urine. Bone images were obtained 3 hr after the injection of Tc-pyro. Serum levels of calcium, inorganic phosphates, acid and alkaline phosphatase, and parathormone (PTH) were obtained. Bone x-ray was obtained and tubular reabsorption of phosphates was calculated.

Blood levels of Tc-pyro were identical at all times for the three groups of patients. In comparison with the controls, the Tc-pyro urinary excretion was increased and the net bone uptake was decreased in patients with PSHT. In contrast, the urine excretion was decreased and the net bone uptake was increased in patients with metastatic bone disease. Tc-pyro images showed all the bone lesions seen on x-ray in addition to several other lesions which were not well appreciated in the bone x-ray. PSHT is a clinical entity where the patient has all the clinical and biochemical features of hypoparathyroidism but increased levels of endogenous PTH fail to alter the urinary excretion of calcium and phosphates. Increased urinary excretion of Tc-pyro suggests that the kidney handling of Tc-pyro in patients with PSHT may be different from that of inorganic phosphates and may be related to raised serum PTH levels. Bone imaging is very sensitive for the early detection of skeletal lesions in PSHT.

Tc-99m-Sn-PYROPHOSPHATE KINETICS AND IMAGING IN PRIMARY HYPERPARATHYROIDISM. G. T. Krishnamurthy, A. S. Brickman, R. J. Huebotter, K. V. Forrest, M. Tubis, and W. H. Bland. VA Wadsworth Hospital Center and UCLA, Los Angeles, Calif.

Kinetics data and bone images were obtained with Tc-99m-Sn-pyrophosphate (Tc-pyro) in (1) 9 patients with primary hyperparathyroidism (PHPT) and (2) 4 patients with metastatic bone disease and compared with the data obtained in (3) 6 control patients with known primary tumors without any bone or kidney involvement. The blood was taken at 10 and 30 min, and 1, 2, 3, and 4 hr after i.v. injection of Tc-pyro. Urine was collected hourly for 4 hr. The blood and urine samples were counted with an aliquot of the injection sample and the results were expressed as percent dose/liter of blood and percent dose excreted in urine. Bone images were obtained 3 hr after i.v. injection of Tc-pyro. Bone X-ray and serum levels of calcium, inorganic phosphates, alkaline phosphatase, and parathormone (PTH) were obtained, and tubular reabsorption phosphate was calculated.

Blood levels of Tc-pyro in all three groups of patients were identical. Compared with the controls, the Tc-pyro urinary excretion was decreased and net bone uptake was in-

creased in patients with metastatic bone disease. In contrast, the patients with PHPT showed increased urinary excretion resulting in decreased net bone uptake. Of the 9 patients with PHPT, 4 showed bone lesions with X-ray and 7 showed lesions with Tc-pyro imaging. Bone lesions were distributed more often in the axial skeleton in patients with metastatic bone disease and in the appendages in patients with PHPT. In patients with PHPT despite decreased net bone uptake, the individual bone lesions that were not seen on X-ray could be delineated with Tc-pyro imaging.

It is concluded that increased Tc-pyro urinary excretion may be due to the effect of increased serum PTH. Bone imaging is the most sensitive diagnostic imaging procedure to detect early bone lesions in primary parathyroidism.

TECHNETIUM-99m PYRIDOXYLIDENEGlutamate - A NEW GALLBLADDER SCANNING AGENT: COMPARATIVE PHARMACOKINETIC STUDY WITH I-131 ROSE BENGAL. H. Kubota, K.P. Poulouse, W.C. Eckelman, and R.C. Reba. Washington Hospital Center and George Washington University, Washington, D.C.

Two agents used for hepatic parenchymal cell studies, I-131 rose bengal (I-131 RB) and Tc-99m pyridoxylidene-glutamate (Tc-99m PG), have been compared in rabbits to determine their relative distributions and therefore, their usefulness for gallbladder studies in man. The distribution of the radioactivity with time in the rabbit indicates that the Tc-99m PG is cleared from the blood by the liver and a fraction is rapidly excreted through the common bile duct into the duodenum. The % dose/gm gallbladder to blood ratios and the % dose/gm intestine to blood ratios are greater than 10:1 within 5 min. after injection. This distribution results in good visualization of the liver, the gallbladder, the common bile duct and the intestine in normal human beings scanned at 1/2 hour. An appreciable amount of the Tc-99m activity is excreted in the urine. Although the I-131 RB clears the blood and the liver at a slower rate, comparable tissue concentration and ratios to that achieved with Tc-99m PG are obtained in rabbits at 2 hrs. The preference for the Tc-99m PG images appear to be related to the physical properties of Tc-99m and not to superior biological properties of PG. Twenty-one studies in man, including 9 normals, were done. Good visualization of the gallbladder and intestines was obtained in all normal volunteers within 30 min. Besides lack of entrance of the tracer into the intestine in extrahepatic obstruction, visualization of the dilated bile duct and non-visualization of the gallbladder were the common features. However, in hepatocellular jaundice delayed liver clearance and delayed visualization of the gallbladder were observed. (Supported by USPHS Grant 20543).

THE MARK IV SYSTEM FOR EMISSION COMPUTERIZED TOMOGRAPHY AND QUANTITATIVE RECONSTRUCTION OF BRAIN RADIOACTIVITY. David E. Kuhl, and Roy O. Edwards, Hospital of the University of Pennsylvania, Philadelphia, Pa.

The Mark IV is designed for high-sensitivity quantification of brain radioactivity in cross-section picture format in order to permit accurate assessment of regional brain function localized in three-dimensions. The improvement in sensitivity over our Mark III instrument was a crucial requirement for proper extension of this study method. The device includes a continuously rotating quad-octal array of 32 collimated NaI (Tl) crystals arranged eight on a side as a box about the head. As the detector square rotates at 50 sec/rev, data are collected continuously, processed in the pulse height analyzers, and extracted from the rotating unit. At the same time, image reconstruction to transverse section format is accomplished with a virtual real-time processing display system. A new grey-shade picture appears, growing in detail and diminishing in noise content, every 50 seconds as the detector unit rotates. Applications of the Mark IV system include absolute determinations of local cerebral blood volume, local cerebral blood flow, and local cerebral metabolism as these new study methods are being developed.

GENERATOR PRODUCED 99m-TcO₄⁻: CARRIER FREE? Myles Lamson, Alan Kirschner, Clifford Hotte, Edwin Lipsitz, and Rodney D. Ice. College of Pharmacy, The University of Michigan, Ann Arbor, Michigan.

The current use of the term carrier-free and its application to generator produced radionuclides is questioned. A solution of Tc-99m, as eluted from a Mo-Tc generator is often referred to as carrier-free. The eluate contains a greater chemical quantity of technetium, however, than that attributable to the metastable isomer alone. The isomeric transition of Tc-99m gives rise to a determinable and chemically significant quantity of Tc-99.

The following equation was derived to determine the fraction of metastable technetium to total technetium in the generator as a function of time between elutions.

$$\frac{\text{Tc-99m}}{\text{Total Tc}} = \frac{\lambda_1 (e^{-\lambda_1 t} - e^{-\lambda_2 t})}{1.162 (\lambda_2 - \lambda_1) (1 - e^{-\lambda_1 t})}$$

This equation was used to calculate a table of technetium ratios (99m to total) which allows one to calculate total technetium based on the radioactivity of Tc-99m at the time of elution and time elapsed since previous elution.

It is apparent that the mass of technetium in a radio-pharmaceutical preparation is always greater than the mass of the metastable isomer alone, and varies with elapsed time between generator elutions. The eluent of a generator eluted after 3 days or 1 week contains, respectively, 13 or 56 times more technetium than indicated by the mass of the metastable isomer alone. Consideration of the actual mass of technetium in solution would eliminate one variable in developing new formulations with this radionuclide.

To overcome the ambiguities of current use of the term carrier-free, the term should be redefined as the maximum specific activity of a radionuclide. It is inappropriate to describe a metastable isomer as carrier free as carrier content increases with time.

RADIOLABELED TUMOR ANTIBODY FOR TUMOR LOCALIZATION. Robert L. Lantieri, Takashi Honda, and Luther Brady. Hahnemann Medical College and Hospital, Philadelphia, Pa.

This project considered the use of I-131 labeled antibody raised in inbred Golden Syrian hamsters against the microsomal fraction of the rat tumor Walker 256 carcinosarcoma. Using biochemical techniques the microsomal fraction of the tumor was separated and solubilized for intraperitoneal injection into the hamsters. After appropriate sensitization, hamster serum was collected and the total immunoglobulin fraction separated. Tumor antibody was retrieved utilizing immunoadsorption. The antibody was labeled with I-131 using a modification of the iodine monochloride technique. The radiolabeled substance was injected into rats bearing the Walker tumor; the animals were sacrificed at various times and organs, tumor and blood (1 analysed for activity/weight. Non-sensitized hamster serum was used in the control study. A second aspect of this study, in progress, considers the use of anti-globulin antibody. Tumor antibody is separated from the serum of rats bearing the Walker tumor utilizing immunoadsorption. This antibody is mixed with Freund's adjuvant and used to sensitize a New Zealand white rabbit. Sensitized rabbit immunoglobulin is collected, labeled with I-131 and injected into rats bearing the Walker tumor. Organ, tumor and blood localization are determined as above. As more specific tumor antigens are discovered and specific tumor antibodies developed, radio-labeled tumor antibodies may be appropriate in the diagnostic and therapeutic armamentarium against tumors.

SOME EFFECTS OF RADIATION FROM Tc-99m ON THE IN UTERO AND NEONATAL MOUSE AND ITS PROGENY. K. A. Lathrop, I. V. Gloria and P. V. Harper. University of Chicago, Chicago, Ill.

Radionuclides decaying by electron capture or isomeric transition incorporated into biomolecules produce greater lethality in cell cultures and greater therapeutic effects than predicted from the energy released. Tc-99m from pertechnetate may be incorporated into such molecules in the mammalian fetus, since when localized here it is not released by perchlorate. Effects of such internally distributed radionuclides on the fetus and its progeny have not been investigated for the materials used in nuclear medicine. Pregnant mice were given daily i.v. injections of

from 5 to 500 μCi of Tc-99m as pertechnetate throughout gestation, gestation and lactation, or lactation. Offspring were weighed at birth, and at 1 and 2 mo. Then male/female litter mates were taken at random to produce the 2nd generation; repetition of the process produced the 3rd generation. Mean weights were calculated for each group and the statistical significance of the deviation from control weights was determined. Animals in the 500 μCi groups consistently weighed less in all generations, except for those from mothers treated only while lactating. However, animals of this latter group were often hairless and infertile. Weight reduction was less in animals from mothers receiving 500 μCi of Tc-99m during both gestation and lactation than from mothers treated only during gestation. This may possibly be explained as radiation effects on the thyroid gland after birth which result in hypothyroidism, since the thyroid uptake of Tc-99m from pertechnetate is less in the fetus than in the neonatal or adult mouse. Weight reduction in 50 μCi groups was almost as great as for 500 μCi animals, and was observed to a lesser extent in 5 μCi groups. A trend toward recovery in the 3rd generations may be due to infertility or death of the animals most affected. The estimated fetal radiation absorbed doses are from 1 to 100 rad. (Supported in part by AT(11-1)-69 and GM-18940.)

MANIPULATION OF SKELETAL LOCALIZATION OF Pb-203 IN THE MOUSE. K. A. Lathrop, I. V. Gloria, P. V. Harper, and H. Krizek. University of Chicago, Chicago, Ill.

Lead-203 ($t_{1/2}=52\text{h}$, $\gamma=279\text{ keV}$) has physical properties favorable for imaging and for radiation absorbed dose. The toxicity of lead from environmental sources is well known, the skeleton being a primary site for its localization. These two facts provoke interest in the biologic distribution patterns of Pb-203 radiochemicals as possible imaging materials and as agents for diagnosis and assessment of therapeutic effects in lead poisoning.

Initial studies in mice of the tissue distributions of carrier-free Pb-203 as chloride, acetate, EDTA, polyphosphate-55, and substituted for Tc-99m in commercial kits for the preparation of tin-polyphosphate (NEN) and EHPD (Osteoscan) show that the skeletal localization is about 30% for the 3 phosphates, chloride, and acetate and, as would be expected, is only about 2% for EDTA. Concentrations of Pb-203 in kidneys, liver, lungs, and spleen are considerably lower for EHPD and PP-55, so that use of these two compounds might be favored. Administration of unlabeled EDTA appears to promote removal of Pb-203 localized from the phosphates, and thus to reduce the radiation absorbed dose substantially. Lead-203 may be useful for skeletal imaging in selected cases, i.e., in obese subjects or in double radionuclide studies where a polyphosphate label other than Tc-99m is needed. As a part of these continuing studies, the effect of previously localized stable lead on the distribution pattern is also under investigation. (Supported in part by AT(11-1)-69 and USPHS Grant GM-18940.)

ASSESSMENT OF PLACENTAL MORPHOLOGY AND FUNCTION WITH RADIOINDIUM. K. A. Lathrop, P. V. Harper, G. Bautovich, H. Krizek, and M. Rich. University of Chicago, Chicago, Ill.

Indium is known to concentrate in mouse and rat placentas to about 35% at 48 h. Such concentration has been difficult to demonstrate in primates or humans because the In-113m ($t_{1/2}=1.7\text{ h}$) used for localization studies is too short-lived, and such subjects do not lend themselves to sacrifice at frequent intervals for *in vitro* assay. By *in vivo* assay of radioindium in the placenta of a stump-tail monkey, the concentration curve has been obtained for a two-week period and found to be similar to the curve for mice. *In vivo* assay was accomplished with positron-emitting radioindium administered with In-111, which was followed for two weeks by means of imaging techniques. The *in vivo* assay was verified by *in vitro* assay of the placenta after delivery by Caesarean section. *In vivo* gamma camera pictures of the placenta in one monkey showed a mottled uptake which was also apparent on images made after removal, and which corresponded with the appearance of the placenta *in situ*. These studies appear to offer possibilities for determining the quantitative uptake of radioindium as an indicator of placental transport and for locating areas of reduced uptake within the placenta. (Supported in part by AT(11-1)-69 and USPHS Grant GM-18940.)

INTESTINAL LOCALIZATION OF Tl-201. K. A. Lathrop, P. V. Harper, I. V. Gloria, and M. Rich. University of Chicago, Chicago, Ill.

The radiation absorbed dose to the intestine may be an important factor in determining the quantity of Tl-201 administered for myocardial imaging. Intestinal localization was observed in a human subject soon after injection and persisted through four physical half-lives. Individual idiosyncrasy of the subject was ruled out when similar observations were made in a baboon.

In order to gain some insight into the origin of intestinal Tl-201, tissue distribution studies were made in mice at daily intervals for 1 week. Concentration in the intestinal wall exceeded that in the contents in all segments. It is not clear whether the localization in the intestinal wall represents secretion into or absorption from the intestinal mucosa. Secretions from stomach and gallbladder may contribute to the intestinal content since both these organs concentrate Tl-201 between 10 and 20 times over the blood level.

The initially high concentration in the kidney relative to the intestine seems to disappear with time, so that, after 1 week, images of the intestine are more prominent than those of the kidneys. In spite of the high kidney concentration, urinary excretion is low, being about 5 to 10% during the first 24 h and a few tenths of 1% thereafter in the two humans studied. It is difficult to find definitive answers for excretion of Tl-201 because of the dependence on potassium metabolism. Ratios of fecal to urinary excretion in one subject began at 0.1 for 74 h and reached approximately constant values of about 5 at six days. These data suggest that human absorbed dose estimates based on animal data may require substantial revision. (Supported in part by AT(11-1)-69 and USPHS Grant GM-18940.)

DEVELOPMENT OF XENON COMPOUNDS FOR MEDICAL USE. E. Lebowitz, M. Greene, A. Ansari, J. Steigman, D. MacKenzie, R. Smol, P. Richards, H. Atkins, N. Solomon, Brookhaven National Laboratory, Upton, N.Y. and Downstate Medical Center, Brooklyn, N.Y.

This project attempts to produce compounds of radioactive xenon with desirable physiological behavior. In such forms, the xenon activity could stay in an organ long enough to permit the study of regional organ perfusion and function. It would then be metabolized to elemental xenon, washed out of the organ, and exhaled from the body, allowing repeated dynamic studies (e.g., multiple views, dual isotopes) in rapid succession via intravenous administration. Thus, one would have a radiopharmaceutical with a convenient shelf-life (the physical half-life of the radioactive xenon) facilitating storage and quality control, but with a short biological half-life (which depends only on the patient's ability to breathe). This would allow the administration of large amounts of activity while minimizing the radiation dose to the patient.

Xenon trioxide and sodium perxenate were sufficiently unstable in-vivo that they gave results indistinguishable from the injection of elemental xenon. Use of these simple xenon compounds might lead to easier handling of xenon in saline, since they have negligible vapor pressures in solution. Barium xenate was shown to be sufficiently stable in-vivo that it bypassed pulmonary excretion and allowed organ visualization after intravenous injection. The kinetics of whole body clearance were also slower than after the administration of elemental Xe-133. Initial studies have been performed with Xe-133, but future work could be performed with Xe-127.

This work has demonstrated the feasibility of producing xenon compounds which bypass pulmonary alveolar excretion and allow organ visualization after intravenous administration. Work is continuing to optimize these radiopharmaceuticals for clinical use.

PLATINUM-195m BLEOMYCIN COMPLEXES FOR TUMOR IMAGING. Francis K.V. Leh and Walter Wolf, Radiopharmacy Program and Cancer Center, University of Southern California, Los Angeles, Calif.

Ever since the discovery that radiolabeled bleomycin localized in a number of soft tumors, attempts have been made to synthesize metal chelates by complexing various radionuclides with bleomycin in the search for more effective tumor localizing agents.

The present study involves the synthesis of two $^{195}\text{Pt}^m$ bleomycin complexes where the metal ligands are PtCl_4K_2 and $(\text{Pt}(\text{NH}_3)_2\text{Cl}_2)$ (*cis DDP*) respectively. Their distribution was studied in mice bearing Ehrlich's Ascites or Lewis Lung carcinoma. The results obtained suggest that these $^{195}\text{Pt}^m$ complexes of bleomycin exhibit similar tumor/non tumor ratios as ^{111}In bleomycin. Whereas the latter dissociates *in vivo*, the present platinum complexes are very stable and are excreted unmetabolized. Studies are in progress to decrease the high blood background and to determine how effective these tumor localizing agents are for different tumor models.

Distribution of $^{195}\text{Pt}^m$ - PtCl_4^m and *cis DDP* labeled Bleomycins in Ehrlich's Ascites Carcinoma.

Time (hrs)	% dose gm^{-1}					
	Blood	Liver	Kidney	Tumor	Muscle	Lung
1	1.53	1.30	3.93	1.36	0.65	1.65
24	0.88	1.63	5.27	1.56	0.56	1.38
48	0.50	1.73	4.23	1.85	0.70	1.30
1	1.57	1.32	3.23	1.32	0.47	1.50
24	1.09	1.52	5.35	1.77	0.49	1.30
48	0.56	1.65	4.40	1.94	0.58	0.95

INVESTIGATION OF SACRO-ILIAC DISEASE. A COMPARISON OF RADIOLOGICAL AND SCINTISCAN TECHNIQUES. Brian C. Lentle, Anthony S. Russell, and John S. Percy. Dr. W.W. Cross Cancer Institute and University of Alberta, Edmonton, Canada.

The radiological progression of sacro-iliitis in ankylosing spondylitis is of bone sclerosis and erosion leading to fusion and obliteration of the joint space. The radiological recognition of early changes such as demineralization and pseudo-widening of the joint space has been shown to be liable to such a degree of observer error as to make the technique of little value.

In an attempt to improve diagnostic precision we have used $^{99}\text{Tc}^m$ -pyrophosphate to obtain bone scans in 55 patients with ankylosing spondylitis and with a variety of other disorders which are associated with sacro-iliitis. Because of the usual visualization of the sacro-iliac joints by this technique, the uptake of the radiotracer has been quantitated by profile scanning through the sacro-iliac joints and sacrum. Normal values have been established in 35 patients without clinical or radiological evidence of sacro-iliitis.

Abnormal findings were present in patients with active ankylosing spondylitis, and other diseases associated with sacro-iliitis. In addition in patients with suspected ankylosing spondylitis and with Reiter's disease and with an elevation of serum HLAw27 (the human transplantation antigen known to be present in increased amounts in patients with these diseases), the scans have been abnormal while the radiographs were normal.

The method appears to be of value in the early diagnosis of sacro-iliitis, and, being quantitative, in evaluating response to therapy.

LIVER SCANNING IN METASTATIC CARCINOMA OF THE BREAST. Stanley M. Levenson, James N. Ingle, Steven D. Richman, Robert S. Frankel, Douglass C. Tormey, A. Eric Jones, Gerald S. Johnston. National Institutes of Health, Bethesda, Maryland

Routine interval liver scanning has been incorporated into the N.I.H. metastatic breast cancer protocols since January 1973. Over 500 studies have been performed in 86 patients. Each scan was compared with concomitant physical examination (PE) and liver function tests (LFT's) to determine the sensitivity of liver scanning in the diagnosis of hepatic metastases. Scans were considered abnormal, raising the suspicion of secondary neoplasm when they fulfilled any of the following criteria: (1) hepatomegaly without a basis for underlying disease, (2) an unexplained nonhomogeneous tracer distribution, or (3) focal defects. SGOT, SGPT, LDH, bilirubin and alkaline phosphatase values were obtained in every case, with the alkaline phosphatase a parameter only in the absence of osseous metastases.

Only those patients with liver metastases documented histologically by biopsy or autopsy were selected for analysis. Twenty-seven (27) patients qualified for this study. All demonstrated a scan abnormality coincident with the first suspicion of metastatic disease. Ten (37%) had normal LFT's and 12 (44%) had a normal PE with a scan abnormality. Seven (26%) of these patients had both normal LFT's and PE in the presence of an initially abnormal scan. In no instance did biochemical or physical findings clearly precede scintigraphic abnormalities. Therefore, in this patient population, liver scanning appears more sensitive than the usual clinical and laboratory parameters in the detection of hepatic metastases.

REFOCUSED GAMMA SYSTEM IMAGES. L.M.Levy, Long Island Jewish-Hillside Medical Center, New Hyde Park, N.Y.; J.D.Baker and F.G.Hughes, Honeywell, Inc., Minneapolis, Minn.; and J.B. Marta, Miller Hospital, St. Paul, Minn.

This study evaluated the capacity of an algorithm developed at Honeywell, Inc. to improve the resolution of gamma camera scintigraphs by refocusing the image in the presence of statistical noise.

Gamma camera scintigraphs of one mm. Co-57 point sources, phantoms, and clinical patients were processed in digital form (64x64 or 128x128 pixels) with a non-linear mathematical operator implemented on small size computer systems (Honeywell 716 or Prime 300). Processed images were displayed by an Ohio-Nuclear 150 system in 128x128 form or by a Prime 300-line printer system in 64x64 form.

Results showed that two point sources too closely spaced to be resolved in the original scintigraph could be separated by the process. Phantom studies indicated that 3/16" spaced bars could be resolved easily although just barely suggestive on the original images, and all 'lesions' of the Picker thyroid phantom could be visualized without magnification. Several clinical studies involving bone, brain, liver, and lung systems were processed. The results showed that where appreciable detail could be anticipated (as in bone images), that application of the algorithm produced definite resolution or sharpening of known anatomical details or of known diseased areas.

We conclude that this algorithm is capable of producing substantial sharpening or refocusing of gamma camera images whose resolution had been degraded by the original imaging system even in the presence of statistical noise without producing significant artifacts.

ACCURATE COMPENSATION FOR DEAD-TIME LOSSES OF A GAMMA CAMERA WITH A FIXED-RATE PULSER. L.M.Levy, S.Hoory, G.W.Moskowitz, and R.J.Martone, Long Island Jewish-Hillside Medical Center, New Hyde Park, N.Y., and Picker Corp., North Haven, Conn.

Previous investigations have shown that dead-time losses in the gamma camera are quite complex and virtually forbid the use of conventional dead-time calculations for correction of dynamic camera studies.

The Picker Dynacamera 2 Series include a fixed-rate pulser which sends a pulse into the summing nodes of the X and Y detection circuits. The pulse amplitude was adjusted so that a point image appeared on the viewing screen with the pulse height analyzer set for Tc-99m. X and Y components were then set to shift the point to an area outside the sensitive field of the camera where it could be recorded digitally without interfering with the camera image. We placed successively zero to ten equal sources of Tc-99m on the camera face and recorded the total image counts in both fast analog and digital modes, and pulser area counts for each case. The ratio of pulser counts with camera activity to pulser counts without camera activity gives the live-time fraction. Dividing the observed camera image activity by this ratio gives corrected image activity. The observed count rates peaked to 30K c.p.s. at a dead-time fraction of 0.74 and declined with higher dead-time fractions.

Corrected counting rates showed expected linearity up to a count rate of 180K c.p.s. (0.84 dead-time), and the lines for fast analog and digital modes were virtually superimposable although the dead-times were different. Above this dead-time fraction, the method was not adequate. Other means of varying the count rate also demonstrated the accuracy of this compensation method.

This fixed-rate pulser live-time meter is a convenient, versatile and accurate means of achieving practical dead-time compensation, and offers many advantages over other estimates.

A MULTIWIRED PROPORTIONAL CHAMBER POSITRON CAMERA: PRELIMINARY IMAGING EXPERIENCE. C.B. Lim, D. Chu, V. Perez-Mendez, L. Kaufman, R. Hattner, D.C. Price, and S.J. Swann, University of California Medical School, San Francisco, CA 94143

A new camera for imaging the opposed 511 keV annihilation gamma rays that follow positron decay has been developed and is now undergoing evaluation. The camera consists of two opposed detectors separated by 50 cm, each detector using a pair of 48 x 48 cm² multiwire proportional chambers (MWPCs). Since the conversion efficiency of 511 keV gamma in the chamber gas is low, the MWPCs are coupled to specially configured lead converters. The present detection efficiency of each detector is 5% and soon it will be upgraded to 10% by adding more converters. The two detectors are operated in coincidence, while each chamber pair in the detector is operated in an anti-coincidence mode to eliminate the background counts due (mostly) to cosmic rays. Coordinates are readout by the delay line method. Data is collected on a small on-line computer, and images are generated later off-line on the desired tomographic planes, both axial and transverse to the detector axis. The full system cost, excluding the computer, is considerably less than that of a new scintillation camera with no data processing accessories. Because of its relatively high detection efficiency and large solid angle coverage the positron camera has a very high sensitivity, which is presently of the order of 675 counts/min-ucI and will eventually quadruple when we add more converters. System spatial resolution on the image plane is of the order of 6-7 mm FWHM. Although energy resolution is not possible when lead converters are used, we find that scattering does not seriously affect image information quality. Early images indicate tomographic capabilities such that images vary significantly when the focusing plane is digitally displaced by 1 cm.

INHALED AEROSOLS AS SCINTIGRAPHIC INDICATORS OF OBSTRUCTIVE PULMONARY DISEASE (OPD). Max S. Lin and David A. Goodwin, VA Hospital and Stanford University, Palo Alto, Ca.

Radioaerosol inhalation lung scintigraphs basically do not measure regional gas exchange. To further understanding the scintigraphy, we have analyzed scintigraphic appearance and nonciliary/ciliary partition (NCP) of pulmonary distribution of inhaled radiocolloids in 28 cases of OPD. A Tc or In colloid was aerosolized with a given modified ultrasonic nebulizer. According to an applicable two-component clearance model, we estimated the NCP as the ratio, 24-hr pulmonary retention/clearance.

Two factors affected the general distribution of the inhaled aerosol: 1. Inhalation technique that may affect inhaled particle size. Compared to a high-output misty aerosol generated in the same nebulizer, a low-output thin aerosol better simulated a single-breath xenon in distal penetration in the same patient. 2. Severity of airway obstruction. With the thin-aerosol technique in 17 cases of COPD, the NCP ratio decreased with increasing obstruction and approximated 3:1 in mild and 1:3 in severe cases.

In severe COPD, the thin-aerosol scintiphoto usually showed a generalized contrast heterogeneity with or without a discrete hyperdeposition in hilar large airways. Massive deposition throughout the central airways was absent. The scintiphoto was helpful in excluding pulmonary embolism, which was suspected as a cause of aggravated respiratory symptoms in these patients. Ischemia over a sizable area was usually associated with a general hypodeposition there.

"Warm" or "hot" areas of hyperdeposition of the thin aerosol were common scintiphotographic findings in the 28 cases. In isolated instances, the hyperdeposition almost certainly occurred focally at sites of partial bronchial obstruction and diffusely by expiratory trapping.

In summary, inhaled aerosols tend to deposit preferentially in conducting airways in OPD and can serve as useful scintigraphic indicators of regional OPD.

DEVELOPMENT OF A CHELATING GROUP FOR SYNTHESIS INTO DRUG AND BIOCHEMICAL ANALOGUES. M.D. Loberg, P.S. Callery, E.B. Harvey, W.C. Faith, M.D. Cooper, University of Maryland Hospital, Baltimore, Md. 21201

The chelating group iminodiacetic acid has been evaluated by determining its chelating strength, in vitro and in-vivo stability, and the effects on target organ specificity when incorporated into drug and biochemical analogs.

Three radiopharmaceuticals, each containing N-substituted iminodiacetic acid, $R-N(CH_2COOH)_2$, were made into kits and labelled with Tc-99m using the stannous reduction method. The R group substitutions were Methyl (M.I.D.A.), 10-carboxydecyl (F.I.D.A.) and N-2, 6-(Dimethylphenyl) carbamoylmethyl (H.I.D.A.). Labelling yields and relative chelating strength were determined using paper and Sephadex chromatography in a variety of solvents. Tissue distribution and imaging studies were obtained in mice and dogs.

Labelling yields greater than 99% were obtained with all three and near quantitative elution from Sephadex G 25 columns occurred with each. Animal studies demonstrated rapid plasma clearance of the radiopharmaceuticals with Tc-99m M.I.D.A. concentrated in the kidneys and excreted into urine in analogous fashion to Tc-99m D.T.P.A. In contrast, greater than 85% of Tc-H.I.D.A. localized in the liver within 10 minutes of iv injection, concentrated in the gallbladder and was excreted into small intestine.

The studies demonstrate iminodiacetic acid forms stable chelates with a strong chemical bond to Tc-99m and that alteration of the R-group substitution fundamentally alters target organ specificity. These characteristics of iminodiacetic acid are a valuable basis for the design of new radiopharmaceuticals using Tc-99m and other metals such as gallium and indium.

RADIONUCLIDE EVALUATION OF INHALATION INJURY IN PATIENTS WITH THERMAL INJURY. Robert J. Lull, Robert N. Agee, James M. Long, Peter A. Petroff, and Jack W. Andrews. Brooke Army Medical Center and U.S. Army Institute of Surgical Research, San Antonio, Tex.

This report summarizes our experience using Xe-133 for clinical evaluation of inhalation injury in burn patients. Inhalation injury is associated with a twofold increase in mortality and requires earliest possible diagnosis.

The study technique is simple, rapid, and requires no patient cooperation. Following intravenous bolus injection of Xe-133 in saline solution, pulmonary washout is monitored with a scintillation camera using sequential polaroid views. Normally, there is even washout which is complete in 90 seconds. Regions of early inhalation injury demonstrate delayed washout of Xe-133.

A total of 154 burn patients were studied using this technique during 1972 and 1973. Xe-133 washout was abnormal in 44 patients. Subsequent clinical evaluation confirmed the presence of inhalation injury in 41 (93%) of these patients. This evaluation included bronchoscopy, radiographic changes, physical examination, pulmonary function studies, and autopsy data. Of the 110 patients with a normal washout pattern, 16 (15%) were felt to have inhalation injury clinically. Several of these "false negative" studies relate to prolonged time between injury and the study. After 72 hours, many washout studies returned to normal.

Typically, the Xe-133 washout study was abnormal several days before radiographic changes occurred and before pulmonary abnormalities could be detected on physical examination. The Xe-133 washout study provides a safe, simple, effective method of diagnosing inhalation injury in its earliest phases. This study can be performed with standard equipment available in most modern nuclear medicine clinics.

BONE SCANNING IN OSTEOMYELITIS, CELLULITIS, AND BONE INFARCT IN CHILDREN. Massoud Majd and Robert S. Frankel. Children's Hospital National Medical Center, Washington, D.C.

Bone scanning is more sensitive than x-ray studies in the early detection of osteomyelitis and its differentiation from cellulitis and/or bone infarct in children. Forty-six patients were examined with bone scans because of suspected soft tissue or skeletal inflammatory disease. Four scan patterns were identified. Pattern I: Early (3 min. post-injection) blood pool scan showed increased activity; delayed (3 hr. post-injection) scan showed intense increased uptake in affected bone. This proved to be osteomyelitis. In this group, 70% had normal radiographs initially. One-half of these developed x-ray changes subsequently. All patients were proven to have osteomyelitis either by

laboratory findings and/or clinical course. Pattern II: Increased early activity with either normal late scans or minimal diffuse increased uptake not localized in bone. This pattern was seen in cellulitis. All patients in this group had soft tissue swelling on x-ray without initial or subsequent bony changes. Clinical course was that of cellulitis. Pattern III: Normal early scan with either decreased or slightly increased uptake on late scan confined to bone, depending on stage of disease. This pattern was seen in patients with sickle cell crisis and bone infarct subsequently proven clinically. X-rays were either negative, showed soft tissue swelling, or showed evidence of previous infarct. Pattern IV: Normal early and late scans. All patients were proven to have no inflammatory or ischemic disease on clinical and laboratory follow-up.

GASTRO-ESOPHAGEAL (GE) SCINTISCAN, A TEST FOR THE DETECTION AND QUANTITATION OF GE REFLUX. Leon S. Malmod, Robert S. Fisher, Gerald S. Roberts, John Capuzzi, and Beth Bloch. Temple University Hospital, Philadelphia, PA.

Existing techniques for evaluating GE reflux do not correlate consistently with clinical symptoms. The purpose of this study was to evaluate the ability of the GE scintiscan (GES) to detect and quantitate GE reflux (GER). Fifteen control subjects and 25 symptomatic patients were studied using a gamma camera on line to magnetic tape and a digital computer. Tc-99m sulfur colloid (Tc-SC), 300 μ Ci/300 ml saline, was instilled into the stomach via a nasogastric (NG) tube. Gamma camera images were obtained for 30 sec. intervals as the GE pressure gradient was increased in increments from 10 to 35 mm Hg using an inflatable abdominal binder. The procedure was performed in both the supine and upright positions. In patients with reflux, the study was repeated without the NG tube. GER was seen in 23 of 25 symptomatic patients. None of the conventional diagnostic studies was as sensitive: acid perfusion test (15), radiographic hiatal hernia (15), fluoroscopic GE reflux (12), histologic esophagitis (14), endoscopic esophagitis (11), phenol red reflux test (11), and lower esophageal sphincter pressure ≤ 10 mm Hg (12), and ≤ 15 mm Hg (20). Fifteen normal volunteers refluxed $2.9 \pm 0.3\%$ of the gastric Tc-SC compared to $11.6 \pm 1.9\%$ for symptomatic patients ($p < 0.01$). The GES study detected reflux with greater sensitivity than did other conventional techniques. The GES test without the NG tube correlated in each case with the test using the NG tube and may serve as a simple nonquantitative study for the detection of GE reflux. In addition, the quantitative technique affords a method for measuring response to various therapeutic modalities.

67GALLIUM SCINTIGRAPHY REVISITED 4 YEARS AND 2000 CASES LATER. Orlando L. Manfredi, and Farouk Ramadan. St. Vincent's Medical Center of Staten Island, N.Y.

The purpose of this paper is to evaluate the usefulness and drawbacks of 67Gallium Citrate scintigraphy.

Carrier-free 67Gallium was injected i.v. in doses of 1.5 - 6 mc.. Scans, scintigrams and dynamic function studies with computerized technique were performed immediately and up to 16 days by utilizing a 5 inch dual total body scanner and a Pho/gamma III scintillation camera interfaced with an MDS Modumed computer using various energy peaks.

67Gallium scintigraphy is highly reliable in neoplastic and inflammatory lesions of the reticuloendothelial system, liver, lung, testes, bone and multiple system melanoma.

It is moderately reliable in brain, thyroid and oro-nasopharyngeal disease.

It is unreliable in disease of the parathyroid, breast, gastrointestinal tract, urinary and gynecological systems.

67Gallium has withstood the test of time and has proven to be a useful tumor seeking radiopharmaceutical as well as a forensic tool in evaluating inflammatory lesions.

PITFALLS OF GALLIUM-TECHNETIUM SUBTRACTION SCINTIGRAPHY OF THE LIVER. Orlando L. Manfredi, Farouk Ramadan, and Peter Watson. St. Vincent's Medical Center of Richmond, N.Y.

The purpose of this study is to demonstrate the inherent errors of the subtraction technique in delineating occult hepatic and subphrenic disease.

Ga-67 was injected i.v. (2-3 mc.) 48-72 hours prior to total body scanning followed by 1.5 - 2 mc. of Tc-99m Sulfur Colloid and imaging was performed 15 minutes later with a computer interfaced gamma camera.

Liver images were obtained utilizing the 140 KeV photopeak of Tc-99m with a 20% window and then placed in memory. Another image of the liver was obtained utilizing either 93 or 184-296 KeV photopeaks of Ga-67 (stored in memory). A third image was produced by subtracting Tc-99m activity from Ga-67 using a predetermined computer program.

A study of 200 patients for subdiaphragmatic and liver related pathology routinely revealed avid Ga activity along the periphery of the liver, porta-hepatis and interlobar fissure rendering an unequivocal diagnosis of intra-hepatic and subphrenic disease difficult.

Although subtraction technique is useful in accentuating target to nontarget ratio which emphasizes only Ga activity in the region of interest the observer must be cognizant of normally occurring activity which may be misinterpreted.

CLINICAL APPLICATION OF REFOCUSED GAMMA CAMERA IMAGES. John B. Marta, Frank J. Hughes, James D. Baker, Barbara Eernisse and Barbara Sturgeon. United Hospitals, Miller Division, St. Paul, Mn. and Honeywell, Inc., Minneapolis, Mn.

Having developed a method of image enhancement utilizing computer refocusing of gamma camera data and having demonstrated this with phantom studies, clinical utilization is being investigated.

All images are recorded on polaroid film and the data recorded on computer tape. The taped data are refocused and displayed on the data set cathode ray tube. The polaroid photographs of the refocused images are compared with the original nonenhanced images. Studies of the brain, thyroid, lung, liver, kidneys and bone are being performed.

Results indicate some subtle lesions are made evident by this technique. This has been best seen in bone and brain studies to date. Bone imaging in particular seems to have the greatest potential use especially with sequential exams and retrospective correlation. The degree of enhancement is data dependent, images having higher counts provide better refocusing of the enhanced photograph. The findings to date are encouraging.

A larger experience and more longitudinal studies will be needed to evaluate the full potential of this promising technique. Slide presentation of the unenhanced and enhanced photographs will provide the audience with a means judging the future value and application of this system.

AN EVALUATION OF THE POSTERIOR FLOW STUDY IN BRAIN SCINTIPHOTOGRAPHY. Thomas R. Martin and Rex B. Shafer. V. A. Hospital, Minneapolis, Minn.

Dynamic flow studies, as a component of brain imaging, have become widely accepted as a significant contribution in the interpretation of brain scans. In many institutions the anterior flow study prior to static imaging has become routine. A modification of this - the posterior flow study may be of added value in certain instances suggested by

the patient's clinical presentation. To evaluate the usefulness of the posterior flow study, a prospective study was instituted. It was presumed that the posterior flow study should be of value in posterior fossa tumors and metastases, posteriorly located A-V malformations, Paget's disease of bone involving the occiput and posterior cerebral infarcts. We report here our experiences in patients who were initially studied by the conventional anterior flow and static images. The addition of a posterior flow study enabled us to better evaluate the vascular nature of the lesion and thereby arrive at the correct diagnosis.

From studies conducted to date we would conclude that the nuclear medicine physician should carefully review each patient's clinical history prior to brain scintiphotography. If abnormality is suspected in the posterior portion of the brain or skull, a posterior flow study should be planned to complement or replace the routine anterior flow study.

TECHNETIUM-99m PYROPHOSPHATE CONCENTRATION IN EXPERIMENTAL MYOCARDIAL INFARCTS. Katalin Martonffy, Keith A. Reimer, Robert E. Henkin, Robert B. Jennings, and James L. Quinn. III. Northwestern Memorial Hospital, Chicago, Ill.

Recent work has shown that technetium-99m labelled phosphates identify sites of myocardial infarction. The timing and factors effecting the magnitude of technetium-99m uptake after coronary occlusion have not been established. We investigated the effect of complete coronary occlusion versus coronary occlusion with reperfusion on technetium-99m pyrophosphate uptake. Acute myocardial infarcts were created in 20 mongrel dogs by temporary or permanent occlusion of the left circumflex artery. At various intervals from 15 minutes to 2 days after occlusion, 25 mCi of technetium-99m pyrophosphate was injected into the left atrium. The hearts were excised and technetium uptake in the left ventricle and septum were scanned and mapped by dividing the heart in 30-40 segments for well counting. Calcium content was measured in the same segments by flame spectrophotometry.

Technetium does not accumulate after brief periods of ischemia, but reaches very high ratios (up to 537:1, infarct vs. normal heart) after longer periods of ischemia, while cell death is occurring.

Uptake in the infarct is much higher after reperfusion than after permanent occlusions, where it is more limited to the periphery of the infarcts. Segments with high technetium also show markedly increased calcium uptake. Thus technetium uptake depends not only on the presence of dying myocardium but also on adequate blood flow to those cells.

The likelihood that technetium uptake is related to calcium uptake is supported by these findings.

THE VENTILATION SCAN IN THE EVALUATION OF CYSTIC FIBROSIS. P. Matin, F. Bittikofer, M. Lischner. University of California, Davis. Roseville Community Hospital.

Cystic fibrosis is a recessive inherited disease of the exocrine glands. It characteristically affects the pancreas, respiratory system, and sweat glands, but chronic pulmonary disease is the chief cause of death.

X-rays and pulmonary function studies have been used to evaluate the degree of lung involvement in cystic fibrosis. However, the Xenon-133 ventilation scan has several advantages over existing methods. 1. It uses little radioactive material so that studies can be performed on a more frequent basis with a minimum of radiation dose. 2. It requires little time or cooperation from the patient so that children can be studied easily. 3. It does not involve the time consuming and often exhausting tests of routine pulmonary function studies.

Ventilation scans using Xenon-133 administered by a system which allows single breath, rebreathing and wash-out studies were performed on children with cystic fibrosis. The children ranged in age from 7 to 13 years and had varying degrees of pulmonary involvement ranging from very mild to severe. The Xenon-133 studies were compared with chest roentgenograms and pulmonary function tests performed on the same day.

The study demonstrated that the ventilation scans not only correlated well with the x-rays and pulmonary function tests, but were the most sensitive means of determining the extent of obstructive airway disease. It was the only method in which the actual anatomic location of the ventilatory abnormalities could be demonstrated.

The ventilation scan appears to be an excellent method for evaluating the extent and progression of the pulmonary involvement of cystic fibrosis.

DIAGNOSTIC AIDE FOR THE DIFFERENTIAL DIAGNOSIS OF BRAIN TUMOR AND CVD BY USING Tc-99m PYROPHOSPHATE
Kengo Matsui, Masahiro Iio, Kazuo Chiba, Hideo Yamada, Masahide Abe and Hajime Murata. Tokyo Metropolitan Geriatric Hospital, Tokyo, Japan.

The purpose of this study is to show the value of combined use of Tc-99m pyrophosphate as a brain scanning agent. Twenty two cases of brain tumor and 28 cases other brain diseases such as CVD abscess, hygroma and etc. were examined by Tc-99m pyrophosphate and Tc-99m pertechnetate.

In 17 cases out of 22, successful visualization of brain tumor are made by both Tc-99m labels. The histologically proven cases were as followed: 2 meningioma, 2 astrocytoma, 1 chondroma, 1 neurinoma, 1 hypothalamus tumor, 1 pituitary tumor, and 4 metastatic tumors. In the case of acoustic neurinoma Tc-99m pyrophosphate was found to be of more value, since it disclosed clearly the size and extent of the lesion which was covered by adjacent activity in Tc-99m pertechnetate scan. Twenty eight cases of the other benign brain disease were also examined with two Tc-99m labels. Only conventional Tc-99m pertechnetate were concentrated in the cases of CVD, and not appreciable uptake of Tc-99m pyrophosphate were noted to the lesions except 4 cases of cerebral infarction. This fact could be used for the early differentiation of CVD from malignant brain tumor without follow up of the case by brain scanning.

In summary, Tc-99m pyrophosphate was successfully applied as an additional brain scanning agent because of its following characteristics. 1) Early blood clearance and significantly fast renal excretion. 2) No accumulation into choroid plexus. 3) No accumulation into the salivary glands. And 4) Probable tumor affinity of this label.

CONSULTATION VIA TELEPHONE TRANSMISSION OF SCAN. William S. Maxfield, August Miale, and Jack S. Krause. Medical Evaluation Laboratory, 1028 Manatee Ave., East, Bradenton, Florida 33505.

Availability of a system which can transmit a scan via standard telephone equipment in 34 seconds makes possible immediate consultation. An Omni Medical Tel-Image transmitting unit (Model #P256) and 2 receiving units (Model #R256) have been in use since August, 1974, for remote consultation. Reports dictated from transmitted images which are deemed technically adequate for interpretation have shown a 95% correlation with interpretation from the original scan. No major abnormality was missed on the transmitted image report nor was there a major false positive report. This data is based on review of 50 cases involving 150 transmissions. In 5% of the transmissions an interpretable image could not be obtained due to interference on the telephone line, mal function of the units, or the consultant thought detail on the transmission required review of the original scan. The majority of the transmissions have been from Bradenton, Florida to Tampa and Miami. The use of the receiver, however, has been tested in Chicago and New York where a consultant was attending meetings. The immediate availability of consultation has frequently saved the patient a repeat study since additional or delayed views were obtained at the consultant's request while the patient was in the laboratory. When needed as an aid for scan interpretation, x-rays can be transmitted over the system. Detail of the transmitted film, however, does not compare as well with the original as does detail for scans. The 34 second transmission time via ordinary telephone and quality of the transmitted images makes remote consultation a clinically practical procedure.

VASCULAR DISPLACEMENT DIAGNOSED BY CEREBRAL RADIONUCLIDE ANGIOGRAPHY. Walter P. Maynard and Fred S. Mishkin. Martin L. King, Jr. General Hospital, Los Angeles, Calif.

With the premise that cerebral radionuclide angiography can detect arterial vascular displacement, we reviewed all cerebral radionuclide angiograms and contrast angiograms that were performed between May 1972 and November 1974 for all studies that were reported as demonstrating vascular displacement on either study. We found a total of twelve patients who had undergone both procedures. A correlation of the contrast angiogram with the cerebral radionuclide angiogram showed a positive correlation for displacement of a major cerebral artery in nine out of ten patients. There were two falsely positive and one falsely negative cerebral radionuclide angiograms. Analysis of our data by major arterial groups reveals that we were able to detect nine of ten shifts of the middle cerebral artery, while we were unable to detect five of eight shifts of the anterior cerebral artery. This apparent lack of sensitivity in detecting shifts of the anterior cerebral artery is probably secondary to a lack of a symmetrical structure that can be used for comparison.

Rotation is the main source of difficulty in detecting a vascular shift. This can be assessed in the arterial phase by observing the cerebral hemispheres for symmetry of size. A rotated venous phase will have a bowed appearing sagittal sinus.

LOW DOSE RADIOIODINE THYROID ABLATION IN POSTSURGICAL THYROID CANCER PATIENTS. K. David McCowen, Fred D. Hofeldt, Nasser Ghaed, Robert A. Adler and Thomas Verdon. Fitzsimons Army Medical Center, Denver, Colo.

Sixty-two patients with histologically proven carcinoma of the thyroid (papillary 28, mixed 18 and follicular 16) were treated with initial high and low dose I-131 therapy from 1960 until 1974. A total of 35 patients in the various histological categories were treated with 30 mCi and a total of 27 patients were treated with higher I-131 doses (30 mCi and in most cases 100 mCi). Nine patients were treated with surgery only for various reasons. After initial treatment, three parameters were used to follow the patients. These include: 1) imaging the neck and body with 1-2 mCi of I-131; 2) PBI-131 conversion rates and; 3) whole body retention studies. The disease free criteria were no imangible tissue in the neck or body, PBI-131 of less than 0.005% at 7 days and whole body retention of less than 3% at 7 days. Of the patients receiving 30 mCi of I-131, 50% with papillary carcinoma, 67% with follicular carcinoma and 67% with mixed carcinoma of the thyroid were rendered disease free. Of the patients receiving higher dose I-131 therapy, 64% with papillary, 50% with follicular and 67% with mixed carcinoma of the thyroid were rendered disease free. Followup time varied between one and 18 years; 50% were followed over 5 years. These data suggest that the low dose I-131 ablative therapy may be as effective as the larger, more routine dose I-131 ablative therapy; theoretical benefits include a decreased risk of aplastic anemia, leukemia and dose related pulmonary fibrosis. In addition, less than 30 mCi I-131 may be given to outpatients with resultant economic savings.

THYROID FUNCTION AND ANTIBODY STUDIES IN PERNICIOUS ANAEMIA. Stuart McHardy-Young, Gerry Krassas and Ian Ramsay. Central and North Middlesex Hospitals, London, NW10, England.

A detailed study of the hypothalamic-pituitary-thyroid axis was carried out in patients with pernicious anaemia and the results analysed with respect to the thyroid antibody status.

An estimation of the circulating level of free thyroxine, effective thyroxine ratio was obtained using a commercially available kit, serum TSH and triiodothyronine were measured by radioimmunoassay and thyroid antibodies by an indirect immunofluorescent technique and the tanned red cell agglutination test. Serum TSH levels were measured following rapid intravenous injection of thyrotrophin-releasing hormone (TRH). Thyroid antibodies were present in 57% of asymptomatic patients. The effective thyroxine ratio was significantly lower in patients with positive antibodies; there was no significant difference in serum T-3 levels. The most significantly abnormal finding was in basal serum TSH levels and TSH response to TRH. Six of 17 antibody positive patients had elevated basal levels greater than 4 microunits/ml and 9 had an exaggerated response to TRH. By contrast, basal TSH levels were normal or

undetectable in 13 antibody negative patients with the TRH response either normal or suppressed.

Basal TSH levels are frequently normal in thyroid antibody positive subjects; thyroid antibodies are therefore a better indicator of underlying thyroid damage. Antibody negative subjects in the older age group commonly had a low basal TSH and an impaired response to TRH.

USE OF SIGNAL DETECTION THEORY IN EVALUATING THE EFFICACY AND COST-EFFECTIVENESS OF LUNG SCANNING. Barbara J. McNeil, Samuel J. Hessel, William T. Branch, Lars Bjork and S. James Adelstein. Departments of Radiology and Medicine, Harvard Medical School and Peter Bent Brigham Hospital, Boston, MA.

The usefulness of various diagnostic modalities in evaluating patients with pleuritic chest pain and in differentiating those with pulmonary embolism from those without was assessed using elements of signal detection theory and the receiver operating characteristic (ROC) curve. The hospital records and radiographic and scintigraphic data of 97 patients under 40 years of age presenting with pleuritic chest pain were reviewed and follow-up information was obtained for 94 patients. Several historical features, physical findings and laboratory and radiographic results were then used disjunctively in establishing an ROC curve. The percentage of patients found to have pulmonary embolism increases monotonically with certain critical pieces of diagnostic data. For example, a history and physical examination alone detect 80% of patients with pulmonary embolism; a chest radiograph raises the percentage to 95%. Addition of a lung scan increases the percentage to 100%. Lung scanning not only increases sensitivity but especially increases specificity by reducing the number of false positive diagnoses. For example, with an abnormal history, physical examination or chest radiograph, the false positive ratio is 40%; the addition of a lung scan reduces this false positive ratio to 5%, i.e. the ROC curve is shifted to the left.

Several cost-effectiveness calculations were made using these data. For example, the financial cost of finding a patient with pulmonary embolism is about \$1000 and the cost of preventing a death from pulmonary embolism is under \$5000. If all patients with pulmonary embolism are to be identified and treated, the marginal cost of identifying the ultimate patient with pulmonary embolism is about \$10,000 and the marginal cost of preventing the ultimate death is nearly \$40,000.

LIKELIHOOD RATIOS FOR DIAGNOSIS OF COLON MALIGNANCY FROM MEASUREMENTS OF SERUM CARCINOEMBRYONIC ANTIGEN. C. E. Metz, P. B. Hoffer, W. H. McCartney, and L. B. Lusted. Dept. Radiology, Univ. of Chicago, and Franklin McLean Memorial Research Institute, Chicago, Ill. (C.E.M. and L.B.L.); Dept. Radiology, Univ. of California, San Francisco, Calif. (P.B.H.); and Dept. Nucl. Med., Wm. Beaumont Medical Center, El Paso, Texas (W.H.McC.).

Although carcinoembryonic antigen (CEA) assay does not in most cases provide a definitive diagnosis of the presence or absence of colon malignancy because of the overlap between assay value distributions in normal and abnormal populations, the method can provide useful diagnostic information regarding the likelihood that a particular patient has colon carcinoma. Conventionally, the CEA assay has been interpreted to indicate a "positive" diagnosis if the resulting serum level exceeds some arbitrary "threshold of abnormality," thereby yielding a rather high fraction of either false positive or false negative diagnoses, depending upon the threshold value chosen. Data on 958 CEA assay studies published by McCartney and Hoffer (*Radiology*, 110: 325-328, 1973) permit more flexible interpretation of the CEA assay result, however, in that the data can be used to calculate the likelihood (or "odds") that a patient has colon malignancy, given the patient's serum CEA level and the prior odds that colon malignancy is present in a member of the population assayed. The likelihood ratios obtained from the data of McCartney and Hoffer in effect quantitate the observation that the "strength" of the indication of malignancy is related to the magnitude of the serum CEA level, and they can be applied to populations having prior odds of colon malignancy different from those of the population used to develop data. These likelihood ratios enhance the value of the CEA assay as a screening procedure and can be combined quantitatively with likelihood ratios associated with other clinical signs and symptoms to determine whether additional diagnostic studies are indicated.

MEASUREMENT OF MYOCARDIAL OXYGEN CONSUMPTION USING HEMOGLOBIN LABELED WITH OXYGEN-15. Judith M. Metzger, Norman S. MacDonald, Carolyn S. MacDonald, and Joseph M. Takahashi. UCLA School of Medicine, Los Angeles, California.

The purpose of these studies was to propose and validate the use of hemoglobin labeled with O-15, a positron emitter of 2 min. half-life, to measure myocardial oxygen consumption by external scintillation detection. Earlier studies indicated that the method lacked sufficient accuracy and precision. The present studies attempted to identify and eliminate sources of error.

Using this method, fractional oxygen utilization of the myocardium is obtained from the externally detected washout curve following intracoronary bolus injection of O-15 hemoglobin. Oxygen consumption is calculated from the product of fractional oxygen utilization, oxygen content of the perfusing blood, and blood flow to the organ. Validation of the technique consisted of comparison against oxygen consumption computed from conventional arterial-venous blood oxygen content differences. These validation studies used the in situ perfused dog heart preparation to maintain blood flow at a known and constant rate.

The accuracy of blood gas analysis was examined in detail. It was found that considerable improvement in accuracy and precision could be obtained by directly measuring blood oxygen content using the Van Slyke technique in contrast to indirect methods which measure oxygen tension. Alternative methods of measuring oxygen content (Lex-O-Con, Severinghaus) were also evaluated. The magnitude of the effect of recirculating tracer was also assessed.

It was concluded that myocardial oxygen consumption can be measured with acceptable accuracy using this method. The short half-life of O-15 allows repeated studies with good counting statistics and without increasing background activity. Since the method does not require coronary sinus sampling, it is the only method which can potentially be extended to regional measurements by positron detection.

PREPARATION AND CHEMICAL CHARACTERIZATION OF *I-BLEOMYCIN. Jeanne Meyers, Kenneth A. Krohn, Anne-Line Jansholt and Gerald L. DeNardo. University of California, Davis, Ca.

Bleomycin is a chemotherapeutic antibiotic that has promise as a tumor radiodiagnostic agent, but the current isotopes (In-111 and Co-57) have serious disadvantages. We have prepared covalently labeled I-123-bleomycin at yields of 85% by the ICl method. The reaction works in either phosphate, borate or citrate buffers, but is more pH dependent than for protein iodination (maxima between pH 6-7.5). Only 0.15 mg of the antibiotic is required so that specific activities of greater than 100 mCi/mg have been obtained. The product deiodinated in neutral buffer at < 0.2%/d at 23°, and chemically and chromatographically, iodination did not alter the molecule. All of our evidence points to the β-hydroxyhistidyl residues as the site at which iodine is binding.

The preparation of I-bleomycin has led to results that have important implications in iodination of other radiodiagnostic agents. Bleomycin does not contain tyrosine, but does contain β-hydroxyhistidine. Histidine can be iodinated at both C and N sites on the imidazole ring, but only C-I bonds are stable. We found that the ICl labeling must be for 1 to 2 hours and that the product must be treated with a mild reducing agent to cleave all N-I bonds before Sephadex purification if the product is to be stable. Chloramine-T gives extensive N-I bonding and is hence unsuitable for bleomycin labeling. Lactoperoxidase gives yields that are too low to be practical. When compared with Ga-67-citrate and other radiolabeled bleomycins, I-123-bleomycin gives the lowest whole body radiation (Ga-67, .27; Co-57, 2-3; In-111, 0.1; I-123, .01 mrad/mCi). Therefore, I-123-bleomycin of all currently proposed labeled bleomycins has the best physical, chemical and biological properties for tumor detection.

QUALITY ASSURANCE IN NUCLEAR MEDICINE: AN IMPLEMENTATION PROGRAM. Marleen M. Moore, John E. Bucher, and William R. Hendee. University of Colorado Medical Center, Denver, Colorado.

With the growing sophistication of nuclear medicine procedures and equipment, the need for quality assurance protocols is becoming increasingly apparent. To help satisfy this need, efforts have been directed towards delineation of rapid and straightforward quality assurance

procedures for specific phases of operation of a nuclear medicine facility. So far, these efforts have resulted in development of cookbook-like protocols for routine quality assurance testing of different models of scintillation cameras, and self-evaluation techniques to verify proper handling of radioactive materials and their preparation as radiopharmaceuticals. Protocols for additional areas of interest are being developed. To encourage the implementation of these protocols and techniques into community nuclear medicine laboratories, they have been presented in a series of "hands-on experience" workshops held in strategic locations in the Rocky Mountain region. Expansion of these workshops into a national program is being pursued in cooperation with the Bureau of Radiological Health and the Technologists' Section of the Society of Nuclear Medicine.

EVALUATION OF Tc-99m BLEOMYCIN SCINTIGRAPHY IN VARIOUS SOFT TISSUE INVOLVEMENT. Toru Mori, Teruo Odori, Itsuo Yamamoto, Tsutomu Sakamoto, Rikushi Morita, Ken Hamamoto, Kanji Torizuka and Hayato Hirotsu. Kyoto University Hospital, Kyoto, Japan.

In some soft tissue and bone lesions differentiation of malignancy from benign condition is not so easy, even by pathological examination. Thirty six cases suspected of having malignancy in peripheral soft tissue or bone were studied by Tc-99m Bleomycin (BLM) scintigraphy. Scintiphotos were taken 30 min after approximately 3 mCi intravenous dose of BLM. In all 10 pathologically proven malignant soft tissue tumors discrete accumulations of BLM were observed and 3 aggressive fibromatosis and 2 recurrent neurinoma cases were also positive. While, benign tumors or inflammatory changes showed negative or limited accumulations. Results in malignant bone lesions were positive in all 8 primary and 2 of 5 metastatic tumors. Generally, benign bone lesions did not accumulate BLM but one each case of Brodie's tumor, chondroblastoma and osteomyelitis showed positive accumulation. In this series Tc-99m labeled P compound (Tc-P) picked up all malignant and benign bone lesions and most of malignant soft tissue tumors, but accumulation in the latter were rather poor and Tc-P failed to show some malignancies without bone involvement. Further, Ga-67 citrate scintigraphies were negative in 3 of 6 malignant soft tissue tumors. Accepting some false positives, BLM scintigraphy in soft tissue involvement is considered quite useful, and parallel examinations by BLM and Tc-P are highly recommended when X-ray finding does not support osteogenic nature of the lesion.

GALLIUM LUNG IMAGING AS AN AID IN THE DIFFERENTIAL DIAGNOSIS BETWEEN PULMONARY INFARCTION AND PNEUMONITIS. Fred S. Mishkin, Albert H. Niden, Ruth A. Pick, and Mohan Khurana. Martin L. King, Jr. General Hospital, Los Angeles, Calif.

The high ventilation/perfusion ratio of pulmonary artery occlusive disease is invalid in the presence of lung parenchymal densities. Pulmonary embolism with parenchymal changes and pneumonitis may often be indistinguishable by routine xenon ventilation studies and lung scanning. Lung changes early in embolic disease represent atelectasis, fluid or blood with little cellular reaction while in pneumonitis they represent fluid and cellular inflammatory response. Since ⁶⁷Ga gallium citrate accumulates in cellular reactive processes, a gallium scan should be abnormal in pneumonitis and normal in pulmonary embolic disease.

Five patients with clinically certain bacterial pneumonitis all showed abnormal gallium accumulation in the site of parenchymal change. Eleven patients with lung infiltrates suspected of having pulmonary embolic disease were studied by angiography, gallium scans, xenon ventilation studies, lung scans and pulmonary function studies. None of the five patients with angiographic evidence of pulmonary embolism had uptake of gallium in the area of embolism although one showed uptake in another area. Four of these five had ventilation perfusion studies demonstrating parenchymal lung abnormalities while only one was considered to demonstrate embolism. Of the six patients without angiographic evidence for pulmonary embolism, three showed gallium accumulation and three did not. The ventilation perfusion studies in these patients suggested embolism in one,

heart failure in one and obstructive airway disease in three, in one of whom coexistent embolism was suspected. These data suggest that when pulmonary infiltrates are present, the gallium scan may be valuable. An abnormal accumulation is associated with an infectious or cellular reactive process, while a normal gallium scan is associated with early pulmonary embolic disease.

RADIOMETRIC ESTIMATION OF SERUM B-12 USING CHICKEN SERUM BINDER. Everett Mincey, Eileen Bonoguro, Shirley Dorais and Robert Morrison. Vancouver General Hospital, Vancouver, BC, Canada

This work was undertaken in order to develop a simple radiometric assay for vitamin B-12 utilizing the exceptional properties of chicken serum as a binder. Chicken serum has a very high affinity for vitamin B-12 and has been used for this assay at 1:1500-1:2000 dilution. Serum samples are boiled in L-glutamic acid buffer in the presence of cyanide ions to denature the endogenous B-12 binding proteins and to free B-12 for assay. L-glutamic acid prevents precipitation of proteins and makes a centrifugation step unnecessary. Glycine buffer, pH 10.0 is then added directly to the test system in the tube used for boiling. This buffer provides the appropriate pH and ionic concentration for optimal binding by chick serum. After incubation, the free radioactive B-12 may be removed by protein coated charcoal. Serum B-12 concentrations in the range 25-2000 pg/ml may be measured by this system. We have determined that maximal binding occurs after 30 minutes at 23°C. This allows for a rapid assay which offers several advantages over the current assay systems using intrinsic factor or human serum as the binding protein. We have compared the B-12 values on 300 serum samples by the present assay method and another radiometric system using human serum as the binder and DEAE cellulose to separate bound and free radioactive tracer. The correlation was sufficiently good to permit the same degree of diagnostic accuracy.

UPTAKE OF 14C-ASCORBIC ACID BY THE ADRENAL AND PITUITARY GLANDS, AND EFFECT OF ACTH OR DEXAMETHASONE ADMINISTRATION. Ali Mohammadzadeh, Lelio Colombetti, U. Yun Ryo, Steven M. Pinsky. Michael Reese Hospital and Medical Center, Chicago Ill.

The distribution of intravenously administered 14C-ascorbic acid (14C-AA) among various tissues of the rabbit and the dog and the effects of dexamethasone or ACTH administration on the distribution were studied.

Two hours after the I.V. dose the concentration of 14C-AA was higher in the adrenal than in any other tissue examined. As a function of time, the difference of 14C-AA concentration between adrenal and surrounding organs became greater, and 24 hours after the dose the adrenal to liver ratio became 5 to 1 in dogs. The concentration of 14C-AA in the pituitary gland gradually increased, reaching a peak at 24 hours and exceeding the adrenal concentration at 48 hours and thereafter.

After suppression by dexamethasone the concentration of 14C-AA in the adrenal gland was significantly lower than the control value, although the hormone had no detectable effect on the concentration in other tissues. Injection of ACTH for three days before administration of the 14C-AA produced no significant effect on the accumulation of 14C-AA in the adrenal. A single dose of ACTH given 1 hour prior to the 14C-AA, however, significantly increased the accumulation in the adrenal.

These results suggest that accumulation of AA in the adrenal occurs through mechanisms that are more complex than those proposed in the literature. The results also suggest that AA may be an effective pituitary scanning agent if it can be labeled with a suitable radionuclide.

AN AUTOMATED XENON-133 SPIROMETER SYSTEM FOR PULMONARY VENTILATION. G.W. Moskowitz, L.M. Levy, and F.J. Sacher. Long Island Jewish-Hillside Med. Ctr., New Hyde Park, N.Y., and Medcraft Instruments, Inc., Rockville Center, New York.

Since xenon ventilation studies often require at least two technicians and a sequence of patient maneuvers, an automated Xenon-133 spirometer system for pulmonary ventilation studies was designed and built.

Instantaneous and remote control is possible with this apparatus during each phase of the ventilation study. A network of afferent and efferent pathways are electronically activated by the use of a combination of pressure sensitive valves, electric solenoid gas valves and a stepper switch assembly. The lead enclosed system reduces the radiation to personnel and scintillation detector. A homogeneous atmosphere within the spirometer system is maintained through constant circulation provided by the use of two internal blowers. This is important for effective exchange of gases between patient and spirometer system.

Data can be accumulated during a single breath maneuver, steady state respiration, with automatic timing mechanisms, or in conjunction with a physiologic gating mechanism. When the spirometer system is used together with a real time dynamic sequencing module (described elsewhere), the examiner can monitor each phase of the pulmonary ventilation study. By means of this dynamic sequencing module, the entire field can be divided into 2 to 64 equal areas of interest. While the study is in progress, dynamic curves for each area are displayed on the sequencer CRT for qualitative analysis.

The advantages of such a system is the wide range of experimental conditions available and the ability to monitor the ventilation study while in progress. Other advantages of the unit include versatility, simplicity, reliability and economy of operation.

APPLICATION OF CONVERGING COLLIMATORS WITH A LARGE FIELD OF VIEW SCINTILLATION CAMERA. R. A. Moyer, P.H. Murphy, J.A. Burdine. Searle Radiographics, Des Plaines, Ill., Baylor College of Med., St. Luke's Episcopal-Texas Children's Hosp., Houston, Tex.

The imaging characteristics of three converging collimators having a 25 cm field of view at 10 cm depth were evaluated using a prototype large field of view scintillation camera. Relative resolution and sensitivity in clinical and phantom images were compared to that obtained with a standard field of view camera and parallel hole collimation. The apparent benefits of convergence include improvement of both spatial resolution and sensitivity, but with an inherent sacrifice in field of view.

Each of these collimators demonstrated better depth response than similar parallel hole collimators. The usual decrease in resolution with depth is partially compensated by increasing magnification. In addition, sensitivity is enhanced with depth because the fraction of the detector viewing the object is increased, and this influence partially counteracts the attenuation of photons by overlying tissues. A combination of these effects are particularly useful in imaging deep seated lesions in the liver, kidney, or brain, as well as providing better definition in count density limited dynamic studies. The potential for image distortion is present for objects which lie in different planes because of varying magnification and changes in relative projection with depth. This has not created a problem in interpretation of more than 800 patient images.

The improvement in imaging with converging collimation and adequate field of view is clinically efficacious.

SENSITIVITY OF LIMULUS TEST AND INHIBITORY FACTORS IN RADIOPHARMACEUTICALS. Hajime Murata, Masayoshi Kobayashi, Masahiro Iio, Hideo Yamada, Kazuo Chiba, Kengo Matsui and Masahide Abe. Tokyo Metropolitan Geriatric Hospital, Tokyo, Japan.

For the purpose to examine the sensitivities and the inhibitory factors in radiopharmaceuticals (RPs), following procedures were employed. 1) Twenty commonly used RPs were examined by dry Limulus Lysate (Pregel-Teikoku-hormon, Japan). 2) In order to detect the inhibitory factors, several doses of endotoxin (E.Coli) were added to RPs before Limulus test and the results were compared with control study using endotoxin in saline.

3) When the pH of reaction solution lay out of a suitable range (6.0-7.5), pH was adjusted by Tris-HCl buffer. As the results, 1) The sensitivity of control Limulus test using Pregel was positive at the concentration of 10^{-3} µg/ml of endotoxin. 2) Limulus test could be applied with its sensitivity and without inhibitory reactions on Tc-99m-O₄, Tc-99m-Albumine, Tc-99m-MAA, Tc-99m-Sn-Colloid, I-131-Hippurate, I-131-Na, Cr-51-Na₂, Ga-67-Citrate and Co-57-Bleomycin as they were supplied. 3) In-111-DTPA, Tc-99m-Phytate, Tc-99m-Pyrophosphate, Tc-99m-DTPA, I-131-PVP, Fe-59-Cl₂, P-32, Au-198-Colloid and Se-75-Selenomethionine needed to be adjusted their pH to avoid inhibition. 4) Bently alcohol in the RP showed the inhibition at the concentration more than 1%. Commonly used Yb-169-DTPA was found to be evaluated by this test with the sensitivity of 2.5×10^{-3} µg/ml due to addition of little Bently alcohol. 5) I-131-BSP showed intense inhibition probably due to protein denaturation by BSP. 6) Contaminations of endotoxin were recognized in almost all of RPs which contain the gelatin or albumine as stabilizer.

HIGH EFFICIENCY LUNG IMAGING. P.H. Murphy, L.A. Monroe, J.A. Burdine. Baylor College of Med., St. Luke's Episcopal-Texas Children's Hosp., Houston, Tex.

The purpose of this investigation was to determine the influence of increased photon utilization on ventilation and perfusion imaging of the lungs.

One hundred-forty patients with a variety of clinical indications were studied using a prototype wide field-of-view scintillation camera and low energy parallel hole collimation. Ventilation was monitored during both inhalation and washout of Xe. The patent air space in the lung was determined following rebreathing of Xe gas. The distribution of perfusion was imaged following IV injection of Xe in saline as well as labeled microparticles.

A marked improvement in Xe images was observed in comparison with those obtained using diverging collimation and a standard field of view camera. This was due to enhanced statistical content (X3 increase in sensitivity) and the superior imaging characteristics of parallel hole collimation. The quality of microparticle perfusion images was also noticeably better. The clinically important matching of ventilation and perfusion on a segmental and subsegmental basis could be accomplished routinely for the first time, thereby facilitating the evaluation of respiratory function particularly in patients with suspected thromboembolism and COPD.

The results of this investigation place new emphasis on the ventilatory portion of lung imaging since the definition approached that of perfusion images. A better overall evaluation of the intrinsic components of pulmonary function is therefore possible.

RESULTS WITH Tc-99m GLUCONATE AS A POSITIVE INDICATOR IN THE DIAGNOSIS OF BRAIN AND LUNG CANCERS IN CHILDREN. G. Carlo Mussa, Istituto Di Puericultura, Torino, Italy.

The employment of Tc-99m gluconate in the diagnosis of brain, lung and bone neoplasias in adults has been investigated by D'Onofrio et al. The advantages of this complex include rapid preparation at room temperature, stability, perfect tolerance, and rapid metabolization. Its labelling, half-life, and body distribution have been studied in the mouse. Renal clearance is high and rapid, with good reduction of circulating activity.

It is excellent as a diagnostic aid for brain and lung tumours. Tc-99m gluconate has shown high positivity in osteosarcoma, rhabdomyosarcoma, and follicular carcinoma of the thyroid. It has proved negative in some cases of lymph node metastasis that were identifiable with gallium, and in benign tumours. Certain examples of simple inflammation, on the other hand, such as subdural haematoma and tuberculosis, have been detected using Tc-99m gluconate. Comparison of this substance with Ga-67 citrate and Co-57 bleomycin shows it has better statistics, while the fact that the examination is brief is important when general condition and age are primary considerations.

The present note deals with the use of Tc-99m gluconate in the diagnosis of brain and lung cancers in children. 5 mCi were given intravenously in 30 mg calcium gluconate. Scans were taken after 90 min and 6 hr. Definition of brain lesions was good, especially in the posterior fossa, and there was little interference from choroid plexus activity. In lung tumours, the results were satisfactory and similar to those obtained with gallium. There were some instances of false positives in patients with non-neoplastic inflammation.

CONTRIBUTION OF THE BLOOD RADIOACTIVITY TO THE POSITIVE BRAIN SCAN. Claude Nahmas, Edmund S. Garnett. McMaster University Medical Centre, Hamilton, Ont.

The purpose of this study was to determine how often radioisotope confined to the blood compartment made a major contribution to the positive brain scan. Every patient studied had an abnormal Technetium-99m Sodium pertechnetate scan and in every case histological proof of the lesion which caused the abnormal brain scan was obtained. A red cell brain scan was done by reinjecting 16 ml of the patient's own blood labelled with 10 mCi of Technetium-99m. A routine brain scan was done after intravenous injection of 10 mCi of Technetium-99m Sodium pertechnetate. The same protocol was followed for both procedures. All the meningiomas were demonstrated by the red cell brain scan, whereas only half of the remaining lesions could be detected. Furthermore, there seemed to be no relation between the results of the red cell scans and the presence or absence of increased vascularity assessed histologically or by angiography. Therefore radioactivity confined to the blood pool makes a relatively small contribution to a positive pertechnetate brain scan. This documents the widely held belief that leakage of pertechnetate from the vascular bed makes the major contribution to a positive brain scan.

A MODULAR APPROACH TO UNIFY NUCLEAR MEDICINE DATA ACQUISITION. Robert J. Nickles, James E. Holden, Aaro J. Kiuru, and Robert E. Polcyn. Dept. of Radiol., UW Medical School, Madison, Wis.

Commercial nuclear medical instruments tend to perform a single clinical task. We have chosen to employ a NIM modular approach to efficiently utilize a limited inventory of research grade electronics chosen for high count rate capability (300 kHz probes needed in cardiac studies), energy and time resolution in β^+ coincidence configurations. Signal outputs of all clinical systems have been made compatible with front-end requirements of our PDP 11/40 computer, equipped with a pair of ADC's and a dedicated CAMAC dataway. Likewise, test pulse inputs have been installed into all clinical detectors. Aside from routine quality control and dead-time correction, these serve as inputs for parallel physiological data desired during fast dynamic imaging. In particular, an ECG signal is used to frequency-modulate a pulser injected into an outer preamp in the gamma camera head. A dot results outside of the circular data field, and flagging this region of interest retrieves the ECG monitored throughout the cardiac study.

The modular perspective emphasizes instrument function, with some surprising spinoffs. Our uncollimated gamma camera admirably reads two-dimensional chromatograms of such pure beta-emitters as ^{14}C and ^{32}P .

The effective computer servicing of all nuclear medical instruments demands standardization of signals and electronic quality. The versatility implicit in the modular approach increasingly outweighs the stand-alone "counter".

INTERCOMPARISON OF MYOCARDIAL IMAGING AGENTS. H. Nishiyama, V.J. Sodd, R.J. Adolph, J.T. Lewis and E.L. Saenger. Nuclear Medicine Laboratory, BRH and Cincinnati General Hospital, Cincinnati, O.

Cesium-129, K-43, Tl-201 and Rb-81 were evaluated as static myocardial imaging agents. Criteria for evaluation are image quality, image initiation time, and absorbed radiation dose under comparable clinical settings. The prerequisite was to utilize the most commonly available instruments, i.e. gamma camera, without modification. Optimal settings of the instrument were

evaluated based on physical characteristics of each agent. Image quality obtained from normal and infarcted dogs was rated by a multiple blind reading; both Cs-129 and Tl-201 were rated the best, followed by K-43 and Rb-81. Time postdose for image initiation was 5 min for K-43, 10-15 min for Tl-201 and 30 min for Cs-129. Imaging time was comparable between Cs-129, Tl-201 using 80 keV x-ray and K-43. The larger number of higher energy photons from Rb-81 preparation made it impossible to obtain an interpretable image without gamma camera modification. Time postdose to imaging for Rb-81 was between that of K-43 and Tl-201 based on blood disappearance studies and imaging time was shorter than the others. Under the comparable activity employed the least absorbed radiation dose to the whole body was calculated to be from Rb-81, followed by K-43, Cs-129 and Tl-201. Interference from adjacent organs is highest in K-43, followed by Cs-129 and Tl-201, and uptake ratio between myocardium and liver favored Tl-201 over Cs-129 and K-43. Taking all of these into account, we concluded that the best static myocardial imaging agent was Tl-201 followed by Cs-129, K-43 and Rb-81.

COMPUTER-ASSISTED Tc-99m - Xe-133 SCINTIGRAPHIC DIAGNOSIS OF PULMONARY EMBOLISM USING CROSSOVER SUBTRACTION. Nicholas G. Nolan. Mayo Clinic, Rochester, Minn.

The presence of essentially normal ventilation in an area of perfusion defect is considered as being a characteristic feature of acute pulmonary embolism. Hence, knowledge of the distribution of both ventilation and perfusion permits distinction of pulmonary embolism from other causes of blood flow defect. Because of the differences in energy of the radionuclides employed (81 KeV for Xe-133 and 140 KeV for Tc-99m), it has been necessary to perform the Xenon study as the initial phase of the investigation in order to avoid degradation of the Xe images by crossover from Tc. The crossover amounts to approximately 43% of the counts recorded in the Tc window. This abstract describes a simple computer crossover subtraction technique which permits the Tc-99m microsphere perfusion scans to be performed prior to a complete Xe-133 ventilation-perfusion study. Since the purpose of the Xe study is specifically to examine the ratio of ventilation to perfusion (V:Q) in non-perfused areas of lung, it follows that the gamma camera should be positioned as closely as possible to the perfusion defect for this phase of the study. This is especially important in view of the limited tissue penetrating ability of the 81 KeV photon. Thus, the Tc perfusion scans should be done prior to the Xe study.

In this study, Tc-99m microsphere scanning is performed initially. If a perfusion defect is seen, then the gamma camera is positioned so as to optimally observe the defect. The pulse-height analyzer is reset to the Xe-133 window, and an image of the Tc crossover distribution is fed into the computer. An Xe-133 ventilation-perfusion study is performed using a modification of Loken's technique. The crossover is subtracted from each frame of the Xe study, and images of the distribution of perfusion, ventilation, and V:Q ratio, and of Xe washout are generated.

CONTINUOUS BREATH ANALYSIS OF $^{14}\text{C}_2-^{12}\text{C}_2$ FROM ^{14}C -FORMALDEHYDE AND PROPIONATE FOR DETECTION OF VITAMIN B12 DEFICIENCY. Thomas Ntundulu, Ngo Tran, and Etienne LeBel. Dept. of Nuclear Medicine and Radiobiology, Centre Hospitalier Universitaire, Sherbrooke, Quebec, Canada.

An ionization chamber-infrared analyzer system was used for continuous measurement of $^{14}\text{C}_2-^{12}\text{C}_2$ in the breath of vitamin B12-deficient and control rats, after intravenous injection of 2.8 uCi ^{14}C -formaldehyde or 1.0 uCi propionate- ^{14}C , within 120 min. Repeat studies were carried out in vitamin B12-deficient rats treated with cyanocobalamin for 60 days (5ug/rat/2-3 days). Results and conclusions show that: 1) About 6.67 ± 0.34 (n=4) and 11.29 ± 0.26 (n=4) % $^{14}\text{C}/\text{mmole } ^{12}\text{C}_2/\text{kg weight}$ were noted in control rats after injection of ^{14}C -formaldehyde and ^{14}C -propionate, respectively; 2) A decreased $^{14}\text{C}_2-^{12}\text{C}_2$ was obtained in vitamin B12-deficient rats after administration of ^{14}C -formaldehyde ($p < .01$) and ^{14}C -propionate ($p < .01$), which was, however, returned to the normal levels ($p > .05$) after treatment of vitamin B12. This indicates that meta-

bolic behavior of formaldehyde might depend on vitamin B12, and that in vivo radiometric method with ^{14}C -formaldehyde could be useful as a sensitive means for detection of vitamin B12 deficiency in man. The method is confirmed by parallel study with propionate oxidation in this vitamin deficiency, which was known previously (J.Lab.Clin.Med. 72: 67, 1968); 3) Surprisingly, an increase in expiratory $^{12}\text{C}_2\text{O}_2$ rates was also noted in vitamin B12-deficient rats ($p < .02$) which was again returned to normal levels after treatment with vitamin B12 ($p > .05$); 4) Our overall results show that not only in vivo oxidation of ^{14}C -formaldehyde to $^{14}\text{C}_2\text{O}_2$, but also expiratory $^{12}\text{C}_2\text{O}_2$, O_2 consumption, and respiratory quotient, may all be useful for both diagnostic and therapeutic follow-up tests of vitamin B12 deficiency in man.

A KIT PREPARATION OF RADIOIODINATED AUTOLOGOUS FIBRINOGEN. Daniel J. O'Connell, Marcia E. Stein, Donald E. Tow, James H. Frisbie, Arthur A. Sasahara and John S. Belko. West Roxbury V.A. Hospital and Harvard Medical School, Boston, Mass.

A kit has been developed for the rapid isolation, purification and radioiodination of autologous fibrinogen. The procedure including blood drawing can be completed in 45-60 minutes.

A tube of blood is centrifuged for five minutes at 1500G with any centrifuge. Plasma is then delivered through a millipore filter directly into a measured volume of ammonium sulphate solution. The filtration assures complete removal of the formed elements of the blood which interfere with iodination. The concentration of ammonium sulphate and the dilution of the plasma protein have been optimized for the yield and purity of fibrinogen. The precipitate, centrifuged at 300G dissolves readily in 0.6 ml phosphate buffer. 50 μl are then removed for a protein determination. A 0.5 ml aliquot is transferred to a tube containing radioactive iodine. Chloramine T is used as the oxidizing agent in a concentration to minimize polymer formation. Preweighed Chloramine T is diluted to the appropriate concentration and added to the reaction tube. After 6 minutes an ammonium sulphate solution is added and the tube centrifuged. This second precipitation further purifies the fibrinogen as well as removes most of the unreacted radioactive iodine. In the final step the dissolved precipitate is passed through a Dowex-ion exchange resin and a millipore filter in tandem directly into the injection syringe.

The final product contains 92-96% clottable radioactivity 1-2% free iodine. The product is stable-clottable radioactivity decreasing by 1% or less in 44 hours at pH 7.4 and room temperature. In vivo distribution and survival studies revealed characteristics similar to longer methods of preparation. The method is simple and reliable. Sterility throughout the procedure is easily maintained.

TWO HOUR OLD MYOCARDIAL INFARCTION IN DOGS IMAGED WITH ERBIUM-165, A LOW ENERGY RADIONUCLIDE. Henry A. Oldewurtel, Dandamudi V. Rao, Christos B. Moschos, Bunyad Haider and Timothy J. Regan. New Jersey Medical School, Newark, N.J.

Erbium-165 Citrate has a greater affinity for infarction tissue than normal myocardium. The nuclear reactor prepared radionuclide was converted to the citrate and administered intravenously to 9 dogs with myocardial infarction following a coronary artery thrombus induced by catheterization of the Left Anterior Descendens with an electrode catheter. Precordial images in the intact dog were recorded with an Anger Camera and high resolution collimator at 2, 8 and 24 hours after administration of the nuclide. The animals were then sacrificed and the heart removed to image the isolated intact heart, and then the left ventricle was cut open and laid flat for imaging.

Precordial scintigrams at 8 and 24 hours demonstrated an unequivocal area of enhanced radioactivity in the region of the heart very similar to that seen on images of the isolated heart taken with comparable geometry. The image of the flattened left ventricle shows the area of increased activity to be identical to the expected infarct. The extent of this infarct has been previously established in this laboratory for this animal model. The 2 hour images were not unequivocally positive when compared to two control studies.

Ratios of tissue counts for infarcted to normal myocardium were 2.5 to 1 at 2 hours, 12.5 to 1 at 8 hours, and 108 to 1 at 24 hours after administration of Er-165.

The studies indicate that early demonstration of myocardial infarction with this agent is very promising.

Erbium-165 has a half life of 10 hours and an absorbed dose less than Tc-99m. The energy peak at 50 KEV makes it ideal for imaging with pressurized multiwire proportional gamma cameras. Other salts or compounds of Er-165 are being explored to find a form with greater relative selectivity for infarcted myocardium.

CHANGES IN THE DISTRIBUTION OF SHORT-LIVED RADIONUCLIDES IN THE KIDNEY: STUDIES BY AUTORADIOGRAPHY. Robert E. O'Mara, Stephen J. Capps, and Jack N. Hall. Arizona Medical Center, Tucson, Az.

Since the introduction of short-lived agents such as Tc-99m DTPA and Tc-99m Fe complexes for renal scanning, a wide variety of compounds have been introduced for this purpose, including Tc-99m glucoheptonate and Tc-99m dimercaptosuccinic acid. A precise knowledge of renal distribution would be valuable both for timing serial images and calculation of absorbed radiation dose to intrarenal structures. One millimeter thick sections of rabbit kidney were obtained at various time intervals after the intravenous administration of a variety of compounds. Contact autoradiographs were then performed on these sections as well as individual well counting of cortical and medullary components. These labeled agents demonstrated rapid clearing of most of the injected radioactivity through the kidney with a significant fraction being retained in the cortex. Amounts retained were in descending order: Tc-99m DMSA, Tc-99m GH, Tc-99m iron ascorbic acid, Tc-99m DTPA. Calculation of the retained percentage in cortex was highest for the DMSA (approximately 50%). The Tc-99m DMSA demonstrated the most rapid complete clearance indicating that adequate scans for cortical lesions may be obtained as early as 20 minutes post-injection.

Prior blockade of the outer cortex by non-radioactive microsphere injection demonstrates similar distribution of all of these compounds in the inner cortex and medullary portions of the kidney. Percentage uptake within the kidney was calculated by exteriorization of the kidney and serial counting of the organ followed injection. The highest obtained uptakes were similar to those demonstrated with autoradiography.

Based on these findings, it is concluded that Tc-99m DMSA is the agent of choice at the present time for renal cortical imaging.

INDIUM-111 BLEOMYCIN AS A TUMOR SCANNING AGENT IN PEDIATRIC ONCOLOGY. Robert E. O'Mara, Kai Haber, James Corrigan, Helen Johnson, and David L. Lilien. Arizona Medical Center Tucson, Arizona.

Increasingly broad experience with In-111 Bleomycin (Bleo) has demonstrated it to be a tumor scanning agent with greatest usefulness in soft tissue primary and metastatic neoplasms. This study was undertaken to determine its efficacy in the pediatric age group. Over the past 18 months, 51 total body scans were carried out in 27 patients. The most commonly encountered neoplasms were neuroblastoma, lymphoma, rhabdomyosarcoma and Wilms' tumor. A site by site analysis was performed basing positive correlations on autopsy, surgical biopsy findings, clinical evaluation and demonstration of neoplasia by other imaging techniques. The true positives were 83%, false-negative sites were 7% and false-positive sites were 10%. It is of particular interest that Bleo was localized in many sites not suspected clinically, which were subsequently shown to have malignant involvement. Several of the cases demonstrated positive accumulation in malignant sites with the Bleo scan that were not seen on Gallium scanning, a condition also found in the adult population.

Calculation of radiation dose estimates were 0.28 rad for total body and 0.92 rad for the liver. The radiation dosage levels are within acceptable limits in patients with pediatric neoplasms.

The main advantages of Bleo scanning in the pediatric population are the lack of significant bowel activity, important with so many neoplasms in children involving the abdomen; accumulation in more types of tumor than Ga-67 citrate; accuracy in assessing efficacy of therapy. The disadvantages of Bleo scanning at the present time are the relatively high cost; less accumulation than other tumor scanning agents making findings subtle at times; non-specificity for tumor. Despite these problems, In-111 Bleo appears to be a quite acceptable agent for pediatric oncological study.

BONE SCANNING IN LYMPHOMA. Robert E. O'Mara, J. P. Schecter, Stephen E. Jones, and James M. Woolfenden. Arizona Medical Center, Tucson, Az.

Over a two year period, 36 bone scans in 24 patients were performed utilizing Tc-99m labeled phosphates. All patients had malignant lymphoma, 9 with Hodgkin's disease, 4 with nodular lymphoma, and 11 with diffuse lymphoma. Scan findings were correlated with clinical laboratory and radiographic findings. Twenty-six (74%) of the scans were abnormal. Bone scans were performed in 10 patients undergoing staging prior to therapy; 4 scans were abnormal altering the final determination of staging in 2 patients. Nineteen abnormal scans were on patients with advanced stage IV disease; 8 were observed in patients with concurrent normal bone radiographs. Poor correlation was obtained with serum calcium levels. Seven patients with abnormal scans had normal serum calcium levels whereas two patients with hypercalcemia (both with diffuse histiocytic lymphoma) revealed normal scan findings. Eighty percent of the patients with positive bone scans presented with some type of bone pain complaint. Four of 5 patients with elevated alkaline phosphatase determinations also had abnormal bone scans.

Serial bone scanning correlated well with response to treatment. In 3 of the cases a change in either planned or ongoing therapy was dictated by bone scanning. In others response in bony involvement to therapy became evident on the scan before any radiographic changes were noted.

In summary, bone involvement by lymphoma as detected by bone scanning correlates well with the histiological type of lymphoma, stage of disease, and presence of bone pain. Bone radiographs and serum calcium levels were less helpful. A clinical rationale for more selective use of bone scans will be presented. Bone scanning is a useful procedure for both the initial evaluation and subsequent follow-up of patients with lymphoma. (This work has been supported in part by American Cancer Society Grant CI-10A).

EVALUATION OF LIVER-SPLENIC PERFUSION STUDIES IN HYPERSPLENIC STATES. Robert E. O'Mara, Marlys Witte, Charles L. Witte, James Corrigan, James M. Woolfenden, and Theron W. O'vitt. Arizona Medical Center, Tucson, Az.

Liver-spleen perfusion has been shown to be markedly altered in a variety of hypersplenic states including pyruvate kinase deficiency, congenital spherocytosis, ITP, histiocytosis, and a variety of liver diseases. Recently, our surgical group has attempted intervention of splenic blood flow by ligation or blockade of the splenic artery rather than splenectomy in an attempt to improve the pathological condition.

In hypersplenic states, there is a marked increase in splenic perfusion and size, as well as a marked increase in Tc-99m-sulfur colloid localization. The use of a perfusion study of these organs accomplished by a bolus injection of the labeled colloid for liver and spleen scanning has allowed pre and post-operative assessment of increased perfusion and any changes produced by the surgical intervention. In all cases undergoing either splenic artery ligation or splenic artery blockade, there has been: 1) reduction in the size of the organ with areas of decreased to absent activity present, 2) marked diminution in perfusion to the spleen in relation to liver perfusion. This simple and safe study allows for immediate post-op evaluation of the effect of the intervention. This is important because clinical response frequently lags by at least two weeks. Return of splenic perfusion via collateral circulation has been seen in unsuccessful cases while continued reduction in splenic perfusion and organ size has correlated with the clinical response in successful cases.

This simple technique offers safe and accurate assessment of both pre-operative and post-operative changes in these clinical conditions.

A STUDY OF PARAMETERS AFFECTING TRANSAXIAL RECONSTRUCTION BY ITERATIVE TECHNIQUES. Bernard E. Oppenheim. The University of Chicago, Chicago, Ill.

The important techniques for transaxial reconstruction (computerized axial tomography) may be broadly classified as either Fourier or iterative techniques. While the latter are slower than the former they are more flexible, and can be readily adapted to handle special problems that arise in nuclear medicine (e.g., compensation for attenuation and

varying line spread function). Iterative techniques, however, do not lend themselves well to theoretical analysis.

In this study the effects of the following parameters on the accuracy of iterative reconstruction in nuclear medicine were investigated: the number of iterations, the number of projections, the order of projections, the number of counts, and the distribution of radioactivity (focal vs. diffuse). "Hot spot" and "cold spot" phantoms simulating the range of activity distributions encountered in nuclear medicine were generated with the computer. Accurate projections of these phantoms were made at 6,9,12,18 and 24 equally spaced angles per 180°. These projections were modified to study the complete range of counting statistics. Reconstructions were carried out using multiplicative and additive forms of the Algebraic Reconstruction Technique (ART) of Gordon et al. as modified by Herman et al. (*J Theor Biol* 42: 1-32, 1973).

It was found that when projections were applied in pseudorandom rather than in serial order, reconstructions could be accomplished with fewer iterations, two iterations being adequate in most instances. Accuracy improved with increasing counts, but statistical artifacts were troublesome when total counts were fewer than 300,000 in projections of the "hot spot" phantom, and fewer than 3 million in projections of the "cold spot" phantom. Accuracy improved as the number of projections were increased to 18, but there was little further improvement with 24 projections, and even slight deterioration when total counts were limited.

ION EXCHANGE DETERMINATION OF THE CHARGE ON THE Tc SPECIES PRODUCED BY THE Sn⁺² REDUCTION OF TcO₄⁻, Azu Ogunwanna, Jacob A. Marinsky and Monte Blau. Roswell Park Memorial Institute and State University of New York, Buffalo, N.Y.

Reduction of TcO₄⁻ by Sn⁺² produces a reactive intermediate (TcIV) which is used in the preparation of many radiopharmaceuticals. The charge on this species has been determined by ion exchange techniques. To determine the charge on an unknown tracer species, its equilibrium distribution between the resin and the solution is measured as a function of the concentration of an electrolyte of known charge. The slope of the displacement curve gives the charge on the tracer species.

Sn⁺² as perchlorate was chosen as the known electrolyte to insure complete reduction of the TcO₄⁻. Tracer amounts of reduced Tc-99m were added to suspensions of Dowex-50 (stannous form) in various concentrations (1-10mM) of Sn(ClO₄)₂ and equilibrated for 24 hours. The slope of the Tc-99m replacement curve indicated a charge of +2. The most likely Tc(IV) species carrying this charge is TcO⁺².

To confirm the validity of this technique similar experiments were carried out on known tracer species, Na-22 and Zr-95, with the Sn(ClO₄)₂-Dowex-50 system. The charge on Na⁺ was confirmed as +1 and the Zr data showed a charge of +2 corresponding to the well established species Zr(OH)₂⁺².

When the experiments are carried out at pH above 1.5 both Tc and Zr show evidence of hydrolysis and the ion exchange data no longer follow the displacement curve of a +2 ion.

DETECTION OF ACUTE REJECTION IN KIDNEY TRANSPLANTS USING RADIO-IODINATED AUTOLOGOUS FIBRINOGEN (R.A.F.) J. Quinlan, M. Loberg, R. Ollodart, M. Cooper University of Maryland Hospital, Baltimore, Md. 21201

A clinical study was performed to determine the value of RAF in the detection of acute rejection and distinction of acute and chronic rejection from other causes of renal failure following transplantation. Fourteen patients were studied sequentially for as long as 61 days post-operatively. Each patient was injected with 100 uCi I-131 RAF / 70 kg b.w. Activity over the heart and graft was measured using a portable detector and expressed as a kidney to heart ratio (KHR). I-131 RAF was reinjected when the count rate over either organ fell to less than ten times background.

Post-operative progress and graft function were monitored by clinical and laboratory studies including a one hour post-transplant biopsy. Subsequent biopsies were performed on the basis of the diagnostic need. Normal KHR was established from 91 observations made when the patients were clinically stable.

Individual patients exhibited an average relative S.D. of $\pm 5.3\%$ about their own means.

8 / 14 patients had acute rejection episodes 4-10 days follow-operation. Two proceeded to infarction and failed to respond to therapy. Intercurrent complications included acute tubular necrosis, hematoma and infection. All patients in whom rejection occurred showed an increase in KHR with an initial increment which exceeded 20% of the normal mean value. The KHR also increased in the presence of hematoma or infection, but was not associated with renal failure. KHR did not increase when renal failure was due to causes other than acute rejection.

RAF - KHR is an effective means of detecting acute graft rejection and for differentiating renal failure in the post-transplant period.

LEAD-203 TRIS AS A MELANOMA LOCALIZING AGENT. Samuel Packer, Richard M. Lambrecht, Alfred P. Wolf and Harold L. Atking. Chemistry and Medical Departments, Brookhaven National Laboratory, Upton, N.Y. and North Shore University Hospital, Manhasset, N.Y.

Lead-203 ($T_{1/2} = 52.1$ hr, $\gamma = 279$ keV, 95%) was evaluated in the Syrian golden hamster as a radionuclide, in the chemical form of lead-203-Tris, for ocular and skin melanoma localization and scintigraphy. The Greene melanoma was injected into the skin and eye of the hamster and studies were performed with 2 to 3 week old tumors. Tissue distributions were obtained as a function of time (1 - 144 hrs) in several organs. Ocular imaging was possible at 24 hours. The uptake in the eye and skin melanoma at 24 hours was 0.5%/g and 0.9%/g, respectively. The tumor eye: normal eye ratio was 25:1. Detailed dissection of the eye at various times indicated the Lead-203 to be principally associated with the choroid and retina.

For comparison Co-57-bleomycin was studied at the same time intervals in the same tumor models. Imaging was possible at 6 hours, but the activity in the melanoma and ocular structures diminished with time. The maximum concentration in the skin melanoma was $1.34\%/g \pm 0.22$. At 6 hours the concentration in eye melanoma was $0.52\%/g \pm 0.14$.

Of the two agents, Lead-203-Tris consistently had a greater tumor (melanoma) affinity. The pharmacodynamic and tissue specificity results suggest that lead-203-Tris may have potential as a radiopharmaceutical for ocular melanoma scintigraphy.

A FOURIER CONVOLUTION FAN-GEOMETRY RECONSTRUCTION ALGORITHM. Sing C. Pang and Sebastian Genna. Boston Univ. Med. Ctr. and Boston V.A. Hospital, Boston, Mass.

The methods of three-dimensional reconstruction of internal tissue X-ray absorption coefficients or radionuclide emissions from their projected measurements derive from two general categories; Fourier techniques and iterative relaxation techniques. The Fourier convolution technique has a more clearly defined theoretical background and yields a faster and more stable computational solution than the iterative techniques. However, published Fourier-convolution algorithms limit its application to parallel-projection-geometries. A fan-beam-geometry algorithm, for example, will permit fuller use of an X-ray beam thus conserving data collection time. In addition, the fan beam can accommodate an extended range of torso sizes.

This paper presents an algorithm for the Fourier convolution solution of a fan-projection-geometry and a comparison, through computer simulation, with a parallel-projection-algorithm. The algorithm for the fan geometry is very similar to that for a parallel geometry. The program provides for any fan angle and any number of m equal subdivisions of that angle. Data generation is similar to that for a parallel beam except that, since the beam paths diverge, full rotation is required. The data is similarly stored in $m \times n$ matrix where n equals the number of rotation angles. The deconvolution is similar except that the image is formed through angular projection. Through simulation, data is generated from a phantom consisting of two concentric circles of any size and density which contain any number of smaller circles of any radii, position and density. Results with a low contrast and a high contrast phantom show that the reconstruction fidelity of the two methods are equal.

THE USE OF DIGITAL TECHNIQUES IN γ -RAY IMAGING USING A ZONE-PLATE APERTURE. Roy Parker, Brian Wilson and David Dance, Royal Marsden Hospital, Sutton, Surrey, United Kingdom.

Coded aperture imaging provides possible gains in sensitivity, resolution and tomography. Stationary apertures are normally Fresnel zone plates which, together with optical decoding methods, afford good spatial resolution but require time-consuming photographic procedures.

The problems of optical reconstruction largely disappear if a numerical reconstruction method is used. This can be linear, reproducible and quantitative. For zone plate apertures we have developed a correlation method which can give a 50% gain in signal-to-noise for a single point source over the maximum obtainable with optical decoding.

Using a line source as the object, computer simulations have been used to examine the effects of noise, solid angle variations, shape of detector, detector resolution and tomographic capability. Satisfactory reconstructions have been obtained of a line source and a thyroid phantom using an Anger camera as detector.

For a 12 cm uniform object the signal-to-noise obtained with the zone plate is comparable to that for a high resolution parallel hole collimator 10 cm from the source. In this case the zone plate aperture provides a gain in sensitivity of approximately 1000.

ANALYSIS OF Tc-99m STANNOUS PYROPHOSPHATE (PYP) MYOCARDIAL SCINTIGRAMS IN 242 PATIENTS. R.W. Parkey, F.J. Bonte, E.M. Stokely, S.L. Meyer, and J.T. Willerson. The University of Texas Health Science Center at Dallas, Texas

Tc-99m PYP was utilized for myocardial imaging in 242 patients admitted to the hospital with chest pain of uncertain etiology. Of the 113 patients with clinical, ECG, and enzymatic evidence of acute myocardial infarction, 108 patients had positive myocardial scintigrams. The remaining 5 patients had negative scintigrams, but all were obtained 7 or more days after myocardial infarction. Of the 129 patients with no clinical, ECG, or enzymatic evidence of acute infarction, 117 had negative myocardial scintigrams. The remaining 12 patients had faintly positive scintigrams. Nine of these patients were admitted with "unstable angina pectoris".

If time (post infarct and post injection) were held constant, visualization was a volume (of damaged myocardium)-related phenomenon. Large transmural infarcts were very positive and smaller subendocardial infarcts were less positive. The most common cause of false negative scintigrams was imaging either before 12-18 hours or after 6-7 days post infarction. False positive images might be encountered with chest wall lesions involving breast, rib, or damaged muscle, but by using three projections, most chest wall lesions can be separated from the myocardium. A radioactive blood pool in the heart caused from either slow clearance of the Tc-99m PYP or free Tc-99m could give a false positive image. The gamma camera has to be well tuned for each exam because a non-uniformity field can give rise to a false positive image. Myocardial imaging with Tc-99m PYP is a simple, safe, accurate, and rapid method of detecting and locating acute myocardial infarction. Detection of an extension and possibly sizing of the infarction are additional benefits.

LOCALIZATION OF POSTERIOR FOSSA BRAIN SCANS. Dennis D. Patton. Vanderbilt University Hospital, Nashville, TN.

Forty-nine patients were reviewed who had posterior fossa brain scans and subsequent surgical or autopsy proof of a posterior fossa (PF) lesion. The scan was positive in 40/49 or 82%. 46/49 posterior fossa lesions were tumors, though the mode of followup (surgery, autopsy) biases the study towards tumor. Scans detected 12/14 gliomas, 5/5 ependymomas, 5/7 medulloblastomas, 5/6 metastases, 6/6

acoustic neuromas, 3/3 meningiomas, 2/5 other tumors, and 2/3 benign lesions. Scan technique for PF views requires full flexion of the head and both posterior oblique views.

The scans were analyzed using a new model for anatomic assignment of PF lesions that includes relationship to base, transverse sinus, and midline, and patient's age, modified after DeLand, et al. (Nuclear-Medizin 9:303,1970). Lesions are localized to cerebellum, cerebellopontine angle, brain stem, or vermis/4th ventricle. The tumor type can often be predicted by the anatomic location.

The "most likely" localization was correct in 35/47 or 74%, the "next most likely" in an additional 10/47 or 21%. Only 4% were incorrectly localized by the model. Anatomic prediction was correct in 26/34 or 76% of lesions localized to the cerebellum (P_0 , or prior probability of this location, is 60%); in 1/1 localized to the CPA (P_0 15%); in 2/2 localized to the brain stem (P_0 9%); and in 6/10 localized to the vermis/4th ventricle (P_0 17%). Localization is sufficiently accurate that the scan may be the only imaging procedure needed to plan the surgical approach.

THE DIAGNOSIS OF THYROID NODULES BY QUANTITATIVE FLUORESCENT SCANNING. J.A. Patton, J. Hollifield, D. Patton, and A.B. Brill. Vanderbilt University Medical Center, Nashville, Tennessee.

A new indicator has been developed which appears to be superior to any other noninvasive diagnostic test in predicting whether a thyroid nodule is benign or malignant. This technique involves quantitative fluorescent scanning of thyroidal iodine pools which has been used clinically in nuclear medicine at Vanderbilt for the past three years. With this procedure the thyroid is irradiated point-by-point with an external source of radiation (Am-241) and the resultant x-rays of iodine emitted from the gland are counted by a high resolution Si(Li) detector. Thus one obtains an intensity map corresponding to the stable iodine distribution in the thyroid. The scanning system is interfaced to a computer and iodine content can be quantitatively determined in the total gland or in selected regions. This technique has provided a new parameter for predicting the histology of thyroid nodules that are "cold" to radioisotope studies. In this method, the ratio of iodine content in the nodule to that in a corresponding area of the contralateral lobe is used as an indicator of the probability of malignancy.

To date, of 42 patients who have gone to surgery, 15 had malignant nodules and all 15 had nodule/normal ratios below 0.60 (\bar{x} = 0.41, σ = 0.13). Ten patients had benign cystic nodules and 9 of the 10 had ratios above 0.60 (\bar{x} = 0.91, σ = 0.36). Seventeen patients had benign solid nodules and 14 of the 17 had ratios above 0.60 (\bar{x} = 0.78, σ = 0.29). Thus an iodine content ratio of less than 0.60 is a good indicator of malignancy with a sensitivity of 100%, a specificity of 79%, and an overall accuracy of 90%. (This work is supported in part by NIH Grant #AM17484-01.)

IMPROVED DIAGNOSIS OF POST RENAL TRANSPLANT COLLECTING SYSTEM ABNORMALITIES BY RADIONUCLIDE STUDIES. Dan G. Pavel, Olga M. Jonasson, Olaf Andersen, Virginia N. Patterson and Barry D. Kahan. University of Illinois Hospital and Northwestern Memorial Hospital, Chicago, Ill.

In the past two years we have tried to establish optimal detection techniques and diagnostic patterns of evolution for collecting system abnormalities post transplant. I-131 Hippuran and Tc-99m were used. A common finding is pelvic hangup of radioactivity that subsequently decreases or disappears on follow-up studies. On the other hand, progressive increase of the pelvic hangup is a matter of serious concern, since these patients are potential candidates for urinary leaks. Localized ureteral distensions, developing in parallel with pelvic hangup have the same significance.

Urinary leaks may be massive and easily detectable but often more subtle signs must be looked for: false "improvement" of a dilated ureteral image, an oddly shaped ureter, changes of the kidney shape or hot areas distant from the bladder. Delayed views are important, as well as imaging of remote areas like flanks or scrotum.

Complete obstruction is often suspected, usually not confirmed, but very difficult sometimes to

differentiate from rejection. The key to the differential diagnosis is delayed views at 1 or 2 hours post-injection. If at that time radioactivity appears in the bladder but the ureter and pelvis are not visualized, obstruction can be ruled out.

Blood clots in the bladder, due to post biopsy hematuria can be best demonstrated by Tc-DTPA imaging which shows the effect as well as cause.

EFFECT OF CEREBRAL COMPRESSION ON THE CEREBRAL BLOOD POOL. D. Pearson, P. V. Harper, F. Brown, B. Mock, P. Krizek, L. Johns, and M. Rich. University of Chicago, Chicago, Ill.

Cerebral blood dynamics as measured by transit time give indeterminate results unless the volume of the cerebral blood pool is monitored simultaneously. In the present study, a technique has been developed for measuring the cerebral blood pool by coincidence imaging, with ^{11}CO used as a blood pool label. Compression of the brain was carried out in rhesus monkeys with an epidural plastic balloon. Blood pool imaging measurements were done before and after compression, using a collimated Anger camera coincidence imaging system with digital matrix and tape storage. A simultaneous comparison was made between the monkey's head and a C-11 standard of similar shape and thickness positioned nearby in the camera field of view. Corrections were made for chance coincidences and differences in attenuation in the animal and standard. Comparison of the standard with a peripheral venous blood sample permitted determination of blood equivalent content of the standard and, by comparison, the amount of blood in any region of interest in the animal's head. Scalp and muscle blood pools were eliminated by stripping of these tissues from the calvarium. Excretion of ^{11}CO during the period of observation was shown to be negligible. Compression of the brain to the point of production of spontaneous pressure waves, with a mean increase in intracranial pressure of 20 mm Hg, decreased the blood pool in the head by 13%. Further compression to the point of cerebral vasoparesis and apnea decreased the pool by 25%. Combining such results with transit time measurements should permit the determination of flow under circumstances which do not too violently alter the anatomy of the circulation. This method permits direct measurement of the intracranial blood pool and its contribution to states of altered intracranial pressure. (Supported in part by USPHS 7376-07 RES, USPHS Grant GM-18940, and AT(11-1)-f9.)

PREPARATION AND TESTING OF TECHNETIUM-99m LABELLED STREPTOKINASE FOR SCINTIGRAPHIC IMAGING OF THROMBI. Bertil R.R. Persson, and Viktor Kempf. Depts. of Rad. Phys., University of Lund, and Centrallasarettet, Östersund, Sweden.

The method for labelling streptokinase with Tc-99m has been studied in great detail in order to obtain a radioactive indicator for rapid scintigraphic visualization of thrombi and emboli.

Streptokinase (KABI AB, Stockholm, Sweden) 50,000 IU was dissolved in saline and Tc-99m eluate was added together with SnCl_2 -solution in varying concentrations and pH-values. The labelling efficiency was studied with the method of gel-chromatography-column-scanning (GCS). The clot-lyzing effect was studied by adding the labelled streptokinase to thrombin coagulated venous blood with known titer of anti-streptokinase.

The efficiency of labelling streptokinase with Tc-99m was found to be highly dependent on both the SnCl_2 -concentration and the pH-value of the reaction-mixture. A pH-value larger than 3 results in a very low labelling-efficiency and a SnCl_2 -concentration higher than 0.5 mM increases the risk of colloid formation and denaturation of the protein. The amount of streptokinase to be labelled each time should correspond to 50,000 - 100,000 IU in order to get a high labelling-yield. The clot-lyzing effect of streptokinase decreases rapidly at about pH 1, but at pH 2 the enzymatic activity of the labelled streptokinase is almost unchanged. Tc-99m labelled streptokinase at a final pH-value of about 2.0 has been used in clinical studies of deep venous thrombosis in man.

A COMPUTERIZED TRANSAXIAL TOMOGRAPH FOR NUCLEAR MEDICINE IMAGING. Michael E. Phelps, Michel M. Ter-Pogossian, Edward J. Hoffman, Nizar A. Mullani and Carol S. Coble. Washington University, St. Louis, Missouri

A transaxial tomograph was designed, constructed and evaluated for imaging cross-sectional distributions of positron-labeled radiopharmaceuticals in human subjects. This system is referred to as a positron emission transaxial tomograph (PETT III). PETT III consists of 48 5 x 7.5 cm NaI(Tl) detectors placed in a hexagonal array (8 detectors to a side) around the cross section of interest. The detector collimation consists of "electronic" collimation established by the coincidence detection of annihilation radiation. Each detector on opposing banks of the hexagon is connected in coincidence to yield 192 coincident detector pairs for the total system. Data are taken during a linear motion of detector banks (5 cm) and at angular increments of 3° over a total rotation of the gantry of 60°. The data are collected, sorted, reconstructed in a convolution-based algorithm and displayed by an on-line mini-computer. The spatial resolution (cross-sectional and slice thickness) is variable from 0.5 to 2 cm. Images with 300,000 counts per 1 cm thick slice are obtained in 2 to 3 minutes with an intravenous injection of about 10 to 15 mCi of activity. This system yields quantitative (+5%) tomographic images with high contrast (hot and cold spot), high resolution, and high statistical quality with the removal of superimposition of information. The positron radionuclides presently employed are Ga-68 (from commercial generator system, Ge-68), F-18, C-11, N-13 and O-15 labeled to a variety of compounds. PETT III is used for studies of the human head and torso, and should prove to be an important advancement in nuclear medicine imaging.

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COMPARISON OF THREE COMMERCIAL KITS FOR DETERMINATION OF SERUM TRIIODOTHYRONINE (T3) BY RADIOASSAY. Robert O. Pick, Douglas Daniels, Jerome A. Waliszewski, and Martin L. Nusynowitz. William Beaumont Army Medical Center, El Paso, TX.

A comparative study was made on three commercially available T3 radioassay kits in order to determine the precision and accuracy of each. One kit (M) uses magnesium 8-anilino-1-naphthalene sulfonate (ANS) for extraction of T3 from serum and a resin strip for separation of unbound from bound T3; the second kit (P) employs a direct double antibody technique; the third kit (N) utilizes alcoholic extraction of serum and a resin column for separation of unbound T3. Determinations were performed in duplicate on serums of 23 normal males by the same technician on each of two different days. An hierarchical randomized complete block analysis of variance design was used to determine precision within and between runs for each assay technique. All three kits showed that individual variation was significantly greater than variation between duplicate determinations ($p < .001$), but kits M and N demonstrated significant variation between runs on different days as compared to the individual results ($p < .01$). The kit (P) with no significant day to day variation had the greatest variation between duplicate determinations as compared to the other methods, and as a result had the largest normal range. Kits M and P were more accurate than kit N as determined by addition of known amounts of T3 to a serum pool. Indeed, the accuracy of kit P was nearly ideal in terms of reflecting added quantities of T3. The normal range for kit P in this study was 38-193 ng/100 ml (95% confidence limits). Thus, precision and accuracy factors and other considerations such as cost, ease of automation, and assay time, lead to the conclusion that kit P (double antibody technique) is best for routine use in the nuclear medicine laboratory.

RELATION BETWEEN BLOOD FLOW AND UPTAKE OF POSITIVE INFARCT IMAGING AGENTS. N.D. Poe, G.D. Robinson, Jr. and J.H. Tillisch. Center for Health Sciences and Laboratory of Nuclear Medicine, UCLA. Los Angeles, Ca.

The relationship between uptake of myocardial specific radiopharmaceuticals and regional perfusion has not been established. The problem was investigated in dogs with ischemia produced by coronary artery ligation. K-43 was the flow indicator and Tc-99m tetracycline (Tc-T) or pyrophosphate (Tc-P) were the positive indicators. Animals were

followed 4 hours to 1 month. Prior to sacrifice, K-43 and a Tc-99m agent were given IV. Multiple myocardial sections were counted to determine relative concentrations.

At 4 hours the Tc-T showed a flat curve but Tc-P rose linearly as flow decreased by 70%, then dropped to normal. By 24 hours the Tc-T curve mimicked the 4 hour Tc-P curve but was increased in areas with perfusion reduced by only 30%. The 24 hour Tc-P values peaked at 50% flow reduction. Only Tc-T was followed a week or more and showed progressively lower uptakes in ischemic regions.

Combined K-43/Tc-P imaging was carried out in 16 patients with suspected infarction. Although a general correlation between ischemia and positive uptake resulted, high Tc-P levels were often found with good K-43 concentrations.

Conclusions; 1) Some perfusion is necessary for positive uptake. 2) Positive uptake does not necessarily indicate irreversible cell injury. 3) Positive uptake can occur with only moderate diminution of flow. 4) A combined study should be useful for infarct staging.

COBALT LABELED BLEOMYCIN - A COMPARATIVE CLINICAL EVALUATION WITH Ga-67 CITRATE IN 50 PATIENTS WITH CANCER. K.P. Poulouse, A.E. Watkins, R.C. Reba, W.C. Eckelman, and M. Goodyear. Washington Hospital Center and George Washington University, Washington, D.C.

Bleomycin has undergone extensive investigation as a cancer chemotherapeutic agent. Previous studies in our laboratory demonstrated significant accumulation of labeled bleomycin in transplanted experimental tumors in mice. Because of the concern regarding use of Co-57 (relatively long physical life), attempts have been made to produce a satisfactory bond with Tc, In, Zn, Cu and Pb, but in vivo and/or in vitro stability has not been achieved. This report is an evaluation of the sensitivity of Co-57 labeled bleomycin as a tumor scanning agent in 50 patients with different types of malignant tumors. The sensitivity of labeled bleomycin was also compared to Ga-67 citrate.

Seven hundred & fifty uCi of Co-57 bleomycin were injected IV and whole body scans were obtained using a rectilinear scanner 24 hr. post injection. Subsequently, 3 mCi of Ga-67 citrate were injected and scans were obtained 48-72 hours later.

Because of the rapid blood clearance of Co-57 bleomycin and excretion through the kidneys radiation dose is relatively low and interpretation of scans performed with Co-57 bleomycin is facilitated.

In terms of sensitivity, labeled bleomycin was found to be a superior agent. Maximum sensitivity for labeled bleomycin was found in epidermoid carcinoma (95%). In adenocarcinoma, the sensitivity was 78%; with Ga-67 citrate, the respective values were only 60% and 50%. In this series Co-57 bleomycin is significantly more sensitive for epidermoid carcinoma and in a wide variety of tumors than is Ga-67 citrate ($P < 0.05$). However, no statistical difference for the small number (14) of adenocarcinomas was found. (Supported by USPHS Grant GM 20543)

MEASUREMENT OF NOISE, RESOLUTION CHANGE WITH SEQUENTIAL SMOOTHING OF GAMMA CAMERA IMAGES. David F. Preston, William C. Servoss, Timothy D. Kennedy, William A. Herrin, Joseph A. Gallagher, Audrey V. Wegst, and Richard C. Riley. Kansas University Medical Center, Kansas City, Ks.

This investigation was undertaken to evaluate simple methods to measure "noise", its effect on perception of artificial cold lesions in flood images and changes in noise and perception with sequential 9 point unweighted smoothing.

Flood images with 5 discrete cold lesions 1 inch (7 cells) in diameter, averaging 10% to 25% less activity than the surrounding flood, were acquired from a gamma camera on line to a PDP-15 computer with color TV output. "Noise" was defined as the square of the difference between observed and predicted counts in a cell. A predicted value was the average of the surrounding 3 by 3 group of cells. 2 by 2 chi-squares were performed on the entire 64 by 64 array and the values summated for each image. Floods with lesions of unknown number, size, position and depth were evaluated by 5 observers. Changing accuracy was compared with changing "noise" levels and summated chi square. (P-0) squared/total counts in image was calculated. Five sequential smooths caused a decrease in depth of lesions from 90% to 95% of surrounding activity.

	(P-0) Squared	Summated 2x2 chi-square	Noise/ Total	Minimum Lesions Correctly Detected
Raw Image	2,098,647	98.23	3.886	1 of 5
1 Smooth	213,556	186.75	0.395	2 of 5
2 Smooth	60759	191.50	0.112	3 of 5
3 Smooth	33824	172.13	0.063	4 of 5
5 Smooth	18344	143.34	0.034	4 of 5

Simple smoothing enhanced detectability of cold lesions in this study and decreased noise. The highest summated chi square values may be associated with the optimal level of smoothing. Greater than 3 or 4 smooths does not enhance perception of cold lesions on color TV display.

COMPARISON OF BONE AND BONE MARROW SCINTIGRAPHY IN THE EVALUATION OF MALIGNANT DISEASE. David C. Price and Robert S. Hattner. University of California School of Medicine, San Francisco, Calif.

Bone scintigraphy is a well proven method to assess skeletal involvement by malignancy. Radiocolloid imaging of the bone marrow can be performed as an extension of the liver scan, and may be useful in detecting marrow displacement by intramedullary tumor. We have studied 60 patients with various malignancies by combined bone marrow and bone imaging, using Tc-99m sulfur colloid in the former study, and Tc-99m pyrophosphate (35 patients), F-18 (21 patients) or Sr-85 (4 patients) in the latter. The bone marrow was evaluated with extensive axial and appendicular skeletal scintiphotos, and bone scans were performed with a dual-head whole body scanner. The average time between studies was 6.6 days, the maximum 36 days. In 34 patients (56.7%) there was exact correspondence between the two studies, 31 being normal and 3 demonstrating identical areas of involvement with both techniques. In 9 patients the bone scan was abnormal with a normal marrow study, and in 4 the bone scan demonstrated more areas of involvement than the marrow study, giving 13 studies (21.7%) with increased yield from the bone scan. On the other hand, 3 patients (5%) demonstrated bone marrow abnormalities with a normal bone scan, and 5 (8.3%) were found to have more extensive involvement on the marrow study than on the bone scan. In 5 patients there were multiple lesions with both techniques, some coinciding and some not. Where the bone scan was more effective, the pathology was usually in the skull, the ribs or the extremities. Prior radiotherapy presented problems in the interpretation of both studies. The addition of bone marrow scintigraphy in the evaluation of malignant disease significantly increases useful information over that provided by bone scanning alone.

ANALYTICAL TECHNIQUES FOR IMAGE SUPERPOSITION. R. Price, S. Hillis, G. Friesinger, and A.B. Brill. Vanderbilt University Medical Center, Nashville, Tennessee.

We have investigated analytical techniques for superimposing images of the same organ made at different times. The images may be either from the same or different instruments with different magnifications and rotations.

Exact superposition is essential for assessing disease progression from sequential images. One can also correct for size distortions in Anger camera images resulting from different isotopes with gamma rays of different energies as well as superimpose different images for anatomical definition.

Knowing the coordinates of a number of corresponding points in the two images, one can define a coordinate transformation and use it to carry out a coordinate mapping of an image from one image reference frame to the other. Corresponding points are obtained by imaging known fiducial markers in each imaging procedure. The complexity of the mapping is dependent upon the number of markers. The mappings may be chosen to carry out translations, magnifications, rotations, and arbitrary distortions.

One of the coordinate mappings we have used is:

$$x' = a_1 + a_2 x + a_3 y + a_4 xy$$

$$y' = b_1 + b_2 x + b_3 y + b_4 xy, \text{ where}$$

(x,y) are the coordinates of the original image and (x',y') are the transformed coordinates.

To investigate the accuracy of externally measured radioxenon clearance rates for identifying the anatomical position of myocardial infarcts, we have superimposed contrast arteriograms with xenon washout parameter images. The arteriograms were digitized by means of a video disc/PDP-9 computer coupling.

These algorithms have proven useful in superimposing scintillation camera images and for overlays of coronary arteriograms and their corresponding xenon washout images.

A SYSTEMS ANALYSIS OF THE MIDWEST SCIENTIFIC INSTRUMENT, INC. COMPUTER FOR THE RADIORECEPTOR ASSAY LABORATORY. John R. Prince, Walter G. Dukstein and William E. White. Research Hospital and Medical Center, Kansas City, Mo.64132

The purpose of this study is to report on our evaluation of the hardware reliability and software quality of a specific computer system as well as the clinical advantages of on line data acquisition and computation versus graphical analysis of radioreceptor assay data. The system uses a Wang 600-14 programmable calculator as the central processing unit and is on line to a Searle Analytic 1185 well counter and an Iso-Cap 300 liquid scintillation counter. Peripherals include a 2048 step read only memory and a two cartridge disk each with a capacity of 131,072 steps. The down time during the first year of operation has been 3% based on data from the maintenance log. Time motion studies have shown that on-line data computation saves 1.25 minutes per patient assay when compared to graphical analysis. In a comparison of 100 digoxin assays we found the following relationship between the computer generated value and the graphical data: (Computer value) = -0.01 + 0.86 (Graph value), r = 0.956 with a standard error of 0.32. This suggests that prior to the computer we were over diagnosing digitalis toxicity. We conclude that this computer system is reliable, the software is adequate and the computer has increased our diagnostic accuracy.

CONJUGATION OF ANTIBODIES WITH COMPOUNDS CAPABLE OF RAPIDLY BINDING INDIUM 111. J. H. Pritchard, M. J. Ackerman, M. Tubis, and W. H. Bland. VA Wadsworth Hospital Center and UCLA, Los Angeles, Calif.

During the past few years, nonradioactive methods have been developed to conjugate antibodies with various compounds in order to facilitate localization of antigen-antibody reactions at the cellular and intracellular level. By using similar methods, compounds having free amino groups and capable of chelating heavy metal atoms can be conjugated to antibodies. Radionuclides such as In-111 can then be bound to the antibody-chelator conjugate without destroying its ability to participate in immune reactions.

We have successfully conjugated transferrin, D-penicillamine, and desferoxamine to antibodies by using glutaraldehyde as the coupling compound. Glutaraldehyde has two reactive sites which couple free amino groups on both the chelator and antibody molecules. To each ml of physiologic buffered saline (PBS), 10 mg of IgG, 0.025 ml of a 0.5% glutaraldehyde solution, and either 0.2 mg transferrin, 0.05 mg desferoxamine, or 0.05 mg D-penicillamine is added and mixed thoroughly. The mixture is allowed to stand at room temperature for 2 hr. The resulting conjugate is dialyzed overnight against PBS at 4°C to remove unreacted glutaraldehyde, then centrifuged at 3000 rpm at 4°C for 30 min to remove any precipitate. The conjugate is stable for several weeks when stored at 4°C. In-111-Cl (commercially available in .05 N HCl) can be added to the conjugate whenever desired. Complete binding of the In-111 by the chelate portion of the conjugate is essentially instantaneous.

Immuno diffusion reactions on Ouchterlony plates of In-111-human IgG-chelator conjugates against goat antihuman gamma globulin antisera results in strong precipitant bands. Similarly, goat antihuman gamma globulin-chelator conjugates produced strong precipitant bands against human gamma globulin. Autoradiographs demonstrate the radioactivity to be concentrated along the precipitant bands.

COMPARATIVE STUDY OF POTASSIUM-43 AND TECHNETIUM-99M PYROPHOSPHATE DISTRIBUTION IN MYOCARDIAL INFARCTION AND THEIR CORRELATION TO CREATINE PHOSPHOKINASE (CPK) DEPLETION. Savita Puri, Gerald S. Freedman, Richard K. Donabedian, Steven Wolfson, and Barry L. Zaret. Yale University School of Medicine, New Haven, CT.

The myocardial concentration of Potassium-43 (K-43), a cold spot myocardial imaging agent, and Tc-99m Pyrophosphate (Tc-99m PYP), a hot spot imaging agent, was studied in myocardial biopsies obtained 24 hours following closed chest canine infarction (MI). These values were compared with tissue CPK levels.

In five dogs with myocardial infarction receiving both tracers, for K-43 the ratio of radioactivity in infarct samples (n = 47 samples) as compared to normal averaged 0.39 ± 0.03 (mean \pm SEM) with a range of 0.07 to 0.88 and for Tc-99m PyP averaged 23.3 ± 3 (range 3 to 68). The values from infarct samples for both K-43 and Tc-99m PyP were of great significance ($p < 0.001$) when compared to ratios in 4 control dogs (n = 60 samples) where K-43 averaged 1.01 ± 0.02 and Tc-99m PyP averaged 1.01 ± 0.04 . However, the correlation between the gradation in magnitude of each radionuclide concentration within the MI was poor. (n = -0.33).

The decrease in K-43 concentration correlated well with the extent of CPK depletion ($r = 0.77$, $p < 0.01$); while no correlation was found between Tc-99m PyP and CPK depletion.

Though tissue concentration of both K-43 and Tc-99m PyP are markedly abnormal in the infarcted myocardium, only gradation in K-43 concentration appears to have a quantitative relation to tissue viability as assessed by CPK depletion while other factors in addition to viability might govern Tc-99m PyP uptake by the MI.

TUMOR LOCALIZATION; ADRIAMYCIN COMPLEXES OF GALLIUM AND MERCURY VERSUS Ga(III) and Hg(II).
G.V.S. Rayudu, R. Kanoor, P.C. Ramachandran, A. Ali, D.A. Turner and E.W. Fordham.
 Rush University Medical Center, Chicago, Ill.

A comparative tumor localization study of Ga-67-adriamycin(A), Hg-197-adriamycin, Ga-67-chloride, Hg-197-acetate was made making use of: 1. Biological distribution in S-180 bearing mice, 2. whole body clearance in normal mice, 3. whole blood clearance in normal rabbits. The complexes were prepared by incubating carrier free Ga-67-chloride Hg-197-acetate with 2-3mg. of adriamycin at 6-7pH. The Ga-67-chloride, Hg-197-acetate solutions were obtained commercially in purest form and pH adjusted to about six. Some of the tumor to nontarget ratios at 24 hours post administration were presented below:

	Ga-67 adriamycin chloride		Hg-197 adriamycin acetate	
Tumor/muscle	11.3	12.3	8.6	10.6
Tumor/blood	3.5	3.5	3.5	4.4
Tumor/liver	0.5	0.7	0.5	0.5

The whole body and whole blood clearances were listed below:

	$E_{ff}T_{\frac{1}{2}}$ whole body (mice)		$E_{ff}T_{\frac{1}{2}}$ whole blood (rabbits)	
Ga-67-A	$3 \pm 0.3d$		$15 \pm 1.5hr$	
Ga-67-chloride	$3 \pm 0.3d$		$15 \pm 1.5hr$	
Hg-197-A	$34 \pm 0.3hr$	$1.7hr(90\%)$, $17hr(10\%)$		
Hg-197-acetate	$32 \pm 0.3hr$	$1.3hr(90\%)$, $13hr(10\%)$		

The results suggest that the Ga-67-chloride, Hg-197-acetate are comparable to adriamycin complexes in tumor localization.

BIOLOGICAL DISTRIBUTION OF RADIOLABELED FIBRINOGEN, PLASMINOGEN, SERUM ALBUMIN AND TRANSFERRIN IN TUMOR BEARING MICE. G.V.S. Rayudu, R. Kanoor, P.C. Ramachandran, A. Ali, D.A. Turner, and E.W. Fordham. Rush University Medical Center, Chicago, Ill.

A systematic study of serum proteins localization in tumors was undertaken. Accordingly biological distributions of iodine-125 labeled fibrinogen(F), plasminogen(P), technetium-99m labeled serum albumin(S) and transferrin(T) were studied in S-180 bearing mice to study the relative affinity of these proteins to this specific tumor.

Labeled F and P were obtained by radioiodination and the technetium labeled S and T were prepared by stannous ion reduction and complexation method. Some of the tumor to nontarget ratios measured in mice at 24 hours post IV are:

	I-125-F	I-125-P	Tc-99m-S	Tc-99m-T
Tumor/muscle	9.1	1.0	12.1	6.9
Tumor/blood	1.0	1.2	1.4	1.3
Tumor/liver	3.2	2.6	1.0	0.2

Some of the concentrations in various organs reported as percent/gm of tissue at 24 hour post IV are:

	I-125-F	I-125-P	Tc-99m-S	Tc-99m-T
Tumor	1.8	2.4	1.6	1.7
Blood	1.6	2.0	1.1	1.3
Muscle	0.2	2.4	0.1	0.3

Fibrinogen exhibited superior tumor localization capability, while plasminogen was inferior than F, S and T due to poor clearance from soft tissue.

DIRECT RECORDING OF RECTILINEAR SCAN IMAGES ON 4 x 5 INCH FILM. Isaac C. Reese and Fred S. Mishkin. Martin L. King, Jr. General Hospital, Los Angeles, Calif.

The reduction of the cost of medical care is a goal which should be pursued with vigor. The cost to produce and store radionuclide scans in nuclear medicine can be reduced by the use of smaller films for recording the images from rectilinear scanners. Presently scan images are normally recorded on 14 x 17 inch x-ray film. The use of 4 x 5 inch film to replace this larger film would result in saving both in the cost of film and in the cost of storage space for the completed studies.

An Ohio-Nuclear Model 84FD dual five-inch scanner was converted for the production of 4 x 5 inch images by the use of Tektronix Model 602 display oscilloscope and C-58 oscilloscope cameras. The X and Y positioning signals were taken from the positioning potentiometer of the scanner by paralleling the input of the 602 scopes with that of the storage scope of the scanner. The power supply from the scanner was disconnected from these potentiometers and replaced by two (2) 1.5 volt rechargeable "D" cells. This resulted in a stable positioning signal which could not be obtained using the scanner's power supply. The Z signals to the 602 scopes were obtained by connecting them in parallel with the Z inputs of the storage scopes.

The 4 x 5 scan images obtained in this way may be viewed directly using a standard X-ray view box, or they may be projected if a larger image is desired. The image quality is excellent and may be used to replace the standard 14 x 17 inch films.

DECLINING NORMAL RANGE FOR THYROIDAL ¹³¹I UPTAKES IN CANADA. Lionel Reese, and Robert MacKenzie. St. Joseph's Hospital and the University of Western Ontario, London, Canada.

A sharp decline in thyroidal uptake of ¹³¹I has been documented in the U.S. and other countries over the past 10 years. Considerable regional variations within the U.S. and marked difference between the U.S. and the U.K. have been documented but the Canadian experience has not been previously published.

A series of 100 euthyroid patients studied in 1964 and 1965 were compared with a similar series of 165 euthyroid patients in 1973 and 1974 using the same technique. A group of 10 normal subjects drawn from the hospital staff were also studied in 1974. Capsules supplied by Frosst were used throughout all studies.

The original series was found to have a mean uptake of 24.2% with a S.D. of 8.0 giving a range of $24.2 \pm 16.0\% = 8.2-40.2\%$ (mean \pm 2 S.D.) In 1974 the group of normals showed a mean uptake of 15.25 with a S.D. of 3.54. The euthyroid patients in 1973 and 1974 had a mean uptake of 16.4% with a S.D. of 6.0%.

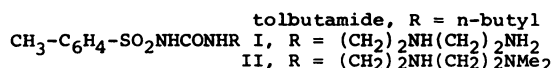
This study confirms the clinical impression that thyroidal uptakes have fallen here as elsewhere. Unlike the situation in the U.S., bread does not appear to be a factor as iodine is not used here in the baking process.

GALLIUM-67 IN THE DETECTION OF METASTATIC BREAST CARCINOMA. Steven D. Richman, James N. Ingle, Stanley M. Levenson, Douglass C. Tormey, A. Eric Jones, and Gerald S. Johnston. National Institutes of Health, Bethesda, Maryland

Gallium-67 scintigraphy was evaluated prospectively as a diagnostic modality in the management of 84 patients with metastatic breast carcinoma. Scintigraphic results were compared with clinical, pathologic, roentgenographic, and organ-specific radionuclide studies. Focal tracer increases and asymmetries were seen in 85 (56%) of 151 scans. Skeletal metastases were detected in 34 (67%) of 52 cases. The confirmation of lung involvement was observed in 10 (38%) of 26 patients. Of 25 patients with secondary hepatic neoplasm, abnormal gallium localization was observed in only five (20%). Two confirmatory studies were obtained in 10 known cases of cerebral metastases. Technetium-99m bone, liver, and brain scans consistently provided information far superior to the gallium for diagnosis and follow-up. Gallium scanning proved to be of limited sensitivity and only of corroborative value. The most promising contribution of gallium was the unique ability to detect occult tumor in the mediastinum. Gallium revealed mediastinal lymph node metastases in the presence of unremarkable clinical and chest roentgenogram findings in eight patients (10%). Tomography performed in six of these cases demonstrated tumor in only one instance. Mediastinoscopy confirmed metastatic breast carcinoma in the four patients who underwent this procedure. Gallium uptake in the mediastinum was most rewarding in localizing accessible biopsy sites, thereby facilitating histologic and hormone-receptor studies. Since gallium proved the most effective non-invasive means for evaluating the mediastinum, the scan has been incorporated into the diagnostic work-up of patients with metastatic breast carcinoma.

PREPARATION OF Tc-99m SULFONYLUREAS AND THEIR DISTRIBUTION IN RATS. Victor R. Risch, H. Donald Burns, Takashi Honda, Marilynne Micalizzi, Luther W. Brady, and Ned D. Heindel. Hahnemann Medical College and Hospital, Philadelphia, Pa.

As part of studies on the development of radiopharmaceuticals for imaging pancreatic beta-cell tumors, new hypoglycemic sulfonylureas were prepared as structural models of tolbutamide, a known stimulator of islet cell secretion. These compounds incorporated basic side-chain moieties capable of chelating Tc-99m in a fashion similar to DTPA. The analogs were screened for retention



of hypoglycemic activity in rat glucose tolerance studies, and the two most active compounds (I and II) were labeled with Tc-99m. Both agents displayed similar tissue distributions. The highest uptake in all cases was in the kidney (6 to 8% dose/gram of tissue) with about 0.3% dose/gram appearing in the pancreas. Several attempts were made to enhance pancreatic uptake involving pre-dosing the animals with Imferon and CaEDTA complex as well as utilization of morphine. Pancreatic uptake was improved to 0.4-0.7% dose/gram and kidney uptake was somewhat diminished over untreated animals. The elevated kidney uptake probably reflects glomerular filtration of chelates rather than active uptake within the kidney tissue itself. (This work was supported by Grant CA 14043 from the National Cancer Institute.)

2-FLUOROETHANOL: HIGH SPECIFIC ACTIVITY, FLUORINE-18 LABELING IN A FLOW SYSTEM. G.D. Robinson, Jr. Laboratory of Nuclear Medicine and Department of Radiological Sciences, University of California, Los Angeles, Ca.

Fluorine-18 labeling of fluorocarboxylates from halocarboxylates by halogen replacement with F-18-fluoride exchange resin has been reported. Although the method gives good yields, use of flame sealed ampules and multiple transfers of labeled product make this approach undesirable for large quantities of F-18. We have modified the basic technique and devised a simple flow system for routine production of F-18-2-fluoroethanol (F-18-FEtOH).

The system consists of a 20 cm x 2 mm ID glass tube in which a 2 cm fluoride exchange column is formed. This as-

sembly is inserted into a small tube furnace. Aqueous F-18-fluoride is transferred, by exchange, to the resin, which is subsequently washed with CH₃OH and (C₂H₅)₂O and dried under N₂ flow. 2-Bromoethanol (BrEtOH) is injected with simultaneous heating of the tube assembly. Interaction between BrEtOH and hot F-18-resin gives a labeled mixture containing F-18-FEtOH. This reaction mixture is collected downstream and F-18-FEtOH is isolated by gas chromatography (GC). Using 50 µl of BrEtOH, 15-20% of the F-18 is recovered from the system with heating at 150°C. Of this activity, 60-70% is recovered as F-18-FEtOH after GC purification. Under these conditions, starting with 50 mCi of aqueous F-18-fluoride, 5-7 mCi of product are routinely obtained at a specific activity of 1.5-3.0 mCi/mg.

The yields (mCi) obtained by this method are comparable to those previously reported since only 40-50 min are required for synthesis and isolation. In the future, yields may be improved by use of an inorganic anion exchanger since thermal decomposition of the polystyrene based resin is a significant problem. Radiation exposure is dramatically reduced since close contact with the bulk of the F-18 is avoided.

4-IODOANTIPYRINE RAPID, DUAL BUFFER KIT METHOD FOR LABELING WITH IODINE-123. G.D. Robinson, Jr. and A.W. Lee. Laboratory of Nuclear Medicine and Department of Radiological Sciences, University of California, Los Angeles, Ca.

4-Iodoantipyrine is a freely diffusible substance which, due primarily to its lipophilic character, readily crosses the intact blood brain barrier. It is cleared, essentially completely, on a single pass through the cerebral circulation. As a result, I-123-4-iodoantipyrine has been proposed as an agent for direct imaging of the CNS.

4-Iodoantipyrine is rapidly and efficiently labeled with iodine-123 by exchange with I-123-iodide under acidic conditions. Use of 0.3 N H₃PO₄ for acidification provides buffering at pH=2. Subsequent addition, after labeling, of an appropriate quantity of NaOH gives buffering at pH 7. "Kits" for use in the clinical radiopharmacy consists of a "labeling vial," 0.3 N H₃PO₄, and 1 N NaOH. The 10 ml labeling vial contains: 4 mg of 4-iodoantipyrine and 4µg of carrier KI.

- 1) 3 ml of the desired quantity of carrier free I-123-iodide (pH=7) is added to the labeling vial.
- 2) The labeling mixture is acidified by addition of 1 ml of 0.3 N H₃PO₄.
- 3) The labeling vial is immersed in boiling water for 15 min and allowed to cool.
- 4) After cooling, the acidified labeling solution is neutralized and buffered (pH=7) by addition of 0.25 ml of 1 N NaOH.

Labeling yields, as determined by TLC, exceed 95% and although minimal free I-123-iodide is easily removed by anion exchange, the product is suitable for clinical use as prepared. All components are pre-sterilized and aseptic technique is used. Alternatively, terminal sterilization is by "millipore" filtration (0.22 µ).

DYNAMICS OF LIPOPHILIC RADIOPHARMACEUTICALS IN THE BRAIN. G.D. Robinson, Jr., J.M. Uszler, and L.R. Bennett. Nuclear Medicine Divisions, University of California and Harbor General Hospital, Los Angeles, California.

Many lipophilic molecules are known to penetrate the intact blood brain barrier (BBB). Such molecules may accumulate in brain tissue and, if labeled with suitable gamma-emitters, are potential agents for assessment of brain morphology and perfusion. I-123-4-iodoantipyrine (IAP) has been suggested for use in direct CNS imaging.

F-18-2-Fluoroethanol (FEtOH), C-11-ethanol (EtOH), I-131-2-iodoethanol (IEtOH) and Tc-99m-trifluoroacetate (TFA) are lipophilic agents. Their tissue distributions and, in particular, brain uptakes were measured and compared with that of I-131-IAP. Quantitative determinations were by direct tissue sampling in rats. Qualitative comparisons were made using a scintillation camera or collimated probe placed over the brain area of dogs or monkeys; and the uptakes and washouts of various test agent were monitored.

EtOH, IEtOH and TFA showed qualitative patterns of rapid brain tissue accumulation followed by slow washout. This pattern is similar to that observed for IAP. Quantitatively, maximum brain uptakes of 0.6 to 0.9% of the injected dose were obtained 20 sec post injection. FEtOH

shows similar rapid accumulation but, in contrast to the former agents, relatively little washout for up to 60 min post injection.

Partition coefficient data indicate that all of these compounds should penetrate the intact BBB. However, the usefulness of lipophilic agents for clinical assessment of regional brain perfusion is affected not only by partition coefficient, but also rates of tissue penetration, accumulation and subsequent washout. In light of these considerations, the most promising of these agents for direct assessment of regional brain perfusion, appears to be F-18-2-Fluoroethanol.

EFFECTS OF ANTACIDS ON GASTRIC EMPTYING. Ralph G. Robinson, Aryeh Hurwitz, Richard Skibba, William Herrin, and Charles Hartman. Kansas University Medical Center, Kansas City, Ks.

The rate of stomach emptying may be quantitated by the oral administration of non-absorbable radionuclides. Using this technique, we have studied the effect of commonly used antacid preparations on gastric emptying rate in patients with acid-peptic disease.

Ten patients with proven peptic ulcer were studied. Subjects were placed in a semi-recumbent position beneath a gamma camera interfaced to a computer, and then drank 100 uCi In-113m chloride in 100 ml water. Each patient was studied on four separate days in random fashion, receiving either water (control), or calcium carbonate, pure aluminum hydroxide gel, or aluminum hydroxide-magnesium carbonate mixture as the antacid in three hourly doses prior to the In-113m chloride. Continuous gastric pH measurements were obtained by telemetry from a swallowed Heidelberg capsule, and serum was drawn in the fasting state and during the measurement of gastric emptying for gastrin levels.

Mean control half-emptying time was 10.3 minutes. All ten patients had a 2.5 times or greater increase in their time to half-emptying (mean $T_{1/2}$ 50.1 minutes) following pre-medication with pure aluminum hydroxide gel ($p < 0.0125$). The increase in pH was greatest with calcium carbonate, but all three antacids maintained pH > 3.5 for similar time periods, due to differences in the rate of stomach emptying. Serum gastrin levels tended to rise during the study, but the changes were not significant.

Pure aluminum hydroxide gel significantly delays gastric emptying in patients with peptic ulcer. This study suggests that the effects of antacids on the rate of gastric emptying should be considered in addition to their in vitro neutralizing capacity in any inter-comparison of antacids available for treatment of acid-peptic disease.

ROUTINE USE OF I-125 FOR THYROID UPTAKE MEASUREMENTS.

R. N. Rocco and H. J. Dworkin. William Beaumont Hospital, Royal Oak, MI.

Our experience with I-125 in the measurement of thyroid uptakes in approximately 3,000 patients (utilizing a specially made neck phantom) has been very satisfactory and has not suffered from the weak photon emission of I-125 and high attenuation. Four hundred patients were chosen at random from our patient files, 301 of which had adequate supporting data to be classified into hypothyroid (12), euthyroid (227) and hyperthyroid (62) categories on the basis of examination and studies, other than thyroid uptake (TU). All hyperthyroid patients had TU $> 40\%$ (normal 24-hr TU is 10-40%). Seven euthyroid patients had TU $> 40\%$, but less than 50%. Overlap of TU between the euthyroid and hypothyroid patients was common and is observed with I-131 TU as well.

Forty-eight patients who were referred for I-125 TU volunteered for an additional 24-hr I-131 TU measurement. The standard for I-125 was counted utilizing the specially made neck phantom. The standard for I-131 was counted in an ORINS lucite phantom. Statistical analysis showed no significant difference between the two sets of TU values. The group mean for the I-125 TU was 30% and for the sequentially measured I-131 TU was 28% ($P > 0.05$). The correlation coefficient was 0.96.

Our study suggests that, in contrast to the theoretical analyses in the literature, I-125 can be used routinely for TU measurements with no unique or complicated corrections for photon absorption. The advantages of I-125 vs I-131 are: decreased rad dose, longer shelf life and convenience in shipping, ease of performing sequential stimulation, suppression or perchlorate discharge studies and lower

energy photon, requiring less collimation, hence, better scanning resolution. Though I-125 gives a higher rad dose than I-123, it is more readily available, more conveniently distributed and is less expensive.

AN ULTRASOUND-GUIDED GAMMA-RAY PROBE. W.L. Rogers and M.A. Wainstock. University of Michigan Medical Center, Ann Arbor, Michigan.

Coordination of diagnostic ultrasound information with that obtained using radioisotopes has proven useful in associating tracer uptake with specific anatomical features. This is normally accomplished by comparing independently acquired ultrasound and isotope images.

This paper describes an ultrasound-guided gamma-ray probe which permits uptake measurements to be obtained at the same time as the ultrasound image. The collimated gamma-ray probe is mechanically coupled to the ultrasound transducer, and the focal point of the collimator is accurately positioned over a region of interest on the ultrasound B-scan image by means of a range mark on the ultrasound beam.

The gamma-ray probe was specifically designed for measuring the uptake of I-125 chloroquine analog by ocular melanomas. In this measurement, the suspected tumor will be counted and the background measured from an adjacent region of normal choroid. Tests using phantoms show that accurate, repeatable, probe placement is readily achieved to within ± 1 mm, and clinical trials are underway.

We feel that this approach will facilitate earlier detection of smaller tumors and may find other applications in nuclear medicine.

ACOMPARISON OF THE IMAGING PROPERTIES OF Rb-81 AND K-43. F. David Rollo and Raleigh F. Johnson, Jr. VA and University of California Hospitals, San Francisco, California and University of Texas, Galveston, Texas.

Line spread function (LSF) and plane sensitivity measurements were made for a series of energy window settings and two collimator types for both Rb-81 and K-43 under scatter conditions using the Ohio Nuclear Dual Head 5 inch Scanner. The LSF data were used to compute corresponding Modulation Transfer Function (MTF) values which, when combined with the appropriate plane sensitivity data yielded Performance Index (PI) information for each condition studied. Since the PI includes both spatial resolution and sensitivity information and measures how well a given imaging system will reproduce a spherical void of activity in the image plane, the resulting data were used to determine the optimum energy window and collimator type for both radionuclides. In addition, the technique allowed a comparison to be made between these radionuclides as to their relative detectability of lesions of various sizes. Scans of a liver slice phantom were also obtained for each condition evaluated in the PI study. The results confirmed the findings of the PI study.

Rb-81 was found to have its best performance with the 38M collimator and an energy window of 400-600 keV while K-43 performed best with the 38 M collimator and an energy window of 320-430 keV. The overall performance of K-43 was significantly better than that of Rb-81 for every condition studied. This was especially true when both radionuclides were evaluated with their optimum energy window and collimator type.

CLINICAL SAFETY OF FIBRINOGEN I-125 (HUMAN) INJECTION FROM SCREENED INDIVIDUAL DONORS. S. Rosenthal, F. Ashkar, G. DeNardo, R. Holmes, A. Serafini, R. Manoli, S. DeNardo, and R. Caretta. Jackson Memorial Hospital and Mt. Sinai Medical Center, Miami, FL; Milwaukee County General Hospital, Milwaukee, Wisc; University of California School of Medicine, Davis, Ca.

The efficacy of Fibrinogen I-125 (Human) for detection of occult deep vein thrombosis in the lower extremities has been demonstrated by numerous studies. A multi-institutional study was undertaken to determine the safety and efficacy of Fibrinogen I-125 (Human) Injection prepared from single donor plasma.

Healthy donors were selected after clinical and biochemical evaluation; these donors are followed routinely to assure that they are in continued good health. Both the initial and followup evaluations include testing for Hepatitis B (Australia) antigen (HBAg) and antibody (HBAb) by radioimmunoassay methods. Hepatitis B negative plasma collections from these donors has been used by a manufacturer to prepare Fibrinogen I-125 (Human) Injection for investigational use in the United States.

Patients at high risk of developing deep vein thrombosis and patients with clinically suspected deep vein thrombosis were evaluated prior to entry into the study and monthly for 6 months after injection. This evaluation consisted of a history, physical examination, liver function studies, CBC, HBAg and HBAb. Patients with a history of hepatitis or evidence of liver disease were excluded from the study.

Of the 129 patients selected for this study, 40 have thus far completed their 6 month followup visits. The remainder of these patients are in various stages of followup. None of the 40 patients have developed clinical or laboratory evidence of hepatitis or any adverse reactions.

Fibrinogen I-125 (Human) Injection appears to be free of hepatitis transmission risk when derived from plasma of a screened donor.

DIPHOSPHONATE DYNAMIC IMAGING OF EXPERIMENTAL BONE GRAFTS AND SOFT TISSUE INJURY. Steven Roser and Ismael Mena. Division of Oral Surgery and Nuclear Medicine, UCLA-Harbor General Hospital Campus, Torrance, Ca.

Tc-99m diphosphonate bone scans were performed in order to evaluate viability of experimental bone grafts. Initially the uptake of diphosphonate in subjacent injured soft tissue was controlled both in normal and previously injured tissues. Identical 2.5 cm submandibular soft tissue pockets were created in 5 mongrel dogs over both bodies of the mandible. Care was taken not to injure its periosteum. Chronic soft tissue scars were present over one of the bodies of the mandible. Mandible bone scans were performed on submental and both lateral projections. A 2 cm lead shield was introduced between both bodies of the mandible. Bone scans were performed 3 hours post injection, preoperatively, on the 1st, 3rd and 8th postoperative days. A transient increased uptake was demonstrated unilaterally on the 1-3 days which diminished by the 8th day. Consistently, the scarred side demonstrated increased uptake as opposed to the normal side sham operated.

Three dogs received grafts in acute unilateral mandibular discontinuity defects and were scanned before, at one day, 2, 5, 8 and 12 weeks; and another 4 dogs at 10 and 13 months. Initially in the clinically viable grafts more uptake appeared in the adjacent host bone compared to the graft site. At 3 months, the activity in the adjacent bone had diminished and the activity in the graft area was intense. Increased uptake was still present in the graft site at one year. In one nonviable graft, there was only increased activity in the adjacent host bone, while the graft remained cold for 5 months. The increased uptake of the chronic traumatized soft tissue is thought to be on the basis of necrosis induced in the scar preferentially. Viability of the grafts can be predicted from the scan findings.

Tc-99m-GLUCOHEPTONATE FOR THE IDENTIFICATION OF ACUTE MYOCARDIAL INFARCTION. David J. Rossman, Jacques Rouleau, H. William Strauss, and Bertram Pitt. The Johns Hopkins Medical Institutions. Baltimore, Md.

This study reports our experience with Tc-99m-glucoheptonate for the detection, localization and sizing of acute myocardial infarction in humans. Twenty-seven patients admitted to the CCU with suspected or confirmed acute myocardial infarction received 15 mCi of Tc-99m-glucoheptonate intravenously 2-48 hours after the onset of chest pain. Scintillation camera images were obtained 1-5 hours after tracer injection. The presence or absence of acute myocardial infarction and extent of the infarct if present was determined by historical, physical, electrocardiographic and serum enzyme criteria. In patients with abnormal scans, the quantity of infarcted tissues was estimated by planimetry of the area of increased tracer uptake.

All eight acute transmural infarctions were correctly identified by the Tc-99m-glucoheptonate scans. Of 7 non-transmural infarctions, 4 were correctly identified by the scans and 3 were incorrectly read as being negative. None of the 7 patients without acute infarction had abnormal

scans. Of 5 patients in whom the occurrence of acute myocardial infarction could not be confirmed or ruled out by the usual clinical criteria, 3 had abnormal scans and 2 had negative scans. In the patients with acute myocardial infarction and abnormal Tc-99m-glucoheptonate scans, a linear correlation with $r=0.77$ was found between the area of abnormal uptake as determined by scan and the peak serum CPK value. Tc-99m-glucoheptonate is useful for the identification and localization of moderate to large size acute myocardial infarction. Small, non-transmural infarcts were not consistently identified. An estimate of infarct size may be obtained as early as 5 hours after infarction. This estimate can be made more quickly by Tc-99m-glucoheptonate scanning than by other radionuclide or non-radionuclide methods now in use.

COMBINED RADIONUCLIDE AND ULTRASONIC APPROACH TO DIAGNOSIS OF BILIARY PANCREATIC DISEASE. Philip P. Ruetz, Robert C. Heade, En-Lin Yeh, and Ron Balint. VA Center, Wood (Milwaukee), WI.

Six-hundred cases in which both radionuclide pancreas scanning and ultrasound scanning of the pancreas and biliary hepatic area are presented. Fifty-one out of fifty-two primary pancreatic malignant tumors were detected by the combined approach. Primary biliary tree malignancy, pancreatitis, pancreatic pseudocyst formation, abscesses and numerous other benign and malignant conditions were also diagnosed. The radionuclide pancreas scan, whether showing focal or diffuse abnormalities, is non-specific in nature. The addition of ultrasound has been found to be a valuable adjunct in differentiating between surgical versus medical jaundice. A 95% confidence range in delineating pancreatic biliary tree abnormalities by the combined approach can be expected.

SENSITIVITY OF THYROID SCINTIGRAM IN DETECTION OF NODULE. U. Yun Ryo, John E. Arnold, Steven M. Pinsky. Michael Reese Hospital and Medical Center, Chicago, Ill.

The thyroid scintigrams of patients who underwent surgical thyroidectomy were reviewed and correlated with the pathological findings to elucidate the sensitivity of the scintigram. Pathological reports with defined size and location of thyroid nodule(s) were available in 87 patients on whom thyroid scintigraphy was performed before surgery. Two histologically different nodules were present in 7 patients. The scintigram was obtained using a gamma camera with 5 mm single hole collimator after 5 mCi ^{99m}Tc -pertechnetate I.V. Among 150 nodules 32 were malignant with 29 papillary Ca from 16 patients and 3 follicular Ca from 2 patients. Of total 118 benign nodules from 70 patients, 79 were described as adenoma and 39 were described as colloid nodule. The smallest malignant nodule detected on the scintigram was 5 mm and largest nodule missed was 16 mm follicular Ca. No malignant nodule smaller than 4 mm was detected by the scintigram. A nodule in the isthmus was often missed on the scintigram. All 22 benign nodules of 5 mm or less were not delineated on the scintigram. Largest benign nodule undetected on the scintigram was a 18 x 10 mm isthmus nodule of adenoma. Overall detectability of nodule by the scintigram was 7% in 28 nodules of 5 mm or less, 56% in 56 nodules of 6-10 mm, 90% in 31 nodules of 11-15 mm, 90% in 19 nodules of 16-20 mm and 100% in 16 nodules of larger than 20 mm. Adenomatous nodules were more often missed on the scintigrams than malignant, or colloid nodules. A careful physical examination could detect a small nodule in some patients which was not delineated on the initial scintigram. Close-up and/or oblique view scintigram over the area of abnormal physical finding could improve sensitivity of thyroid scintigram significantly.

RADIONUCLIDE VENOGRAM-POSITIVE FINDINGS AND THEIR SIGNIFICANCE. U. Yun Ryo, Lelio G. Colombetti, Stanton G. Polin and Steven M. Pinsky. Michael Reese Hospital and Medical Center, Chicago, Ill.

To elucidate the mechanism of radionuclide venogram findings, in vivo and in vitro venograms were obtained in dogs. Both femoral veins were surgically exposed in anesthetized dogs and thrombin soaked silk was sutured on venous wall to induce thrombus formation. Twenty-four hours later, 2 mCi of ^{99m}Tc -labeled macroaggregates (MAA)

or microspheres (MS) were injected into each leg via a superficial foot vein with a tourniquet in place. After a series of venograms, dogs were euthenized and both femoral veins were isolated. The labeled protein particles were also injected through the foot vein of patients before a varicotomy procedure. Scintigrams were obtained from isolated veins. Thrombi and areas of crush-injured venous wall were dissected from and observed under a microscope.

Areas of gross thrombus formation were delineated as areas of decreased radioactivity on the respective venograms in all 7 dogs studied. Areas of increased radioactivity on venograms corresponded well to venous stasis. Scintigram obtained from isolated, blood drained veins showed radioactivity remained in the veins was minimum and the distribution to be entirely different to the respective in vivo venograms. Scintigrams of isolated veins did not delineate thrombi or injured vein or valve area. Microscopic examinations failed to demonstrate MAA or MS adhered on a surface of abnormal or normal intravascular structure.

Contrary to many recent reports, results from this study suggest that delayed clearance of radioactivity on a venogram represent a stasis due to incompetent venous flow or a turbulent flow at the area of a thrombus or a venous valve. No significant difference was noted between venograms obtained using labeled MAA or MS.

EVALUATION OF ^{99m}Tc -RBC, IT'S LABELING PROCEDURE AND IN VIVO STABILITY. U. Yun Ryo, Ali Mohammadzadeh, Lelio Colombetti, Aslam Siddiqui, and Steven M. Pinsky. Michael Reese Hospital and Medical Center, Chicago, ILL.

In vivo stability of ^{99m}Tc -RBC was studied in patients and in dogs, and the procedure of RBC labeling with ^{99m}Tc -pertechnetate was evaluated.

Packed RBCs from 10 ml venous blood were mixed with 20 mCi ^{99m}Tc -pertechnetate and were incubated for 20 min. with a gentle agitation in a 37°C water bath or on a rotator at room temperature. Then 100 μg SnCl_2 was added and incubated for additional 15 min. The labeled RBCs were washed twice and resuspended in a physiologic saline for the infusion. The labeling yield of ^{99m}Tc -RBC averaged 54% with blood samples in which efficiency of plasma removal before the labeling was 73%, and the average yield became 66% when 85% of plasma was removed. Difference in incubation temperature did not affect the labeling yield. Ninety-five percent of the radioactivity was found to be bound to RBC and this radioactivity distribution in the circulating blood showed no measurable change throughout the study.

In vivo half-life of the labeled RBC showed marked individual variations. Mean biological half-life of the labeled RBC in 12 patients was 16.8 hrs. and calculated effective half-life was 4.42 hrs. The half-life of ^{99m}Tc -RBC was also studied in dogs and compared to ^{51}Cr -labeled RBC. In all 5 dogs, the rate of radioactivity disappearance from circulating blood showed 2 slopes, early rapid and late slow disappearance suggesting that these labeled cells are damaged in some degree. Up to 2 hrs., disappearance rate of ^{51}Cr -RBC and ^{99m}Tc -RBC showed no significant difference, however, 24 hrs. later, higher proportion of ^{99m}Tc -RBC was found to be disappeared from the circulation comparing to that of ^{51}Cr -RBC. A series of study carried out to find a factor(s) which damages the RBC during the labeling procedure revealed that a mechanical trauma; gentle agitation or rotation, induces noticeable damage to the RBC.

INADEQUACIES OF GAMMA CAMERA PERFORMANCE AND QUALITY CONTROL. E.L. Saenger, V.J. Sodd, J.G. Kereiakes and R.J. Van Tuinen, Radioisotope Laboratory, University of Cincinnati Medical Center and Nuclear Medicine Laboratory, BRH, FDA, Cincinnati General Hospital, Cincinnati, Ohio.

Over the past several months, our laboratories have maintained an active quality control program on 6 gamma cameras of 3 of the leading manufacturers. More recently, camera accessories are available which allow quantitative evaluation of performance. It has been demonstrated that these cameras are not operating within acceptable specifications when evaluated for performance with respect to uniformity, resolution or linearity. Although manufacturers' field representatives have repeatedly serviced these imaging devices, sustained high quality performance has not been achieved. Quality control data will be presented which corroborates the inadequate performance of the cameras in clinical use.

The need for guidelines and standards for both manufacturer and user will be emphasized.

A POTENTIAL METHOD TO DETECT BONE CHANGES OF FEMORAL HEAD IN PATIENTS WITH CUP-ARTHROPLASTY. Vidya V. Sagar, Paul Ramsey, Dorothea Kurman, and Josephine Piccone. V. A. Hospital, Wilmington, DE.

Until very recently, a common surgical treatment for relief of symptoms from degenerative disease of the hip joint was insertion of a vitallium cup over the femoral head. When patients with cup arthroplasty develop hip pain, conventional X-rays offer no diagnostic help because the femoral head is within the metallic cup. Nuclear imaging could offer some help for these patients. In order to evaluate the attenuation of gamma rays due to the metallic cup, fifteen patients were studied. The patients had preoperative bone scans of the hip using Tc-^{99m} Polyphosphate. All patients had severe disease of the femoral head on one side or both. The patients were given 10mCi of Tc-^{99m} Polyphosphate two hours prior to surgery. When the femoral heads were removed at surgery for the insertion of total hip prosthesis, they were brought to the Nuclear Medicine Laboratory. Count rates were taken with and without the cup. Some of the femoral heads were also counted with a 2" probe and scaler. The data accumulated from fifteen femoral heads is presented. There is an average reduction in count rate of about 30% with the cup.

Patients with the cup in-situ have been followed with bone scans in our laboratory. To date, two patients, who had no uptake within the cup postoperatively, subsequently developed symptoms and repeat scans showed increase in uptake. Both femoral heads were surgically removed and both showed severe degenerative disease histologically. Conversely, lack of increased uptake over an in-situ cup correlated well with no recurrence of symptoms. This data suggests that bone imaging may be helpful in detecting underlying bone changes in patients with cup arthroplasty.

LABELING OF LYMPHOCYTES WITH Ga-67, In-111 AND Hg-197. G.B. Saha, E.T. Schell, and P.A. Farrer. Royal Victoria Hospital, McGill University, Montreal, Quebec.

The present study was undertaken to establish optimal physicochemical conditions for labeling human lymphocytes with Ga-67, In-111 and Hg-197.

Lymphocytes were separated from human blood by the Hypaque-Ficoll method and suspended in saline or RPMI 1640 medium. Viability of the cells was determined by Trypan Blue (>90% viable). Known amounts of Ga-67, In-111 or Hg-197 were added to 1 ml cell suspension and the mixture incubated at given temperature and incubation period. The cells and supernatant were separated by centrifugation and radioassayed. Experiments were carried out to compare the labeling efficiency with different amounts of added tracer, change in temperature, duration of incubation, cell concentration and stimulation by phytohemagglutinin.

Lymphocytic uptake was slightly greater in RPMI 1640 than in saline for In-111 (+11%), but no difference for Ga-67 and Hg-197. For incubation periods of 0.5, 1, 2 and 3 hrs., Hg-197 showed maximum uptake of 57% at 1 hr; Ga-67 and In-111 showed 5.5% and 22%, respectively, at 2 hrs. Incubation at 0°C and 37°C showed slightly higher uptake at 37°C for all three tracers. Lymphocytic uptakes of all three tracers increased linearly with increasing amount of added tracer between 1.5 μCi and 3.0 μCi at a constant cell concentration. A linear increase in uptake was also found with increasing cell concentration ranging from 1×10^6 cells/ml to 1×10^7 cells/ml. PHA stimulation increased the uptake by factors of 1.6 and 1.4 for Hg-197 and In-111 respectively, but had no effect on Ga-67. Lymphocytic uptake was about 1000 times higher than that of RBC under all conditions for the three tracers.

This study establishes the optimal conditions for labeling lymphocytes with Ga-67, In-111 and Hg-197; the latter exhibited the highest cell labeling.

COMPARISON OF DELAYED 99m TECHNETIUM DTPA AND PERTECHNETATE CAMERA BRAIN IMAGES. Ivan T. Sakimura, Alan D. Waxman and Jan K. Siensen. University of Southern California School of Medicine and Rancho Los Amigos Hospital, Downey, Calif.

The superiority of delayed technetium-pertechnetate (Tc-^{99m}) as compared to early studies is generally accepted. We have recently demonstrated that delay of brain images after administration of 99m technetium DTPA (Tc-DTPA) also significantly improves lesion visualization and detection. (J Nucl Med 15:12, 1135, 1974).

The purpose of the present study is to compare the delayed images of Tc-DTPA to those of delayed TcO₄ (with sodium perchlorate). Twenty miclicuries were used in either case and scintiphotos in four standard projections obtained three hours after injection using a Pho/Gamma III HP camera with high resolution collimator. 500,000 counts were obtained with TcO₄ and 200,000 counts with Tc-DTPA. The Tc-DTPA study was followed in 2 to 7 days (average 4.2) by the TcO₄ study.

Twenty-six patients with proven abnormalities were studied. The results in 21 infarcts are tabulated. The five additional patients with miscellaneous lesions are too small for analysis.

Abnormality Identified	Infarct
Tc-DTPA = TcO ₄	10
Tc-DTPA >> TcO ₄	6
Tc-DTPA+ TcO ₄ -	3
Tc-DTPA- TcO ₄ -	2

In spite of the low count rate of the Tc-DTPA study, 9 of 19 demonstrable infarcts (47%) were significantly better seen with Tc-DTPA, 3 of which (16%) were completely missed with TcO₄. In no instance was the TcO₄ study superior to the Tc-DTPA study.

The superiority of delayed Tc-DTPA over TcO₄ images in this series appears to be in the detection of deep parietal lesions adjacent to the choroid plexus and to lesions in close proximity to regions of high extracerebral uptake.

68-I-131-IODOMETHYL-19-NOR CHOLEST-5(10)-EN-3β-OL (NP-59) CONCENTRATES IN THE ADRENAL GLAND BETTER THAN I-131-19-IODOCHOLESTEROL. Salil D. Sarkar, Rodney D. Ice, Wm. H. Beierwaltes, Garabed P. Basmadjian, Kenneth R. Hetzel, and Wm. P. Kennedy. Univ. of Mich. Hospital, Ann Arbor, Mich.

Iodine-131-I-19-iodocholesterol has an "impurity" by chromatography, not iodide, that accounts for 10-25% of 19-iodocholesterol. Basmadjian, Hetzel, Ice and Beierwaltes have identified this impurity as 68-I-131-iodomethyl-19-norcholest-5(10)-en-3β-ol (NP-59) and have described its synthesis. We now report that I-131-NP-59 administered intravenously to rats results in a 10% (kg) dose/gm at 24 hrs or 5X that of I-131-19-iodocholesterol.

Each of 15 mature female Sprague-Dawley rats weighing 200-225 gms was given 25 μCi, sp. act. 1330 μCi/mg, of NP-59 intravenously. The rats (3 for each time interval) were sacrificed 2 hrs, 24 hrs, 5 days, 10 days and 15 days, respectively, after the dose. Tissue samples were weighed, counted in an automatic gamma well counter and the % (kg) dose/gm was calculated. For comparison, an identical study was carried out with I-131-19-iodocholesterol (NM-145), (sp. act. 1350 μCi/mg) at 24 hrs and 5 days.

Peak concentration of NP-59 in adrenals occurred at 24 hrs (10% kg dose/gm) and remained high at 15 days (7% kg dose/gm). The uptakes at 24 hrs and 5 days were respectively 5 and 3 times greater than those of NM-145. The highest concentration in the thyroid (22% kg dose/gm at 24 hrs) was half that of NM-145 (44% kg dose/gm). The highest adrenal/liver ratio was 771 (at 15 days). At 24 hrs it was 2.5X and at 5 days, 17X that of NM-145.

Thus NP-59 showed a higher adrenal uptake as compared to NM-145, probably less in-vivo deiodination (concentration in thyroid less than that with NM-145), and superior target-to-nontarget ratios. I-131-NP-59 also demonstrated superior adrenal scans in the first 2 dogs studied.

SE-75-19-SELENOCHOLESTEROL, A NEW AGENT FOR ADRENAL IMAGING Salil D. Sarkar, Rodney D. Ice, William H. Beierwaltes, Garabed P. Basmadjian, William P. Kennedy and Stephen T. Mosley. University of Mich. Hospital, Ann Arbor, Mich.

Iodine-131-19-iodocholesterol has been the only available radiopharmaceutical for adrenal imaging. Se-75-selenocholesterol would give a lower β dose and higher photon yield.

Each of 55 mature female Sprague-Dawley rats, weighing 220-260 gms, was given 25 μCi (sp. act. 4.2-4.8 mCi/mg) of Se-75-selenocholesterol intravenously. Five rats were sacrificed at each of 11 time intervals ranging from 2 hrs to 20 days following the dose. Tissue samples were weighed, counted in an automatic gamma well counter and the % kg dose/gm was calculated. For comparison, an identical study was performed using I-131-19-iodocholesterol (sp. act. 1.4 mCi/mg) at 24 hrs and 5 days following the dose.

Four mature female mongrel dogs, weighing 8-10 kg and given 100 μCi/kg of the compound were similarly studied at 1,2,4 and 15 days respectively. Adrenal scintiscanning was also performed.

In the rat, the peak adrenal concentration, 6.7% kg dose per gram, occurred at 4 days with a gradual decline to 4% kg dose/gm at 20 days. The uptakes at 1 and 5 days were 2X those of I-131-19-iodocholesterol. The highest adrenal to liver ratio was 149 (at 15 days); at 5 days, it was 2X that of I-131-iodocholesterol.

In the dog, the concentration in the adrenal medulla at 1,2, and 4 days were respectively 2X, 8X and 2X that in the adrenal cortex. Adrenal scanning yielded good quality images.

Thus Se-75-selenocholesterol produced an adrenal cortical concentration and target-to-nontarget ratio comparable to I-131-iodocholesterol, a greater concentration in the medulla than in the cortex and good quality adrenal images. Further evaluation of this agent as a potential scanning agent for the adrenal medulla seems indicated.

MYOCARDIAL UPTAKE AND ORGAN DISTRIBUTION OF THALLIUM-201 AND ITS USE FOR MYOCARDIAL IMAGING IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION. Heinrich Schelbert, Pierre Rigo, Hartmut Henning, Depew Chauncey, Subhash Khullar, Robert O'Rourke and William Ashburn, University of California, School of Medicine, San Diego, Calif.

Thallium-201 (Tl-201) has been introduced recently as a potassium analog for intravenous (IV) myocardial perfusion imaging (MPI). Therefore, we have analyzed its distribution and kinetics following IV injection in 5 patients with acute myocardial infarction, in 7 open chest dogs (6 with acute coronary artery occlusion) and compared with Rubidium (Rb-86) in 84 rats. In the rat heart, Tl-201 achieved higher concentrations than Rb-86 (2.2 vs. 1.4% of dose at 10 min.). Myocardium-to-blood ratios for Tl-201 were higher (51 vs. 33) at 10 min., (49 vs. 26) at 30 min. and (32 vs. 2) at 48 hrs. Also, hepatic uptake was less for Tl-201 than for Rb-86 (5% vs. 9.8% of dose). In the dogs, the distribution of Tl-201 within the heart followed closely that of microspheres (r = .92) injected into the left atrium. In all 5 patients, high quality perfusion images were obtained. The location of perfusion defects noted on all scans corresponded to the infarct location on ECG. Repeat scans 24 hrs. post-injection were still of diagnostic quality. Blood levels 15 min. after injection were low (1.06% ± .41 SD of dose/l), but decreased with a T_{1/2} biol. of 3.41 ± 7 days. Urinary excretion rates/24 hrs. ranged from .6 to 6.5% of the given dose with an average excretion of 8.7 ± 2.2% within 72 hrs.

Tl-201 with its high myocardial to background ratios, its uniform distribution in normal and decreased uptake in ischemic myocardium appears promising for MPI with the gamma camera. Following injection, no adverse effects were observed. The slow clearance and relatively high radiation dose to the kidney however might limit its use for repeat studies.

COMPARISON OF LEFT VENTRICULAR EJECTION FRACTION BY RADIONUCLIDE ANGIOGRAPHY AND BY ECHOCARDIOGRAPHY IN PATIENTS WITH CORONARY ARTERY DISEASE. Heinz Schelbert, H. Henning, Robert O'Rourke, John Verba, Michael Crawford, Joel Karliner and William Ashburn. Department of Medicine, University of California, San Diego, San Diego, Calif.

Echocardiography (echo) and radionuclide angiography (RNA) currently are employed for non-invasive assessment of left ventricular (LV) performance. Ejection fraction (EF) by echo is calculated from the internal diastolic and systolic LV diameters by assuming that the LV represents a regularly shaped ellipsoid of revolution. Calculation of EF by Tc-99m RNA is based upon end-diastolic and end-systolic count rates as noted on the LV time-activity curve and is virtually free of any geometrical assumptions. Accordingly, EF was obtained by both methods in 77 patients (pts) with coronary artery disease. In 31 pts with normal heart size, as measured from a standardized end-diastolic X-ray, and normal wall motion (heart wall motion video-tracking) both methods correlated well (r = .86, p < .0001) with complete separation between pts with normal and reduced EF (< .52). However, when cardiomegaly and/or wall motion abnormalities were present (46 pts), EF by echo correlated poorly with EF by RNA (r = .33). In only 12 (26%) of these pts EF was normal by both techniques, while in 27 pts (59%) echo EF was normal, but RNA EF was reduced. In 25 of 27 pts in whom there was a lack of agreement between the two methods, wall motion abnormalities involving the

anterolateral LV wall were not apparent on echo. We conclude that EF by echo and by RNA is equally accurate when heart size is normal and no wall motion abnormalities are present. On the other hand, EF by RNA, which previously has been shown to correlate closely with EF by biplane cineangiography, appears to be a superior method in pts with coronary artery disease, particularly in those with previous myocardial infarction.

THERMOGRAPHY IN THE DETECTION OF PERIPHERAL VENOUS THROMBOSIS IN PATIENTS WITH ABNORMAL LUNG SCANS. M. Schreyer, Kovaleski, K. Vanags, J. Homesley, J. Franco. Department of Nuclear Medicine, O'Connor Hospital, San Jose, California.

In a search for peripheral vein thrombosis, we have studied patients with abnormal lung scans by means of leg vein thermography. Thermography shows the temperature differences of an object using the natural infrared radiation emanated from the subject. The thermographic examination was conducted in a room with the temperature maintained around 68°F. The patient is exposed below the pubis, remains so for 10 minutes before thermographic examination. About 6 minutes are needed to expose the different pictures.

We have so studied 21 patients suspected of pulmonary embolism. Four patients had normal lung scans, x-ray venograms and thermography. The clinical course of those 4 patients did not suggest pulmonary embolism. Seven of the 17 patients who had positive thermography and abnormal lung scans had also x-ray contrast venography which did demonstrate unilateral thrombosis in the leg veins. One false negative was found in a patient who had a positive lung scan, negative thermogram and abnormal x-ray venography suggestive of a pre-existing thrombus.

In our limited experience this modality represents a major advance in the diagnosis of patients with peripheral venous thrombosis. One limitation to this approach would be that some patients have thrombosis in the iliac veins and these would not show up as abnormalities in the leg thermogram. While thermography will not recognize every instance of thrombosis in the iliac-femoral system, it seems likely to demonstrate most instances of deep venous thromboses in the legs.

RADIOLABELLING OF GRANULOCYTES TO LOCALIZE ACUTE INFLAMMATION BY SCINTISCANNING. John R. Scott, Brian C. Lentle, and T. Alexander McPherson. Departments of Nuclear Medicine and Medicine, Dr. W.W. Cross Cancer Institute, Edmonton, Canada.

Human granulocytes in heparinized whole blood were found to be preferentially labelled when incubated with technetium-99m sulfur colloid (Tc-99m-S.C.).

In vitro experiments have shown that labelling efficiency is dependent upon the formulation and volume of Tc-99m-S.C., incubation time and temperature and upon the number of granulocytes. The labelling efficiency was found to range from 60% to 90% when Tc-99m-S.C. was incubated with samples of normal heparinized whole blood in a ratio 1:20 for 0.5 hours at 25°C. After removal of excess Tc-99m-S.C. by washing with normal saline, density grade centrifugation and autoradiography indicate that greater than 80% of the radioactivity is concentrated in granulocytes. Viability of granulocytes, determined by trypan blue exclusion, was greater than 90% after labelling.

Twenty granulocyte scans were done; 17 on patients with evidence of acute inflammation, and three on normal volunteers. Scintiscans were done 1.5-2.5 hours after injection of radiolabelled granulocytes. Fifteen scans showed focal accumulation of radioactivity, and 13 out of 15 could be positively correlated with objective evidence of acute inflammation. The ability of granulocytes to ingest Tc-99m-S.C. and remain viable, allied with the excellent physical properties of the radionuclide, suggest this method might be of value in the localization of acute inflammation.

A NEW RADIOPHARMACEUTICAL APPROACH FOR AN ADRENAL IMAGING AGENT. James E. Seabold, Wm. H. Beierwaltes, James F. Zakem, Donald M. Wieland, and Rodney D. Ice. University of Michigan Medical Center, Ann Arbor, Mich.

This investigation was undertaken to evaluate the feasibility of using an enzyme inhibitor as a potential agent for imaging the adrenal glands. When given in physiologic doses, aminoglutethimide has been shown to inhibit the conversion of cholesterol to pregnenolone, an intermediate of all steroid hormones synthesized in the adrenal cortex. It has also been shown to affect the conversion of norepinephrine to epinephrine in the adrenal medulla, and therefore might concentrate in both cortex and medulla.

Tissue distribution studies were performed at 0.2, 0.5, 1, 2, 4 and 24 hr time intervals following I.V. injections, 0.1 µCi/gm in each rat and 0.04 µCi/gm in each dog, of H-3 labeled aminoglutethimide, (specific activity 1 mCi/mg). In the rat, a peak adrenal concentration of 2 % kg dose/gm was achieved within 30 minutes. In the dog, maximum concentration in adrenal medulla was 1.1 % kg dose/gm at 0.5 hrs, while that in the cortex was 0.6 % kg dose/gm, maintained from 0.5 to 2 hrs. This compares with 1.6 % kg dose/gm of C-14-dopamine (sp. act. 0.04 mCi/mg) at 2 hrs. in the medulla and 1 % kg dose/gm of I-131-19-iodocholesterol (sp. act. 1.35 mCi/mg) between 1-5 days in the adrenal cortex.

The target-to-nontarget (T/NT) ratios for the adrenal versus liver, ovaries, blood were 9, 11 & 13 in the rat and 3, 6 & 6 in the dog. The biologic half-life had 2 components (2 & 12 hrs). These results not only support a new approach to organ specific radiopharmaceuticals but hold promise for a new imaging agent for detection of adrenal medullary and cortical lesions. A gamma emitting analog of aminoglutethimide should markedly decrease the time between injection and optimum tissue levels for imaging. Also the short biologic half-life should decrease radiation exposure to patients.

I-131-IODOCHOLESTEROL IMAGING IN ADRENAL NEOPLASMS. James E. Seabold and David E. Schteingart. University of Michigan Hospital, Ann Arbor, Mich.

Normal ipsilateral and contralateral adrenal tissue has not imaged in patients with cortisol secreting carcinomas and adenomas. Only in patients with hyperfunctioning aldosteronomas has the normal adjacent and contralateral tissue been observed to image. We wish to report that androgen secreting adrenocortical carcinoma also allows normal imaging of the ipsilateral and the contralateral adrenal cortex and report tissue data that supports previous observations.

We obtained tissue from 5 patients with cortisol secreting and 2 patients with androgen secreting adrenal carcinomas following 2 mCi iodocholesterol scans. We assayed 0.1 gm slices of tissue for radioactivity and compared the results with the data obtained from 15 patients with aldosteronomas and 3 patients with cortisol secreting adenomas. The adrenal carcinomas had a tenfold decreased concentration of radioactivity (0.002% dose/gm or less) compared with 0.01-0.03% dose/gm in tissue adjacent to aldosteronomas and in tissue adjacent to an androgen secreting carcinoma. Radioactivity was also decreased (0.0006-0.008% dose/gm) in normal adjacent tissue of patients with cortisol secreting carcinomas or adenomas and in adrenal tissue obtained from 3 patients on dexamethasone suppression. Cortisol secreting adenomas had high normal or increased tissue concentrations (0.03-0.13% dose/gm) whereas levels in aldosteronomas were 0.01-0.06% dose/gm. Patients with cortisol secreting adrenal cortical carcinomas failed to image tumor or non-involved adrenal tissue. Patients with androgen secreting carcinomas had decreased uptake of the nuclide in the tumor but had normal concentration and imaging of ipsilateral and contralateral adrenal tissue. It would be expected that an androgen or estrogen secreting adenoma would present adrenal images identical to aldosteronomas.

MINICOMPUTER ENHANCEMENT OF GAMMA CAMERA IMAGES USING FAST FOURIER TRANSFORM (FFT) TECHNIQUES. Mark J. Sebern, James D. Horgan, Robert C. Meade, Charles Kronenwetter, Philip P. Ruetz, and En-Lin Yeh. VA Center, Marquette University and Medical College of Wisconsin, Milwaukee, WI.

The purpose of this study was to develop methods using a minicomputer to enhance lesions in scintillation camera images. This has been accomplished with a PDP-12 digital computer interfaced to a Pho-Gamma HP camera and programmed to carry out two dimensional frequency domain analysis and processing. Significant enhancement of image defects has been obtained.

A phantom was constructed consisting of groups of "lesions" ranging from one to four cm. in diameter. Four groups absorbed 10, 20, 30, or 40% respectively of the Tc-99m 140 Kev gamma. Phantom and liver data are stored on magnetic tape or disk in a 64x64 matrix, and flood corrected.

A two dimensional FFT of the data is generated yielding two 64x64 matrices in the frequency domain. A one dimensional frequency spectrum is generated. An interactive program allows the operator to use a simple joystick to graphically construct a filter and apply it to the data matrix. An inverse Fourier transform produces an enhanced image in the spatial domain. Processing time 2-1/2 minutes. The filter chosen for best results was a mid band-pass filter. The results of phantoms and liver images with enhancement are shown. Various filters will be demonstrated.

Although similar results have been obtained with large computers, this study makes enhancement by FFT techniques available to nuclear medicine laboratories using small computers.

REGIONAL VENTILATION IN CHRONIC OBSTRUCTIVE LUNG DISEASE.
Roger H. Secker-Walker, Philip O. Alderson, Rexford L. Hill, Joanne Markham. Washington University School of Medicine, St. Louis, Mo.

This study compares measurements of relative regional ventilation with measurements of regional fractional exchange of air in healthy subjects and patients with C.O.P.D.

Regional ventilation was measured during the washin and washout of Xenon-133 using a gamma camera interfaced to a PDP-12 computer. Relative regional ventilation was determined as the distribution of tidal volume per unit lung volume from the first 42 seconds of the washin. Regional fractional exchange of air was calculated from the washout curve, after tissue background correction, using the height/area approach.

In 17 normal subjects both methods showed a similar gradient of ventilation from the upper to lower zones. In 22 patients with C.O.P.D. the gradients differed and were more uneven with the fractional exchange method. The regional values for each zone were all significantly different from normal, using the fractional exchange method, but not with the relative ventilation method.

In patients with C.O.P.D. the whole lung fractional exchange of air was shown to correlate positively with F.E.V₁ and with M.M.F.R. (r=0.70) and negatively with PaCO₂ (r=-0.67). No significant correlations were found in the normal subjects.

Measurement of relative ventilation provides an indication of how much air enters a region in relation to its volume and this corresponds closely to the fractional exchange of air in healthy lungs. In the presence of C.O.P.D. this is not so, the difference reflecting the inefficiency of gas exchange. Methods of measuring regional ventilation based on the exchange of air provide more meaningful information than methods based on the distribution of air.

REGIONAL MYOCARDIAL BLOOD FLOW (RMBF) IN CORONARY ARTERY DISEASE (CAD) WITH AND WITHOUT VENTRICULAR ASYNERGY. Jackie R. See, Peter F. Cohn, B. Leonard Holman, Barbara R. Roberts and Douglass F. Adams. Peter Bent Brigham Hospital and Harvard Medical School, Boston, Mass.

RMBF in areas of asynergy was assessed in 44 patients. Ten were normal controls, 13 had CAD and no asynergy at angiography, 14 had CAD and antero-apical (AA) asynergy, 7 had CAD and postero-lateral (PL) asynergy. RMBF was studied after selective injection of Xe-133 into the left main coronary artery. Washout from the tissue supplied by the proximal and distal left anterior descending (LAD) and left circumflex (LCX) arteries were monitored with an Anger scintillation camera. Functional images were constructed using a PDP-11/20 computer. Values for total heart flow showed a definite trend, the normal controls had higher mean flows than patients with CAD and no asynergy. In patients with CAD and AA or PL asynergy, total mean flow was less than those with CAD and no asynergy. This trend was again seen when the lower quadrants were analysed; mean flow was highest in normal controls and lowest in CAD with AA or PL asynergy.

Flow (ml/100 gm/min, mean±S.E.M.)

	Whole Heart	Lower LCX Region	Lower LAD Region
Normal controls	82.1±7.1	91.5±8.8	85.7±7.0
CAD, no asynergy	75.1±6.7	77.1±5.4	77.4±5.8
CAD, AA asynergy	67.4±4.3	71.1±5.9	67.9±5.7
CAD, PL asynergy	67.8±4.2	69.6±5.9	73.4±6.0

There were, however, patients both with and without asynergy in whom RMBF was not reduced, suggesting that various interventions to simulate stress may be necessary to more clearly define regional hemodynamics in the presence of CAD with or without asynergy.

IONOPHORES: A NEW GROUP OF RADIOPHARMACEUTICALS. David Semenoff, Luigi Marzilli, H. William Strauss, Katharine Harrison, Buck A. Rhodes and Bertram Pitt. The Johns Hopkins Medical Institutions, Baltimore, Md.

Ionophores are a group of natural or synthetic compounds which complex metal ions and facilitate their transport through membranes. These bound ions are sequestered within the ionophore, so that when complexes are administered to animals, the distribution is significantly different from that of the ion alone. The property of specific ion binding suggested that the ionophores may be useful as radiopharmaceuticals, particularly to image the myocardium.

The distribution of two ionic nuclides, Lead-203 and Thallium-201 were investigated in mice, both with and without complexation to ionophores. Groups of 6 mice were sacrificed 10 minutes after intravenous administration of the substances under evaluation, and the activity in the heart, blood, lungs, liver and kidneys expressed as percent of the dose/organ. The results were:

Substance	% Dose/Organ (mean of 6 values for each point)					
	Thallium			Lead		
	Ht	B1	Lu	Ht	B1	Lu
IONIC	1.79	0.38	1.57	0.15	14.0	--
FILIPIN	2.17	0.19	1.55	0.66	2.51	3.2
BACTRACIN	1.95	0.20	1.78	0.51	0.91	1.68
X-537A	1.84	0.19	1.70	2.59	0.47	0.45
18-C-6	4.0	1.2	1.7	5.08	1.48	3.27
DB-18-C-6	3.4	1.3	1.4	0.65	1.96	0.71
B-15-C-5	3.1	0.19	1.5	2.6	0.74	0.57

Thallium and Lead were found in greater concentration in the myocardium after complexation with ionophores, than after administration in ionic form, suggesting that these substances may be useful as new myocardial imaging agents.

IODINE-123 ROSE BENGAL IN THE EVALUATION OF THE JAUNDICED PATIENT. Aldo N. Serafini, Homer B. Hupf, Dale Lindberg, William M. Smoak, and Albert J. Gilson. Mount Sinai Medical Center, Miami Beach, Fla.

We have evaluated the usefulness of I-123 Rose Bengal in the diagnosis of primary hepatocellular disease and extrahepatic obstruction. Each of ten normal healthy volunteers and 30 jaundiced patients were injected intravenously with 2mCi of I-123 Rose Bengal. Blood clearance curves and a 24-hour urinary excretion level were performed. These show that the radiopharmaceutical is cleared with a T_{1/2} clearance time of 12.9 minutes which is comparable to the value obtained with Iodine-131 Rose Bengal by previous investigators. Using the Anger scintillation camera with a high energy parallel hole collimator, sequential scintiphotos to include cardiac pool, liver, biliary system and intestines were taken at various intervals throughout the day. Time activity curves were generated from various selected regions of interest using an on-line computer, and the pattern of uptake in the liver, gallbladder and subsequent excretion into the GI tract observed. The dynamic pattern of normals as seen on scintiphoto scanning with I-123 Rose Bengal has been reported previously by the present investigators.

This study outlines our findings in the jaundiced patients either with primary hepatocellular disease or secondary to extrahepatic obstruction. Significant findings were that an overall improvement in the quality of the images was possible even in the face of severe jaundice probably because of the higher administered dose possible. In addition, there is a marked reduction in the total study time for the patient possible because of the improved information density. The overall radiation to the patient is considerably less than for Iodine-131 Rose Bengal.

THREE-DIMENSIONAL (TOMOGRAPHIC) MYOCARDIAL RECONSTRUCTION USING INTRACORONARY RADIOLABELLED PARTICLES. James B. Seward, James F. Greenleaf, Nicholas G. Nolan and Robert G. Tancredi. Mayo Clinic and Mayo Foundation, Rochester, Minn.

The aim of this study was to validate the technique of three-dimensional reconstruction with the use of isotope phantoms and non-living heart preparations. Tc-99m labeled microspheres (30 micron diameter) injected into coronary arteries of dogs distribute in the myocardium in proportion to blood flow. Using a gamma camera, interfaced to an on-line computer, 37 static views of the phantom or heart are obtained at 5 degree increments and mathematically analyzed to obtain the three-dimensional distribution of isotope. We have developed and successfully used an algebraic reconstruction technique (ART) to generate tomographic images of isotope phantoms and isolated heart preparations.

Reconstructed transverse (tomographic) cuts of isotope distribution within a phantom were compared to the true distribution. Using the computerized ART, the regional distribution of isotope was accurately reproduced. Reconstruction of beef myocardium, following the intracoronary injection of tagged microspheres, was made and compared to scintigraphic cut sections of the heart. Myocardial anatomy was accurately depicted using this reconstruction method. The ART shows great promise in its ability to reconstruct the three-dimensional distribution of isotopes in perfused organs.

We are presently developing these same techniques for myocardial reconstruction in the closed chest living animal. The long term goal of this work is to apply these techniques to the study of myocardial perfusion in the human and to study how it is affected by pathologic, physiologic and pharmacologic changes.

Tc-99m POLYPHOSPHATE SCANNING IN CALCINOSIS UNIVERSALIS OF DERMATOMYOSITIS. George N. Sfakianakis, Eleni Damoulaki-Sfakianaki, Jack C. Bass, William C. Earl and Xavier J. Riccobono. Columbus Childrens Hospital, Columbus, Oh.

Calcinosis universalis is common in dermatomyositis (DMS) and scleroderma (SCD) in children. Findings in five children suffering from DMS or SCD studied with serial Tc-99m polyphosphate scans for soft tissue calcifications are reported. Evidence of soft tissue Tc-99m polyphosphate accumulation at least fifteen months before x-ray detection of developing calcinosis characterized the first case (11 y.o. boy with DMS). Stabilized long standing nodular calcifications of the soft tissues with grossly abnormal radiographs gave relatively less pronounced accumulation of the radiocompound repeatedly in the second case (12 y.o. girl with DMS). A prominent soft tissue hyperactivity in the developing stage changed into a nearly normal scan in full accordance with the radiographic studies in a case of spontaneous resolution of the previously extensive calcinosis (13 y.o. girl with DMS). The fourth case (11 y.o. boy with DMS) demonstrated soft tissue accretion identical with the early findings of case 1, which persisted for over a year. This was probably due to an occult degree of calcinosis, which never became radiographically evident. In the last case (14 y.o. girl with SCD) unilateral focal hyperactivity over a sclerosing cutaneous lesion of the thigh with lack of calcification by biopsy could be explained on the basis of abnormal kinetics of the radiocompound within the lesion. The polyphosphate Tc-99m scan appears to be a suitable test for early detection and accurate followup of soft tissue calcification in DMS.

PANCREATIC SCAN: A DOUBLE BLIND RETROSPECTIVE ANALYSIS. George N. Sfakianakis, Lawrence R. Fulmer and Xavier J. Riccobono. Ohio State University Hospitals, Columbus, Oh.

Of 708 patients with conventional pancreatic scans 207 (group A) had surgery or autopsy; group B (463 patients) had only a clinical diagnosis, which may have been influenced by the scan re-

sults; cases without diagnosis (38) were rejected. A double blind retrospective analysis of 526 available scans was performed. Reinterpretation by three ABNM specialists agreed in 90.3% with the original interpretation on a positive or negative basis. Reinterpretation had generally a higher rate of positives with an increase in false positives. The analysis appears in the following table.

Diagnosis		% of Positive Scans Per Group of N Patients							
		Original inter.				Blind inter.			
		A		B		A		B	
Other Tumor	N	%	N	%	N	%	N	%	
Adenocarcinoma	44	75			36	86			
Other Primary	9	11	25	92	6	17	21	90	
Metastatic	9	56			8	75			
Pseudocyst	19	95			13	100			
Duct Obstruction	5	80	85	65	5	60	73	66	
Inflam. Fibrosis	14	64			13	54			
Partial Resection	10	100			8	75			
No Pancreatic Dis.	97	15	353	8	75	27	285	19	

The pancreatic scan was more sensitive in detecting the above pancreatic disorders than clinical history, serum enzymes or routine U.G.I. series. The specific configuration and the time of optimal visualization of the pancreas had no correlation with the diagnosis. Accordingly, a normal gland will result in a negative scan about 80% of the time. A patient with pancreatic disease will have generally a positive scan 73% of the time.

ACUTE CHANGES IN THYROID FUNCTION IN PATIENTS TREATED WITH RADIOACTIVE IODINE. Rex B. Shafer and Frank Q. Nuttall. Veterans Administration Hospital, Minneapolis, MN.

Many patients treated with radioactive iodine for thyrotoxicosis eventually become hypothyroid. An occasional patient may develop thyroid storm shortly following I-131 therapy. Thyroid function in these patients has been reported from a few months to many years following treatment, but as yet there has been no documentation of acute changes in the immediate post-therapy period. The widespread availability of RIA for measurement of thyroid hormones now enables monitoring the immediate changes in thyroid function following I-131 therapy. Eight unselected patients with thyrotoxicosis were studied prospectively. Six patients had diffuse toxic goiter, one patient had multinodular toxic goiter and in one patient the thyroid gland was felt to be normal. Six patients received therapeutic amounts of I-131 (7,000-10,000 rads), while two patients received ablative doses (30,000 rads). Total serum T-3, serum T-4 and TSH were measured one week prior to therapy; at 8, 24, 48, 72, 96 and 120 hours and at 6 weeks following therapy. Results showed an abrupt rise in TT-3 and TT-4 at 24-48 hrs, with a return to pretreatment levels at 96-120 hrs. Mean TT-3 increased from 252 to 356 ng% with an increase in mean TT-4 from 21.9 to 27.7 ug%.

These data document for the first time an increase in circulating thyroid hormones following I-131 therapy. This may explain why an occasional patient develops thyroid storm shortly following I-131 therapy.

TECHNETIUM-99m DIPHOSPHONATE CHEST IMAGING: A VALUABLE DIAGNOSTIC AND PROGNOSTIC TOOL IN METASTATIC OSTEOSARCOMA. R. Sham, E.P. Cortes, A. Mundia, H. Klein, V. Azueta, and L. Silver. Queens Hospital Center Affiliation of Long Island Jewish-Hillside Medical Center and School of Medicine State University of New York at Stony Brook, New York, N.Y.

Chest roentgenogram is the procedure of choice in following a patient with pulmonary metastases from osteosarcoma. The recent widespread use of Tc-99m labelled radiopharmaceuticals for bone scanning has demonstrated that these agents also concentrate in the primary as well as in metastatic osteosarcoma. In an effort to compare the diagnostic and prognostic usefulness of radionuclide chest imaging techniques to standard chest roentgenogram, 3 patients with detectable pulmonary metastases from osteosarcoma on chest x-ray had periodic chest imaging. Scans were performed 3 hours following intravenous injection of 15 millicuries of Tc-99m diphosphonate before and during chemotherapy, using a dual probe wholebody scanner and a gamma camera. The lesions in all 3 patients were detected by chest imaging. One patient who had symptomatic improvement with combination adriamycin and 5-fluorouracil had

resolution of some metastatic lesions on chest imaging. These changes did not occur until 5 months later on chest roentgenogram. Another patient with a solitary pulmonary lesion detected by chest x-ray and tomogram showed 2 lesions on chest imaging. The presence of these 2 lesions was confirmed at thoracotomy. While chest roentgenogram failed to show the developing subcutaneous metastases on the chest wall of this patient, the lesion was demonstrated vividly by chest imaging. The chest imaging technique using Tc-99m disphosphonate appears to be a valuable tool in diagnosing and prognosticating a patient with metastatic osteosarcoma. Its periodic use, therefore, is recommended to supplement the chest roentgenogram in following an osteosarcoma patient.

QUANTITATION OF MYOCARDIAL INFARCT SIZE WITH Tc-99 PYROPHOSPHATE AND CORRELATION BETWEEN MYOCARDIAL CPK DEPLETION AND RADIONUCLIDE UPTAKE. David M. Shames, Elias Botvintick, Harris Lappin, Ronald Townsend, John Tyberg and William Parmley. University of California, San Francisco, California.

This study was undertaken to quantitate infarct size non-invasively and to determine the relationship between myocardial CPK and Tc-99 pyrophosphate uptake. Discrete infarcts were created in 13 closed-chest dogs by placement of occlusive catheter plugs in branches of the left coronary artery during fluoroscopy. Scintiphotographs were taken 48 hours post occlusion (2 hours after IV injection of 15 mCi of Tc-99 pyrophosphate) using a scintillation camera interfaced to a small digital computer.* Clear images of each infarct over 5 gm were obtained which correlated well with ECG localization (11 anterior, 2 inferior) and the site of occlusion. Following sacrifice the intact and opened hearts were also imaged in vitro. Biopsies of infarcted, borderline and normal tissue were analyzed for radioactivity, CPK content and histology.

Significant radioactivity was found only in regions of histologically confirmed infarction. There was a good correlation between the area of the in vivo infarct image measured by the computer and actual infarct weight in gm determined pathologically (LAO view, $r = .92$, $p < .005$). There was also a good negative correlation between myocardial Tc-99 radioactivity and CPK content ($r = -.85$, $p < .005$).

In conclusion, Tc-99 pyrophosphate localized specifically in areas of infarcted myocardium in amounts proportional to the degree of CPK depletion. This imaging technique provided good in vivo quantitation of infarct size and lends strong support for the clinical application of this technique in the detection and quantitation of acute myocardial infarction.

* Gamma 11R, Digital Equipment Corporation

Tc-99m-EHDP AND F-18 SCANNING AND EXTERNAL COUNTING IN THE EVALUATION OF DISODIUM ETIDRONATE (Na-EHDP) TREATMENT OF PAGET'S DISEASE. Bernard Shapiro, Irvin Stein, Robert E. Cantor, and Bernard Ostrum. Albert Einstein Medical Center, Philadelphia, Pa.

The purpose of the present work was to use scanning and counting techniques to demonstrate and quantitate the effect of Na-EHDP on pagetic bone. The scans were recorded by a whole body rectilinear dual probe scanner with 5" NaI crystals, appropriate collimators, and 5:1 minification at 2 hours after injection of 12 mCi of F-18 and at 3 hours after injection of 15 mCi of Tc-99m-EHDP. External body counts were obtained with a 2" NaI crystal single probe and flat field collimator over the forehead, sternum, right and left hips and sacrum after each scan. In all patients, at least one of these areas was normal and at least 2 were diseased. Ratios of counts over each area to counts over the normal area were calculated. Thirteen patients with advanced Paget's disease were studied before, during and after 6 months of Na-EHDP, 20 mg/kg. All patients showed some reduction of bone activity on scan and external counting during and after treatment. Serum alkaline phosphatase and urinary hydroxyproline changes paralleled the external counting results. Bone x-rays showed little change except for severe demineralization in several pagetic areas in 2 patients. Tc-99m-EHDP and F-18 gave similar results except that Tc-99m-EHDP scans demonstrated better resolution. It is concluded that Tc-99m-EHDP scanning and counting can be used to demonstrate and quantitate the effect of Na-EHDP on pagetic bone. The scan

changes noted confirmed previous reports (JAMA 230: 562, 1974) in which F-18 and Sr-87m scanning was employed. External counting provides a simple reproducible method of quantitation and correlates well with biochemical changes produced by the drug in this disease. Return of activity in the diseased areas 6 months after withdrawal of Na-EHDP was delayed or absent in some patients.

UTILIZATION OF INDIUM-113m FOR THE DETECTION OF OCCULT GASTROINTESTINAL BLEEDING. Stuart H. Shapiro, Frank P. Castronovo, Ronald J. Callahan, Christos A. Athanasoulis. Massachusetts General Hospital, Boston, Massachusetts.

In patients treated with intra-arterial infusion of vasopressin for upper GI hemorrhage, it is often difficult to assess whether the bleeding has completely stopped. Small amounts of bleeding may go undetected by angiography. Repeated endoscopy is not practical and the nasogastric aspirates may be falsely positive due to clots in the stomach. In order to develop a more reliable diagnostic test, Indium-113m (InCl3) was utilized. Previous work with this radionuclide has shown that when injected at pH 4.0 it becomes bound to transferrin. Our animal data demonstrated 113mIn-transferrin is not secreted by the wall of the gut and therefore as a blood pool agent might be effective for diagnosing and monitoring GI bleeding. In-113m (100-150 uCi) was administered IV and 3-5 NG aspirates were isolated 5-30 minutes after injection and the radioactivity measured in each. In patients who were not bleeding, there was essentially no activity in the aspirate whereas in a bleeding patient the content of radioactivity in the aspirate was 100 times greater than background levels. The short $T_{1/2}$ of In-113m allows for sequential studies in the same patient. This method is simple and reproducible and may also replace the more cumbersome Cr-51 tagged red blood cell method used in the detection of small intestinal bleeding.

MASSIVE ARTERIOVENOUS SHUNTING IN A HYPERNEPHROMA: VERIFICATION AND CLINICAL IMPORTANCE. Michael E. Siegel, Frank A. Giargiana and Henry N. Wagner, Jr. The Johns Hopkins Medical Institutions, Baltimore, Md.

Intra-arterial injections of radioactive albumin microspheres were used to verify and quantitate, for the first time in a human, the presence of arteriovenous communications in a hypernephroma.

Lumbar and renal arteriograms were performed on a male with a left hypernephroma and no cardiovascular symptomatology. Early opacification, within 1-2 sec., of the renal vein and inferior vena cava suggested, although not necessarily verified, as we previously demonstrated in patients with peripheral vascular disease and similar type of arteriographic findings, the presence of arteriovenous communications. After arteriography, with the catheter remaining in the arterial supply to the tumor, known quantities of supernatant and 99mTc microspheres (15-30µ in diameter) were injected. A known quantity of the spheres were also given i.v. to represent 100% shunting. With simultaneous monitoring over the lung, during the injections, the percent of arteriovenous shunting was calculated. Calculations revealed that 82% of the perfusion to the tumor was being shunted through arteriovenous communications greater than 15µ in diameter. Qualitative verification was obtained in subsequent scintillation camera views. Areas of decreased activity, indicating arteriovenous shunting of the particles, correlated well with hypervascular areas on the arteriogram.

We conclude that massive arteriovenous communications, greater than 15µ in diameter can exist in a hypernephroma. This finding, in addition to clarifying a pathophysiologic process, is of particular clinical importance to those who advocate the use of radioactive spheres for the delivery of therapeutic radiation because it emphatically suggests the need for determining the presence and extent of arteriovenous communications prior to the use of this therapeutic approach.

PHYSIOLOGIC RELATIONSHIP OF LOWER AND UPPER AIRWAYS. Edward B. Silberstein, Jeannine T. Lewis, and David J. Quenelle. University of Cincinnati Medical Center, Cincinnati, Oh.

Currently available data suggest the presence of laminar flow of air through the nares to the ipsilateral lung and/or reflex hypoventilation of the ipsilateral lung in unilateral nasal obstruction. We have tested these hypotheses by examining the distribution of Xe-133 inhaled through a specially designed facemask with a midline septum permitting separate control of each nostril's inspiratory content. Ten seated subjects with normal lung volumes and pulmonary mechanics inhaled 3-15 mCi Xe-133 through the left nostril up to total lung capacity with room air entering the right nostril, then vice-versa, and finally via a mouthpiece with the nose clamped. Total counts from each lung were obtained from a gamma camera with data storage accessory, then analyzed statistically. Comparison of counts in right and left lungs in the time frames 0-5 sec. and 55-60 sec. with breathholding showed no significant differences, excluding significant intrapulmonary gas flow post-inhalation as a source of error, and permitting a larger number of counts to be analyzed per study.

In all 10 normal subjects there was a significant difference, $p < 0.01$, between right and/or left lung counts with nasal inhalation compared to oral. In 6 of 10 subjects right nasal inhalation produced significantly greater right-to-left lung ratios; in 2, left nasal inhalation paradoxically increased the R/L lung ratio, and in 2 there was no difference.

Under the conditions employed, intra-pulmonary distribution of nasally inhaled gas varied significantly from oral inhalation in all subjects, and also was significantly different between left and right nares in 8 of 10. Laminar flow was an unlikely explanation as Xe-133 content was significantly greater in the ipsilateral lung in only 6 of 10 subjects. The existence of naso-pulmonary reflexes cannot be excluded by these results.

QUENCH CORRECTION FOR TRITIATED RADIOIMMUNOASSAYS Edward A. Silverstein, A. Michael Zimmer, Richard A. Holmes The Medical College of Wisconsin, Milwaukee, Wisconsin

The counting of tritiated radioimmunoassays by means of a liquid scintillation counter is often assumed to be under conditions of constant quench, in particular for the tritiated digoxin assay. Corrections for quench are sometimes recommended for hemolyzed or otherwise severely discolored samples while samples that appear uncolored are assumed to need no quench correction. In addition, when quench correction is applied it is often by means of the internal standardization method.

In the present work in our laboratory, the quenching obtained under typical clinical conditions was investigated and methods of quench correction were developed. Two types of quenched tritium standard sets were prepared, one with bilirubin in serum, the other with hemoglobin from hemolyzed blood samples. Quench curves were plotted for channels ratio and external standards ratio. The bilirubin and hemoglobin quench curves were found to be identical, (and linear over the clinical range) showing that the quench arising from the coloration of either of these agents may be corrected by a single curve.

Examination of the results of 11 runs with a total of 100 patient samples in duplicate led us to conclude:

1. Visual inspection is insufficient to ascertain if a sample needs quench correction, since 6 samples did not appear discolored but needed significant quench correction.
2. Significant quench corrections were necessary for a total of 17 samples (17% of total).
3. External standard ratios and sample channels ratio both gave adequate correction for quench, and are superior to internal standardization both in accuracy and convenience. The sample channels ratio method is the simplest to apply but can have larger statistical errors for small counts.

RADIOPHARMACEUTICAL DISTRIBUTION STUDIES USING A LINEAR WHOLE BODY SCANNER. Guy H. Simmons, Frank H. DeLand, Sylvia Magoun, Robert Beihn. V.A. Hospital and University of Kentucky Medical Center, Lexington, Ky.

The purpose of this study is to evaluate the application of a new linear total body scanner for the study of spatial and temporal radiopharmaceutical distribution for clinical and dosimetric purposes. The linear total body scanner is

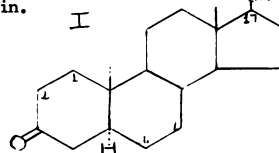
a stationary detector-moving bed type with banks of four NaI(Tl) crystals above and below the bed. The crystals are five inches in diameter and three inches thick. Resolution in one dimension is obtained via variable width slit collimators. The eight detector outputs are summed, digitized and stored in a PDP-11/40 computer for subsequent display and processing. A 256 channel energy spectrum is stored for each transverse body section at 2.5 cm intervals. The data are transferred to disk during data acquisition. Data are presented from long-term retention studies of Yb-169-DTPA administered intrathecally for cisternography. Brain dose estimates of 1.1 to 1500 rads/mCi from this radiopharmaceutical have been reported. Whole body linear scans were obtained following injections of one mCi for periods of up to 30 days depending on the length of hospital stay. Data from three patients whose cisternograms were normal show a two compartment curve for both the head and total body. The long-lived components in both organs have 26 day effective half-times which implies a biological half-time of near infinity. The short-lived components have effective half-times of approximately one day. The initial concentration of the long-lived component is about 6% of that of the short lived component for the head and about 8% for the total body. Application of the MIRD schema for dose calculations yields a dose of 1.4 rads/mCi to the brain. Analysis of the profile scans provides clinical information on cerebral clearance of the radionuclide (quantitative and temporal) which reflects cerebral transit.

STRUCTURAL REQUIREMENTS FOR POTENTIAL STEROIDAL PROSTATIC IMAGING AGENTS. R. W. Scott Skinner, Rodney V. Pozderac, Raymond E. Counsell, and Paul A. Weinhold. VA Hospital and University of Michigan, Ann Arbor, Michigan.

The design and development of a radiopharmaceutical for imaging and possibly for treatment of prostatic carcinoma and its metastases has been undertaken by this laboratory. An in-vitro screening system has been developed to measure the inhibition of tritiated 5 α -dihydrotestosterone binding to rat prostate tissue by various commercially-available and newly-synthesized steroidal compounds. This was done to obtain basic information on the structural requirements for steroid binding to receptor protein in prostate.

Twenty-four selected testosterone analogues were evaluated using prostatic tissue from Sprague-Dawley rats. Inhibition of tritiated 5 α -dihydrotestosterone (I) binding to receptor protein was determined in the cytosol fraction and the nuclear component of prostatic tissue.

The results indicate that a geometrically planar molecule is desirable and that an appropriate radiolabeled function may be attached to positions 1, 2, 6, 7, or 17 of the ring structure without significantly interfering with the active binding sites of the synthesized compound to the receptor protein.



CHEMICAL EFFECT OF Tc-99 ON Tc-99m LABELED RADIOPHARMACEUTICALS. Terry D. Smith, Joseph R. Steimers, and Powell Richards. Brookhaven National Laboratory, Upton, N. Y.

During the recent development of a simplified kit for the preparation of Tc-99m labeled red blood cells (RBC's), Tc-99m solutions containing large quantities of Tc-99 produced low labeling yields. The purpose of this study is to determine the chemical quantities of technetium in representative generator and instant technetium solutions and to determine if there is a correlation between Tc-99 quantities in these sources and radiopharmaceutical labeling yields.

When a series of RBC labeling kits (each containing 1 μ g of Sn⁺⁺) were treated with increasing increments of Tc-99, labeling yields decreased when more than 1.48 x

10^{14} atoms of technetium was added to the kit. Using this data in conjunction with liquid scintillation assay of Tc-99 in various technetium solutions, good or poor labeling yields could be predicted for a given technetium source. The significance of this finding is that the quantities of Tc-99 which caused lower yields were often exceeded in generator and instant technetium solutions.

Several commercial radiopharmaceuticals which contain stannous ion have been selected for a similar evaluation. Although most commercial radiopharmaceutical kits contain more than 1 μ g of stannous ion, it is likely that not all of the added stannous is available for the reduction of technetium.

From this study one should be able to determine the maximum stannous ion required in any radiopharmaceutical for those technetium solutions containing the largest quantities of Tc-99.

AN INVESTIGATION OF THE Sr-89 and Sr-90 CONTAMINATION IN FISSION-PRODUCT Mo-99 - Tc-99m GENERATORS. V.J. Sodd and D.L. Fortman. FDA, BRH, Nuclear Medicine Laboratory, Cincinnati General Hospital, Cincinnati, Ohio.

Technetium-99m generators made from fission product (FP) Mo-99 are usually preferred because they yield a high specific activity product. However, concern has been shown for the radionuclidic contamination of the Tc-99m obtained from these generators. While gamma ray emitters can be easily detected by spectroscopy in the nuclear medicine laboratory, the measurement of alpha and beta emitters is usually not done. It has recently been reported [South. Med. J. 67 1392 (1974)] that the alpha emitters Pu-238, Pu-239 and Pu-240 are not present in significant quantities in eluates from these generators. We have directed our attention to the beta-emitting impurities of which Sr-89 and Sr-90 are of primary concern.

In this study, first eluates from 16 generators and total eluates from 9 other generators of the two distributors were analyzed for Sr-89 and Sr-90 contamination. These generators were manufactured from FP Mo-99 produced during July, August, September and October 1974, at the Sterling Forest Reactor, Tuxedo, New York.

The results showed that the greatest quantities of Sr-89 and Sr-90 found in the eluates were 5.2×10^{-7} and 6.0×10^{-8} μ Ci/mCi Tc-99m. These levels of contamination are, at worst, 3 orders of magnitude less than the limits established by the AEC; namely, that not more than 6×10^{-4} μ Ci Sr-89 and 6×10^{-5} μ Ci Sr-90 per mCi of Tc-99m should be present at the time of administration to each patient.

It is concluded that if the FP Mo-99 is produced and processed in the same manner as the production runs involved in this study, then the Sr-89 and Sr-90 contamination in the Tc-99m eluates is not significant.

MULTI-ISOTOPE STUDIES WITH 'SOFTWARE' ENERGY SELECTION AND COMPTON CORRECTION. F. Soussaline, A. Todd-Pokropek and C. Raynaud. Service F. Joliot, CEA Orsay, France. University College Hospital, London, U.K.

Multiple isotope studies are of considerable interest in Nuclear Medicine. As originally proposed by Di Paola, the solution of digitizing the X, Y, position, AND, Z, energy signals, has been adopted. A Toshiba Jumbo camera has been used together with an Informatek data processing system. The camera was modified so that all events within a large (50-550 KeV) window are recorded. It is therefore possible to choose, a posteriori, the energy window required and the sampling rate in time. The linearity of the energy response of this Toshiba camera facilitates the problem of correcting the Compton crosstalk. A method of linear combination of images from different energy windows has been previously described. An important extension to this technique has been the incorporation of resolution correction, established from phantom studies using the same combination of isotopes. This correction is particularly significant in large organs where the contributions from scattered photons are much greater.

These techniques have been validated in studies of renal uptake of Hg-197Cl₂ in man. A study also has been performed in pigs where 3 isotopes were

used simultaneously. These techniques have now been employed when comparing the renal uptake of Hg-197Cl₂ and of Tc-99mDMSA. Lung studies have been performed using these methods where, simultaneously, a Tc-99m microsphere image and a Ga-67/Hg-197 image were recorded. The experimental studies were chosen to validate the technique in large organs. The resolution correction has been found to be essential.

COMPARTMENTAL MODEL OF PERTECHNETATE ACCUMULATION IN SUBDURAL HEMATOMAS. Richard P. Spencer, Dept. Nuclear Medicine, University of Connecticut Health Center, Farmington, Conn.

Reports that the detection of subdural hematomas can be improved by delayed scanning, prompted construction of a compartmental model to investigate the kinetics of pertechnetate accumulation, and the ratio of subdural to blood activity. The model assumed perchlorate blockade of the thyroid, salivary glands and choroid plexus. Following intravenous administration of Tc-99m-pertechnetate, blood disappearance values were set to mimic literature data, such as that of Apfelbaum and coworkers (1973). Blood content of pertechnetate was, over the first several hours, most readily described by 2 components. The first blood component (B1) had a $T_{1/2}$ of 20 minutes and accounted for 40% of the injected dose. The second blood component (B2) exhibited a $T_{1/2}$ of 300 minutes and was used to quantify the other 60% of pertechnetate radioactivity. The model was tested on an analogue computer. We assumed that B1 + B2 represented total blood radioactivity, that a small portion of the amount in the blood entered the subdural hematoma (represented by a distinct rate constant), and that there was an "outward leak" or backward passage of radioactivity from the subdural hematoma to the blood stream. There were thus 4 rate constants in the final model. The curves generated closely matched known data. That is, the peak of subdural radioactivity occurred at about 2 hours, but a slightly more favorable subdural to blood ratio of activity could be obtained by a further time delay. The use of such models to study intracranial disorders might aid in optimizing the time at which to scan. (Supported by USPHS CA 17802 and by American Cancer Society DT-34E).

THE SMALL SPLEEN: A STUDY OF ETIOLOGY AND PATHOGENESIS. Richard P. Spencer, Dept. Nuclear Medicine, University of Connecticut Health Center, Farmington, Conn.

While the enlarged spleen attracts attention on physical examination, the small spleen (more than 2 std. dev. below the mean for that age) is usually detected only by means of spleen scans or specialized procedures. Over 12 clinical disorders, and several animal models, have now been recognized as being associated with a small spleen. On the basis of accumulated data, and our own experience (principally by use of Tc-99m-sulfur colloid or heat denatured Cr-51-RBC), a tentative classification of the causes of a small spleen has been evolved. 1. Failure of the spleen to develop prenatally: familial hypoplasia, Fanconi's anemia (some cases) and maternal pyridoxine deficiency in animals. 2. Failure to develop postnatally: marasmus (infections may contribute). 3. Impairment of blood supply: sickle cell anemia, thrombocytopenia, possible overwhelming infections with thrombosis. 4. "Atrophy of disuse": chronic blood removal in animals. 5. Internal radiation: thorotrast administration or use of larger radioactive microspheres. 6. External radiation. 7. Medication effects. 8. Mechanisms unknown, but may have associated gastrointestinal-illness: some cases of celiac disease, dermatitis herpetiformis, and ulcerative colitis. 9. Immunologic: end results of graft-versus-host reaction. Estimation of splenic size by conventional (R.E.) scanning agents is feasible only when active accumulation of the radiocolloid occurs. In other cases, blood pool scanning agents, intrasplenic injection, or specialized radiographic procedures may have to be used (and these are illustrated, particularly in Fanconi's anemia). Finding of a small spleen, when coupled with data as to R.E. function, may be important evidence in evaluation of complex clinical situations. (Supported by USPHS CA 17802 and by American Cancer Society DT-34E).

ANALYSIS OF SEQUENTIAL "LOW DOSAGE" RADIOIODIDE THERAPY OF HYPERTHYROIDISM. Richard P. Spencer and Vincente J. Caride. Dept. Nuclear Medicine, University of Connecticut Health Center, Farmington, Conn. and Yale-New Haven Hospital.

Records of 39 patients with hyperthyroidism and diffuse enlargement of the gland, treated with sequential "low dosage" radioiodide, were reviewed. Age range was 21-74 years (mean 47), and 30/39 were women. Patients, seen at intervals of 3 months, were given 1-4mCi I-131 (mean 2.9) each time until there was evidence of a euthyroid or hypothyroid state. Thirty-four of the 39 patients had two or more doses (mean number=2.8). Clinical follow-up was from 1 to 4.5 years. In addition to the clinical status at each visit, we noted the weight of the thyroid (estimated from the scan), the uptake value, and turnover (or used a mean of $T_{1/2}$ =4 days). From these values, the amount of radioiodide in the thyroid (μ Ci/gm) was calculated, as well as the radiation dose given (in rads). A plot was made of cumulative % cured of hyperthyroidism (made euthyroid or hypothyroid), as a function of total radioiodide concentration in the thyroid (μ Ci/gm) achieved in the treatments. A sigmoidal curve resulted, with the 50% cure at an amount just over 100 μ Ci/gm in the thyroid. The curve was linearized by a logit transformation. This may be a useful tool in comparing populations treated by different regimens. A plot of the % radioiodide uptake in the thyroid at each visit, as a function of the total radioiodide concentration (μ Ci/gm) during the multiple treatments, showed a break in the curve at just over 100 μ Ci/gm in multiple cases. Since treatment doses were administered over a long period, several concepts related to the "nominal standard dose" were applied. That is, correction was made for the fractionation of the dosage. Disadvantages of the sequential schedule are the number of patients still hyperthyroid after 1 year, and the whole body radiation dose. (Supported by USPHS CA 17802 and by American Cancer Society DT-34E).

DISTRIBUTION OF IODO-FOLATE AND ITS DISPLACEMENT BY METHOTREXATE. Richard P. Spencer and Robert E. Miller. Dept. Nuclear Medicine, University of Connecticut Health Center, Farmington, Conn.

The enzyme folate reductase occurs in many malignant tissues. Inhibitors of folate reductase are known to be of use in the treatment of certain leukemias, and selected tumors such as choriocarcinoma. A form of folate which carried a gamma ray label might permit localization of the enzyme and determination of its turnover, or its displacement by a more avid folate reductase inhibitor such as methotrexate. The recent commercial synthesis of I-125 or I-131-folate (the iodotyramide complex of the more distal acid group), has made a radiolabeled folate available for *in vivo* studies. The material, in a small amount of dimethylformamide, has good storage characteristics. Upon intravenous injection into dogs, the blood disappearance of I-125-folate approximates that of I-131-3'-iodoaminopterin in man (J. Nuc. Med., 9:530, 1968). At 2 to 3 hours after administration, the ratio of activity per gram tissue to activity per gram blood was: spleen 3.8, urine 4.2, lung 5.0, liver 6.5, bile 84.6. Most of the radioactivity is, thus, in the liver and bile. If a large dose of methotrexate is injected intravenously after 2-3 hours, blood levels of radioactivity promptly increase. This strongly suggests release of I-125-folate from bound sites; also, tissue sites are depleted of radioactivity. With I-131-folate, or preferably the I-123-compound, it should be feasible to follow the sites and rates of uptake of the compound in man, and displacement of the radiolabel from tissue sites by aminopterin or methotrexate. (Supported by USPHS CA 17802 and by American Cancer Society DT-34E).

MERCURY ADDUCTS OF UNSATURATED FATTY ACID ESTERS: AN APPROACH TO GAMMA RAY-LABELED LIPIDS. Richard P. Spencer, Robert E. Miller. Dept. Nuclear Medicine, University of Connecticut Health Center. Farmington, Conn.

Aside from iodinated fatty acids, which are often dehalogenated, there are no readily available lipids which carry a gamma ray emitting radionuclide. Since mercury addition products are well known in the chemical literature, we studied the preparation and biological handling of the Hg adducts of the esters of unsaturated fatty acids. Mercuric acetate was prepared from Ag acetate and HgCl₂, and reacted with compounds such as methyl linoleate or

methyl oleate. Products were studied by elemental analysis and by thin layer chromatography using silica gel and a solvent system of hexane-dioxane-acetic acid. Inorganic forms remained at the origin while the fatty acid esters and mercury adducts readily migrated. Compounds were re-synthesized with Hg-203. For animal studies, products were placed in ethanol and Tween, and given intravenously. Blood disappearance of methyl linoleate-Hg-203 showed at least 2 components (initial $T_{1/2}$ =1 hour) in dogs. At 3 hours, highest specific activity (counts/gm) was shown by the bile. Relative specific activities were bile 1.00, liver 0.78, lung 0.22, spleen 0.12, kidney 0.11, blood 0.03. Among the variations in producing such Hg-addition products are the chain length, site and number of unsaturated bonds, and side groupings. Addition of Hg-197 or Hg-203 to unsaturated lipids may open the way to creation of a number of radiotracers of value. The Hg-products are of particular interest since, in rodents, fatty acid esters can produce a "chemical splenectomy". (Supported by USPHS 17802 and by American Cancer Society DT-34E).

COMBINED CHEMICAL AND ENZYMATIC SYNTHESIS OF C-11 ACETYL PHOSPHATE. L. Spolter, C.C. Chang, D. Bobinet, M.B. Cohen, N.S. MacDonald, A. Flesher and J. Takahashi. VA Hospital, Sepulveda, Calif. and Univ. of Calif., Los Angeles, Calif.

The synthesis of biologically active substances labeled with short-lived radioisotopes may be more directly achieved by the use of appropriate enzymes, and several N-13 labeled amino acids have been synthesized in this manner. This report presents a combined "wet chemical" and enzymatic procedure for the synthesis of C-11 acetyl phosphate, a compound which may be of direct interest and which can serve as a precursor in the enzymatic synthesis of a number of acetyl-group-containing substances, e.g. acetyl coenzyme A, acetylcholine, and N-acetylglucosamine. A study of the distribution of this compound in the rabbit has been made.

C-11 carbon dioxide was produced in the UCLA Biomedical Cyclotron by irradiation of nitrogen gas in a p, α reaction. Carbon-11 acetate was synthesized by the reaction of C-11 carbon dioxide and methyl magnesium bromide and purified on an AG 1-X8 column. The labeled acetate was incubated with ATP, MgCl₂, cysteine, tricine buffer, pH 7.4, and acetate kinase (EC 2.7.2.1) for 6 minutes at 37°. The C-11 acetyl phosphate formed was separated from C-11 acetate on an AG 1-X8 column. Under our present incubation conditions, 20-25% of the incubated C-11 acetate is converted to C-11 acetyl phosphate as demonstrated by column chromatography and paper electrophoresis. C-11 acetyl phosphate (1-2 mCi) has been administered to rabbits intravenously and tissue distribution and scintigraphic studies have been obtained.

Acetyl phosphate was observed to be distributed in most tissues of the body. Although C-11 acetyl phosphate does not appear to be a useful agent for imaging studies, it may be used as a precursor for many biologically active compounds which could have great utility in Nuclear Medicine.

QUANTITATIVE HEPATIC SCINTIANGIOGRAPHY. Robert C. Stadalnik, Gerald L. DeNardo, Nathaniel Matolo. University of California School of Medicine, Davis, Calif.

Hepatic scintiangiographic images have enhanced the specificity of diagnosis of space occupying lesions of the liver. However, this technique provides only semi-quantitative information, so that a study has been initiated to obtain quantitative information. Using a dog experimental model, scintillation camera, and Tc-99m sulfur colloid, regions of interest were digitally stored and replayed through a rate meter with strip chart recording. The transit of radioactivity into the normal liver is characterized by a shallow initial slope (20-35°) of short duration due to hepatic artery (HA) influx followed by a steeper slope (60-65°) of longer duration due to portal vein (PV) influx. The venous/arterial slope ratio was 2.5 and the count ratio was 3.0. Occlusion of the hepatic artery or portal vein caused disappearance of the initial or second slope respectively. 41 patients were studied: 18 with no liver disease (NLD), 5 with cirrhosis, 9 with metastases (M), and 9 patchy cirrhosis vs. metastases (PCM). In NLD venous/arterial slope ratio (V/AS) = 2.6 ± 1.0 and venous/arterial count ratio (V/AR) = 7.3 ± 4.6; in cirrhosis V/AS = 0.6 ± 0.2, and V/AR = 2.0 ± 2.0; in metastases V/AS = 0.7 ± 0.3, and V/AR = 1.8 ± 2.2; in PCM V/AS = 0.7 ± 0.4, and V/AR = 2.0 ± 3.4.

These indices reflect an effort to characterize quantitatively the contribution of hepatic arterial and portal venous flow to the total radioactivity in the liver region, and these indices may be of objective value in distinguishing the etiology of space occupying processes within the liver and in following the quantitative changes in the liver during the course of the underlying disease process.

ISOTOPE BRAIN IMAGING AFTER INTRODUCTION OF THE EMI SCAN: EXPERIENCE IN A 230 BED COMMUNITY HOSPITAL: John C. Stauffer, Harold H. Macumber, and Michael J. Brown. Community Memorial Hospital, Ventura, Calif.

This study was undertaken to evaluate the impact of the EMI scan on the utilization of isotope brain scans.

EMI Scans became available in July 1974 at Community Memorial Hospital (CMH) in Ventura. A 160 matrix was installed in December. The CMH plus the 225 bed General Hospital of Ventura County serve this area of 100,000. The Nuclear Medicine Service of CMH serves both hospitals. EMI and Isotope brain scans are available without delay to the physicians of the community. EMI scans are done without and with contrast in the majority of patients. Similarly, extra delayed views (usually rectilinear) are taken of any borderline brain scan, or negative scan in the presence of an abnormal cerebral perfusion study.

A retrospective study of isotope brain scans was carried out comparing utilization during the 6 months prior to (Period I) and the 6 months following introduction of the EMI (Period II).

The number of brain scans done fell from an average of 78 per month in period I to 41 in period II. Brain scans accounted for 37% of the total imaging studies in Period I but only 19% in Period II. However, the total number of brain scans interpreted as abnormal did not change. Thus the incidence of abnormal brain scans was 11% in Period I and 24% in Period II.

These results indicate a trend toward the combined clinical application of the radionuclide and EMI scans in brain imaging.

THE IMPORTANCE OF THE PROTEIN SULPHYDRYL GROUP IN HSA LABELING WITH TECHNETIUM-99m. Joseph Steigman Hazel P. Williams and Nathan A. Solomon. Downstate Medical Center, Brooklyn, N.Y.

This research is concerned with the effect of chemical modifications of the protein's free sulfhydryl group on the efficiency of labeling human serum albumin with Tc-99m.

Pertechnate-99m was reduced with ascorbic acid and ferric chloride; at pH 9 the HSA was added, the pH was lowered to 2-2.5, incubated, and then raised to 5-6 (method of Stern, McAfee and Zolle, modified by Richards and Atkins). The labeling efficiency was determined by Sephadex (G-25m) gel chromatography.

There are 17 disulfide groups and one free sulfhydryl group in mercaptalbumin. The latter group can be blocked by reaction with reagents like N-ethylmaleimide (NEM) and mercuric chloride. Pre-treatment of HSA with NEM reduced the efficiency of labeling with Tc-99m from almost 100% to 24%, and with mercuric chloride to 10%. In addition, if the pH of the labeling mixture was raised to 12 (instead of being lowered to 2), the labeling efficiency was 91%, reduced to 32% on HSA pre-treatment with NEM.

It was concluded that the free sulfhydryl group of HSA is essential for the successful labeling of the protein by Tc-99m.

ALTERATION OF THE CEREBRAL BLOOD FLOW STUDY DUE TO ANOMALOUS VENOUS RETURN FROM THE UPPER EXTREMITIES. Jehuda J. Steinbach, and Adel G. Mattar. Veterans Administration Hospital and Buffalo General Hospital, Buffalo, N.Y.

The cervical flow during the early part of the cerebral blood flow study is usually considered arterial in nature. Consequently, alterations of this part of the study are interpreted as such. The recognition that these alterations could also be due to anomalous venous drainage from the upper extremities is the basis for this report.

Ten patients were studied with the gamma camera using the sequential imaging technique following a bolus administration of 10-15 mCi of sodium Tc-99m pertechnetate in the left antecubital vein. Images of the cerebral flow study and subclavian flow study were obtained in the anterior projection. Vertex flow study was obtained in some of the patients. Two patterns of abnormalities are presented.

1. In this group (7 patients), reflux into the left internal jugular vein occurred as documented by the subclavian flow study. The cerebral blood flow study demonstrated a linear column of activity rising to various levels in the neck which terminated abruptly. The actual arterial phase was delayed but appeared symmetrical. 2. In this group (3 patients), complete or high grade obstruction in the region of the left innominate vein, documented by the subclavian flow study, resulted in reversal of the flow in the left internal jugular vein followed by activity seen to descend in the right internal jugular vein. Similarly, the anterior cerebral blood flow study demonstrated an ascending column of activity in the left jugular vein followed by a descending column of activity in the right jugular vein. Crossover of the activity was seen through the sigmoid and transverse sinuses as demonstrated on the vertex flow study. The recognition of these two patterns as venous rather than arterial in origin is important to avoid misinterpretation of the cerebral blood flow study.

ABNORMAL RADIONUCLIDE CEREBRAL ANGIOGRAMS AND SCANS DUE TO SEIZURES. Jeffrey S. Stevens and Fred S. Mishkin. Martin L. King, Jr. General Hospital, Los Angeles, Calif.

Pertechnate Tc 99m radionuclide cerebral angiograms and brain scans were performed on 9 patients at varying intervals, usually less than one day, after seizures. The findings were occasionally subtle, but in 8 out of 9, the angiogram was abnormal, showing increased activity over the affected hemisphere. In 6 out of 9, the delayed scan images were abnormal, also showing increased activity over the affected hemisphere. In no patient were both components of the study normal. The changes are thought to represent relative increase in perfusion to metabolically hyperactive cortex in the case of the angiogram, and breakdown of the blood-brain barrier in the case of the delayed scan. In one case, the seizures were caused by a lesion which was itself undetectable at the time of the original study. A normal study after control of seizures was followed three months later by a third scan which revealed a focal abnormality, subsequently confirmed by contrast angiography. This patient, then, fortuitously acted as her own control.

Patient	Flow Study	Scan	Interval after Seizures	Duration of Seizures
1	+	+	0	Repetitive focal before and during scan
2	+	+	<1 day	Single focal
3	+	+	<1 day	Single focal
4	+	+	2 days	Single generalized
5	+	0	1 day	Single focal
6	+	0	<1 day	2 focal
7	0	+	6 days	2 generalized lasting 30 minutes
8	+	0	1 day	Single generalized
9	+	+	1 day	16 generalized over 4 days

+ = abnormal 0 = normal

ESTIMATION OF ACUTE MYOCARDIAL INFARCT SIZE IN EXPERIMENTAL ANIMALS USING Tc-99m PYROPHOSPHATE (PYP) SCINTIGRAMS. E.M. Stokely, S.E. Lewis, L.M. Buja, R.W. Parkey, F.J. Bonte, and J.T. Willerson. The University of Texas Health Science Center at Dallas, Texas

This study investigates the feasibility of estimating myocardial infarct weight from the anterior, left anterior oblique (LAO), and left lateral Tc-99m PYP scintigrams of experimental animals. Six mongrel dogs received proximal left anterior descending coronary artery ligation and subsequent acute anterior myocardial infarction. One day later the animals were imaged with a scintillation camera one hour after intravenous injection of 3 mCi (5 mg) of Tc-99m PYP. Three views from each animal were collected on magnetic tape using a digital computer. Each image was retrieved, preprocessed to improve infarct contrast, and a Colay digital computer method for detecting boundaries was applied to demarcate the infarct peri-

meter. The projected area of the infarct in each view was measured, along with the projected area of the whole heart blood pool. Morphological measurements of infarct size were also made by sacrificing the animal and excising the heart. Transverse sections of the heart were examined using PAS staining, areas of infarction were identified, and the weight of infarcted tissue in each section was determined.

Several mathematical techniques were investigated for processing these data. At least two of the methods provide reasonably good estimates of infarct weight using the projected area measurements. These preliminary findings suggest that infarct weight or volume can be estimated from the projected areas of myocardial scintigrams.

Tc-99m LABELED STANNOUS IMIDODIPHOSPHATE (Tc-99m-IDP): EVALUATION OF A NEW BONE IMAGING AGENT. G. Subramanian, J. G. McAfee, M. Rosenstreich and M. Coco, Upstate Medical Center, Syracuse, New York

In recent years several Tc-99m labeled phosphate compounds have been developed for skeletal imaging including polyphosphate, pyrophosphate and two diphosphonates (EHDP, MDP). Compared with F-18, however, they all have relatively low skeletal uptake.

We have studied a new bone imaging agent, imidodiphosphate, an analog of pyrophosphate and diphosphonate with P-N-P bond instead of P-O-P or P-C-P linkages, which shows considerably higher uptake in bone than the previous agents.

Stannous imidodiphosphate was prepared optimally in a freeze-dried kit form containing 10 mg imidodiphosphonic acid and 200 ug of stannous chloride adjusted to pH 6.5. This is quantitatively labeled with (98%) Tc-99m by adding up to 6 ml of pertechnetate. Radiobioassay of this agent was carried out in rabbits simultaneously with Sr-85 from 15 min to 24 hours after I.V. injection, using a dose range of 0.05-0.5 mg/kg imidodiphosphonic acid.

Tc-99m IDP showed 20% higher concentration than Sr-85 in the bone (which is comparable to F-18 uptake) and its soft tissue and blood levels were lower. For example Tc/Sr ratios were 1.23 and 1.34 for femur and pelvic bones respectively compared to 0.8-0.9 for pyrophosphate or diphosphonate at 2 hours. The blood levels were similar to those of pyrophosphate but higher than for Tc-99m MDP. Intravenous acute toxicity of Tc-99m IDP was similar to diphosphonates (LD50 in rabbits: 45-50 mg/kg as acid).

In summary, Tc-99m stannous imidodiphosphate seems to be a promising new bone imaging agent with considerably higher bone uptake compared to previous agents. But its blood level seems to be higher perhaps due to impurities present in the current sample of IDP (98% pure). A purer sample might give better blood clearance.

RADIOXENON GAS AND RADIOAEROSOL INHALATION LUNG IMAGING IN OBSTRUCTIVE AIRWAYS DISEASE. G.V. Taplin, D.P. Tashkin, O. E. Anselmi, D. Elam and R. Detels. UCLA, School of Medicine, Los Angeles, Ca.

This investigation was performed to compare the relative sensitivity of the two radionuclide inhalation imaging procedures with each other and with the results of selected pulmonary function tests (PFT's) as indicators of chronic obstructive airways disease (COAD). All studies were performed on the same day in the Pulmonary Function and Nuclear Medicine Research Laboratories at UCLA. The 60 subjects were all ambulatory volunteers selected from a larger group previously classified as having no, mild or definite evidence of respiratory disease from previous screening studies in a mobile laboratory (Breathmobile).

The results of the aerosol studies on 60 subjects showed abnormal lung images in 48 and normal patterns in 12. By comparison the xenon findings were abnormal in 53 and negative in 7. Both radionuclide procedures provided evidence of COAD more frequently than the PFT's, which were positive in only 44 of the 60 individuals examined. Moreover, by separating the entire group into several categories, additional information was disclosed. In the group of 43 subjects in whom both radionuclide procedures were either definitely positive and/or moderate to severely abnormal, the PFT's were positive in 38. On the other hand when only the aerosol or the xenon findings were regionally abnormal in 15 cases, the PFT's were negative in 9. The capability to detect small areas of COAD explains

to a large extent the apparently higher sensitivity of the radionuclide procedures over conventional tests of total lung function.

It is concluded that radioxenon and radioaerosol lung imaging examinations are highly efficient screening procedures whenever COAD is suspected.

RADIOAEROSOL LUNG SCINTIGRAPHY-AN EFFICIENT INDICATOR OF OBSTRUCTIVE AIRWAYS DISEASE. G.V. Taplin, D.P. Tashkin, L. Ramanna, R. Detels and O.E. Anselmi. UCLA School of Medicine, Los Angeles, Ca.

Seventy subjects, having either no, mild or definite evidence of chronic obstructive airways disease (COAD) on screening studies made in a breathmobile, volunteered to undergo detailed pulmonary function tests (PFT's), respiratory disease questionnaires, physical examinations, and Indium-113m aerosol inhalation and technetium-99m MAA perfusion lung imaging at the pulmonary function and Nuclear Medicine Research Laboratories at UCLA. All examinations were made on the same day and provided a unique opportunity to compare the results of selected PFT's (maximal mid-expiratory flow rates, single breath oxygen and closing volume) with those of the two lung imaging procedures.

Twenty four subjects had normal aerosol and PFT findings. Abnormal aerosol lung images were found in 30 of 32 subjects with positive PFT's: whereas PFT's were positive in only 30 of 44 subjects with abnormal aerosol deposition. Aerosol lung images were abnormal more frequently than respiratory questionnaire responses, findings on physical examination, chest xray films and perfusion lung images. In addition, on delayed lung imaging in 19 subjects having normal PFT's and positive aerosol patterns, only three were shown to be false positives of technical origin. Furthermore, regionally abnormal aerosol patterns were found in nine of fourteen subjects with normal tests of total lung function.

In conclusion, radioaerosol lung imaging is a highly efficient screening procedure in suspected COAD. It appears to be more sensitive for this purpose than PFT's, most probably because it provides evidence of regional and overall involvement in COAD. Also, it is definitely more sensitive than routine chest roentgenography and is frequently positive when lung perfusion images are normal.

SECRETION OF TECHNETIUM-99m PERTECNETATE INTO ISOLATED LOOPS OF RAT BOWEL. Andrew Taylor, James Henry, Naomi Alazraki. VA Hospital, San Diego and University of California, San Diego.

In scanning patients for Meckel's diverticulum, we and others have observed that the colon appears to visualize more rapidly than would be expected simply by gastric secretion and intestinal transit. To pursue these observations, 10 Sprague-Dawley rats were subjected to surgery and segments of the gastrointestinal tract were isolated by severing between double ligations. The abdomen was closed and the animals sacrificed at 45 and 150 minutes after the intravenous injection of technetium-99m pertechnetate. The stomach, upper and lower small intestine, appendix, colon and their contents were removed and counted.

By 45 minutes after injection, technetium-99m pertechnetate could be clearly imaged in the upper small intestine, appendix and colon. In addition, technetium-99m pertechnetate concentration in the stomach, colon, and appendiceal contents increased significantly during the period of study ($p < .005$) while at the same time, concentration of Tc-99m pertechnetate in the blood was decreasing ($p < .01$). These results suggest that Tc-99m pertechnetate is actively secreted by both large bowel and stomach mucosa.

Abdominal scans in patients with suspected Meckel's diverticulum should be interpreted with additional caution since significant amounts of Tc-99m pertechnetate can accumulate physiologically in the gut independent of gastric secretion. Additionally, these results further clarify the mechanism by which the colon becomes the target organ after Tc-99m pertechnetate administration.

DIFFERENTIATION: AVASCULAR NECROSIS AND DEGENERATIVE JOINT DISEASE. Nancy Telfer and Marvin Meyers. Los Angeles County-University of Southern California, Medical Center, Los Angeles, California.

Avascular necrosis of the femoral head (AN) occurs spontaneously, or associated with a variety of conditions or medications such as chronic steroid administration, alcoholism, and Legg Perthes' disease. Radiographic changes may be difficult to distinguish from degenerative joint disease (DJD) and the two may occur together and cause hip pain.

AN shows a patchy distribution, with areas of necrosis surrounded by ischemic areas. Since ischemia stimulates increased osteoblastic activity, a cortical bone scan may show increased activity when compared with the contralateral normal hip. However, some measure of blood flow should show a decrease.

We have done a cortical hip bone scan with 18-F or 99m-Tc-Diphosphonate (DP) to show osteoblastic activity, and a 99m-Tc-sulfur colloid (SC) hip bone marrow scan as an indicator of vascular supply in 25 patients with unilateral hip pain and abnormal radiographs. We have compared findings in the painful hip with those of the presumably normal non-painful hip, and have found four different patterns: hips with AN have decreased SC and increased DP activity. Decreased SC and DP are indicative of disuse, and are associated with DJD. An increase in both SC and DP is associated with some healing process. Both studies may appear normal in DJD.

Radiographic and clinical agreement, or disagreement, with these four patterns will be shown. Final diagnosis was by bone biopsy, definitive surgery, or benign clinical course.

THE POTASSIUM-43 MYOCARDIAL SCAN AS A PREDICTOR OF IMPROVEMENT IN PATIENTS UNDERGOING SURGERY FOR CORONARY ARTERY DISEASE. B. Termini, M. Cooper, L. Scherlis, R. Singleton, J. McLaughlin. University of Maryland Hospital, Baltimore, Md.

Myocardial scanning with K-43 was evaluated to determine its predictive value in anticipating the results of surgery for coronary artery disease.

Sixteen patients with documented coronary artery disease were studied before surgery, during the immediate post-operative period, and six to twelve months following surgery. Scans were performed both at rest and immediately following exercise and compared with the results obtained from cine-angiography. Saphenous vein bypass grafts were attempted in all patients.

Ten patients had normal pre-operative resting studies. All of these patients did well at surgery, and all except one had normal scans during the immediate post-operative period. At the most recent follow-up, five of the six patients on whom clinical data was available considered themselves to be markedly improved while one patient noted slight improvement. Long-term follow-up scans were normal at rest in five of these patients, and with exercise, there were three normal and three abnormal studies.

Six patients had abnormal resting studies pre-operatively and three of these patients died during surgery. Of the three survivors, one died of an unrelated cause several months after surgery, one was slightly improved, and no long-term follow-up is available on the remaining patient due to the recency of his surgery.

These data suggest that a normal resting myocardial scan in the pre-operative period is a predictor of a good response to surgical correction of coronary artery disease. An abnormal pre-operative resting scan indicates severe impairment of functioning myocardial cell mass and a poor surgical prognosis. Exercise studies do not appear to add to the predictive value of the resting scan.

A NEW RADIODIAGNOSTIC AGENT TO EVALUATE GASTRIC EMPTYING TIME. Michael C. Theodorakis*, Robert M. Beihn**, George A. Digenis†, Frank H. DeLand ††, Manvandra Shambhu†, Leonard C. Wilson†. *University of Kentucky Medical Center, and †VA Hospital, Lexington, Ky.

The purpose of this study was to prepare, test the stability of and clinically evaluate polystyrene-TETA-Tc-99m complex for gastric emptying time. Chloromethylated polystyrene was heated with pyridine and TETA for the chemical preparation for large quantities of the polystyrene TETA resin. Tc-99m labeling was performed by stirring the polystyrene - TETA with sodium pertechnetate in aqueous solution for one hour. The polyamine polymer, having complexed 99% of the Tc-99m, was then filtered, washed and dried for mixing with a test meal. The Tc-99m

labeled polymer complex was tested for stability with pH conditions similar to those found in gastric contents. A total Tc-99m elution from the polymer of 4% was observed at a pH of 1.3 with lower release percentages as the pH approached neutrality. The labeled polymer complex has been tested both in dogs as well as humans for the evaluation of gastric emptying. Disappearance half times (human) 40 min to 150 min have been observed. The present study demonstrates the insoluble polystyrene-TETA-Tc99m complex is simply prepared with high retention of label as well as being clinically stable for use in gastric emptying time.

AN INTEGRATED PATIENT CONTROL AND COMPUTER DATA BASE SYSTEM FOR NUCLEAR MEDICINE. J. Thrall, S. Pinsky, R. Corcoran and M. Johnson. Walter Reed Army Medical Center, Wash. D.C.

Technical and clinical quality control and record keeping are on going problems in Nuclear Medicine practice regardless of department size. An integrated control and recording system has been developed for Nuclear imaging procedures based on an optimized flow scheme which considers each step from patient arrival to final reporting of results. The practical basis of the system is a series of prescription forms, color coded by organ, which serve as mini flow charts for each patient. A philosophy of direct physician monitoring and tailoring of procedure to problem is emphasized by the form. Space is provided to record pertinent clinical data and, for flexibility, a choice of radiopharmaceuticals, doses, instruments, and imaging protocols is offered. All dose administration data (amount, type, time) and technical data (instruments, time of study) are recorded. In the flow scheme, completed studies return to the monitoring physician for review and the forms allow specification of repeat or additional views, when indicated. In all cases the monitor must finally approve the completed study. The official interpretation is then entered on the form along with a diagnostic code, follow-up requirements and comments. Thus, the prescription forms are both guides and controls for the respective procedures and the completed forms are comprehensive patient records.

To facilitate data review, the prescription forms are used directly for input of 14 study parameters to a free text data base on a CDC 3500 computer. Up to 4000 characters per patient may be entered and the free text searches initiated on any Boolean expression. The system has proven to be a useful manager for clinical research efforts and permits a rapid statistical review of clinical workload.

THE PREPARATION AND EVALUATION OF DIPHENYLHYDANTOIN-C-11 AS A TUMOR SCANNING AGENT. R.S. Tilbury, S. Stavchansky, C.T. Ting, J.M. MacDonald, E. Maughan, B.R. Freed, G.R. Russ, L. Helson, R.S. Benua, H.B. Kostenbauder, and J.S. Laughlin. Memorial Sloan-Kettering Cancer Center, New York, N.Y. and College of Pharmacy, University of Kentucky, Lexington, Ky.

Diphenylhydantoin (DPH) the anti-epileptic drug, was synthesized from benzophenone and C-11 labeled hydrogen cyanide. From 1.5 curies of HCN, 60 mCi of DPH-¹¹C were made 70 minutes after cyclotron irradiation. The metabolite of DPH, p-hydroxyphenylphenylhydantoin was also synthesized from HCN and p-hydroxybenzophenone and the distribution of both these C-11 labeled compounds was studied in 5 rhesus monkey experiments and in mice. The healthy monkeys were studied with a gamma-camera and with a rectilinear scanner, the output of both instruments being analysed quantitatively by computer. The radioactivity was measured as a function of time for the first 20 minutes after i.v. infusion. The brain, the heart and lungs and the liver and bowel regions were studied. Then whole body scans were performed. One monkey was sacrificed at 45 minutes and counts/min/g measured for brain, liver, pancreas, colon and heart after injection of HPPH-C-11. Blood samples were taken for 72 hours after administration and DPH measured by gas chromatography.

Positive uptake of DPH occurred in the brain. Rosenblum and Stein (Biochem. Pharmacol. 12: 1453, 1963) reported 2 to 4 times the concentrations of DPH in 7 human astrocytomas and one meningioma. Consequently a clinical trial of DPH-C-11 has been started to evaluate it as a brain tumor scanning agent. The first patient, with neuroblastoma, showed no increased uptake of DPH-C-11 in the tumor. This was confirmed with human neuroblastoma growing in nude mice. No increased uptake in the pancreas was observed. HPPH-

C-11 showed a different distribution pattern compared with DPH-C-11, and the administration of HPPH prior to DPH-C-11 caused increased uptake of DPH-C-11 in the brain, and an increased brain:liver ratio.

SPECIFIC BOUNDARY DETERMINATION OF RADIONUCLIDE SCINTISCAN DATA BY COMPUTER ANALYSIS. Roger P. Tokars, Jack N. Hall, and Robert E. O'Mara. Arizona Medical Center, Tucson, Az.

The objective of this work was to develop a computer program for delineating the outline and abnormal areas of static organ images from an Anger camera by the linear inflection point method.

Two-dimensional count-rate contours obtained from an Anger scintillation camera were digitalized into a 4096 matrix and processed with a CDC-6400 computer. A computer program was constructed utilizing the zero of the second derivative along an X and Y linear profile. The program contained statistical data smoothing, crystal non-uniformity correction, and sensitivity parameter routines. The two-dimensional binary-coded scintiscan matrix systems of increased sensitivity were superimposed and subsequently analyzed using a statistical weight factor routine to determine a specific image boundary. The computer analyzed image matrix was then scaled to a 10 by 10 inch coordinate axis of 100 by 100 matrix units and plotted on a Calcomp-665 plotter.

The plotted scans appear to possess the same geometry and dimension within a wide range of camera to object distances. Consequently, this program makes the scintillation camera more than just an organ surface imaging instrument with the multi-hole collimators. For example, defects situated in the depth of an organ such as the liver may be seen with well circumscribed boundaries on the computed scintiplot. In addition, the computed scintiplots clearly illustrate variations in the planar activity of the scintiscan. The output of this program is aesthetically pleasing and requires little experience to interpret studies.

RADIONUCLIDE STUDIES ON BRONCHOGENIC CARCINOMA OF THE HILUM. Kanji Torizuka, Harumi Itoh, Yasushi Ishii, Teruyasu Suzuki, and Tsutomu Sakamoto. Kyoto University School of Medicine, Kyoto, Japan.

Although plain chest film is certainly useful for detecting abnormalities in the thorax, the lesions in the hilar area are often obscured by the mediastinal silhouette. Laminagraphy is the most simple and valuable method to recognize the hilar masses, bronchial stenosis and oligemia of the lung field which are caused by bronchogenic carcinoma among various roentgenological methods.

Meanwhile, Ga-67 citrate scintigraphy is found to be quite useful for seeking the hilar and mediastinal masses, particularly those of bronchial carcinoma. Perfusion and inhalation scintigraphies with radioactive particles are also valuable for detecting oligemia and bronchial stenosis respectively, which are often difficult to recognize on the plain radiogram. But each of these three scintigraphies can not provide specific findings for bronchogenic carcinoma, if applied separately. Therefore, it is reasonable to consider that the combined study of them would enhance diagnostic probability of bronchial carcinoma by demonstrating the hilar masses and changes of the bronchovascular system simultaneously.

Correlative features of the combined scintigrams with the laminagram were evaluated on 25 cases of bronchogenic carcinoma. All of three scintigrams showed abnormal findings which were also confirmed by the laminagram. It was evident from this study that the Gallium-67, inhalation and perfusion scintigraphies were useful for screening bronchogenic carcinoma of the hilum.

KIDNEY PHANTOM TO TEST COMPUTER ASSISTED BLOOD BACKGROUND SUBTRACTION TECHNIQUES AND MEAN TRANSIT TIME CALCULATION METHODS. Juan J. Touya, L. Stephen Graham, and Leslie R. Bennett. University of California, Center for Health Sciences, Los Angeles, Calif.

This investigation was undertaken to design a kidney phantom for evaluating computer assisted blood background subtraction techniques and deconvolution methods used for obtaining the frequency distribution of mean transit times.

The phantom consists of a blood pump, an arterial line, a venous line, two artificial kidneys, a device simulating the tissues surrounding the kidney, two ureters and a bladder.

The glomeruli of each kidney were simulated with a Model 4 Cordis Dow Artificial Kidney (CDAK) having 1.3m² of filtration area. Its dialysate input was closed and its dialysate output was connected to the arterial input of a second CDAK with its dialysate compartment blocked. The fibers of this second CDAK simulated collecting tubules and its venous terminal, connected to a drip chamber simulated the renal pelvis. The vascular bed of tissues surrounding the kidney was represented by the fibers of a third CDAK. An auxiliary line joins the venous line to compensate for fluid volume lost by filtration. The ultrafiltration rate is adjusted by changing the transmembrane pressure by means of clamps on the venous lines. Radio-pharmaceuticals may be injected in the incoming line to the pump.

Clamping the arterial line of one kidney may be used to simulate renal arterial strictures. Decreasing the transmembrane pressure either in one or both kidneys simulates conditions of unilateral or diffuse parenchyma disease. Clamping the ureter tubing results in the simulation of obstructive syndroms. (Supported by USPHS Grant GM01920-06.)

RADIOMETRIC ASSAYS OF LYMPHOCYTE CARBOHYDRATE METABOLISM IN RESPONSE TO MITOGENS. N. Tran, M. Chen, P. McIntyre, S. Larson, and H.N. Wagner, Jr. The Johns Hopkins Medical Institutions. Baltimore, Md.

After the initial report of stimulation of lymphocyte (lymphs) carbohydrate metabolism by phytohemagglutinin (PHA) (J. Nucl. Med. 15: 510, 1974), it was discovered that oxidation of glucose-1-¹⁴C (G-1-¹⁴C) to ¹⁴CO₂ by contaminating granulocytes (PMN) was also being stimulated, accounting for up to 50% of the ¹⁴CO₂. The present study was done to evaluate radiometric detection of changes in carbohydrate metabolism in purified lymphs in response to mitogens, i.e. PHA and concanavalin A (Con. A). A Ficoll-Hypaque technique was used for preparation of fractions containing 90-95% lymphs and less than 1-2% PMN. ¹⁴CO₂ output was quantified by an ionization chamber. 2x10⁶ lymphs or 0.1x10⁶ PMN were incubated with or without mitogens with 1.0 μCi G-1-¹⁴C, G-6-¹⁴C or G-U-¹⁴C in modified Hanks plus 5.0 mM Mg⁺⁺ at 37°C for 360 minutes. Results showed: 1) Lymphs ¹⁴CO₂ production from G-1-¹⁴C plus PHA (Gibco 3.12-6.25 mg) was increased at 0-2 hours (n=9, p<0.001); 2) Lymphs ¹⁴CO₂ production from glucose was increased by incubation with PHA (Difco) with ¹⁴CO₂ production greatest from G-1-¹⁴C, intermediate from G-U-¹⁴C and least from G-6-¹⁴C; 3) Similar changes in lymphs carbohydrate metabolism were noted after incubation with Con. A; 4) No significant change in glucose oxidation was detected in PMN with PHA; a slight increase in ¹⁴CO₂ (p<0.025) occurred only from G-1-¹⁴C when PMN were incubated in Con. A but this PMN metabolism would have accounted for less than 2% of the ¹⁴CO₂ produced by lymphs under identical conditions. These results show that both PHA and Con. A stimulate lymphs carbohydrate metabolism and that glucose oxidation by contaminating PMN did not contribute significantly to ¹⁴CO₂ detected. This study may be of potential importance for development of automated in vitro tests of lymphocyte immune responsiveness.

RADIOMETRIC DETECTION OF EFFECTS OF ANTIRHEUMATOID DRUGS ON SH GROUPS IN BLOOD. Ngo Tran, Thomas Ntundulu, and Etienne LeBel, Dept. of Nuclear Medicine and Radiobiology, Centre Hospitalier Universitaire, Sherbrooke, Quebec.

Radiometric measurement of non-enzymatic oxidation of DOPA in the presence of isolated tissues was considered as a possible means for detection of SH groups in these tissues (J. Nucl. Med. 15: 539, 1974). We demonstrate here that both salicylate and indomethacin can interfere with SH groups in blood, which can be useful as a possible means for rapid quantification of these drugs in clinical applications. An automated indicator system (Bactec) was used for measurement of ¹⁴CO₂ release from 0.1 μCi DOPA-1-¹⁴C incubated with 0.1-2.0 ml human blood, with and without various amounts of indomethacin and salicylate in 20 ml

0.1 M phosphate buffer, pH 7.0, at 37°C, for 90 min. Results and conclusions show that: 1) Non-enzymatic oxidation of DOPA inhibited by human whole blood ($n=10$; $p < .001$) was significantly prevented by 9.4 mg salicylate ($n=10$; $p < .001$), 4.7 mg indomethacin ($n=10$; $p < .02$), respectively; 2) Non-enzymatic oxidation of DOPA without blood was, however, unchanged in the presence of 4.7-9.4 mg salicylate ($p > .05$) and 4.7-9.4 mg indomethacin ($p > .05$), respectively. Results obtained from 1) and 2) show that effects of antirheumatoid drugs, i.e. salicylate and indomethacin in blood were specific, and that these drugs were probably bound to blood SH groups which might subsequently prevent the inhibition of non-enzymatic oxidation of DOPA; 3) A reversed $^{14}C_2$ production from DOPA- ^{14}C by salicylate and indomethacin in blood may be considered as a sensitive index for radio-metric detection of antirheumatoid drugs in blood; and 4) The method may be useful for rapid detection of SH metabolism in blood of connective tissue disorders, subsequent to administration of antirheumatoid drugs. Abnormality in SH metabolism was previously known in these disorders.

REGIONAL LUNG FUNCTION IN CHILDREN WITH VENTRICULAR SEPTAL DEFECT (VSD) AND PULMONARY ARTERY BAND (PAB). S. Treves, R. Sade, R. Williams and A. Castaneda. Harvard Medical School and Children's Hospital Medical Center, Boston, Mass.

Pulmonary artery banding has been used to reduce pulmonary blood flow (PBF) in patients with VSD. PAB however, can produce new physiological disturbances. Ventilation and perfusion studies using xenon-133, a gamma camera and a computer were performed in a group of twelve patients who had previous placement of a PAB. Eleven patients had increased PBF to the left lung (mean=60.28±6.91% of total PBF) and one was decreased (44%). The ventilation perfusion ratio (\dot{V}/\dot{Q}) of the lung with higher flow was reduced (0.74±0.08). Nine of these patients were restudied after operations at which the PAB was removed, the pulmonary artery widened with a patch, and the VSD closed. Post operatively, the distribution of perfusion between the two lungs was normal in three patients, returned toward normal in two patients and was unchanged in three. In one patient the perfusion was reduced below normal on the left lung. The average percent of blood flow to the left lung in the post operative patients was 50.55±8.13%. The \dot{V}/\dot{Q} of the lung with higher flow was .80±0.10%. We conclude that 1) PAB causes blood flow imbalance with relative hyperfusion of the left lung and 2) corrective surgery may not always reverse the abnormality created by the PAB.

TRACE RADIOIODINATED CHLORPROPAMIDE FOR PANCREAS STUDIES. Manuel Tubis, G. T. Krishnamurthy, and John S. Endow. Veterans Administration Wadsworth Hospital Center; and School of Pharmacy, University of Southern California, Los Angeles, Calif.

The purpose of this study is to develop a pancreatotropic radiopharmaceutical containing a suitable gamma emitter for scanning. Chlorpropamide (CPA) has been trace-labeled with I-131 by a simple, rapid exchange procedure to form I-131 chlorpropamide, I*CPA, that can be made with I-123 also. I*CPA is essentially CPA containing an amount of I*CPA equivalent to the carrier-free radioiodine used and should thus behave analogously physiologically like the widely used, hypoglycemic drug. The I*CPA is water-soluble and prepared as an injectable solution, of very low toxicity.

The distribution of I*CPA was studied in mice and shows a significant accumulation in the pancreas and other organs within 5 min. The distribution with time is somewhat similar to that of the water-insoluble iodine analog, iodopropamide I-125, in the hamster, and very much greater than that in the dog at later times, as reported in the literature.

While studies so far in mice indicate a pancreas-to-liver ratio of 1:3, this may represent a species difference which will be determined. The toxicity is low indicating that a potential human dose can be increased to several mCi using I-123 as the tracer. Computer subtraction techniques using Tc Sulfur Colloid and I-123 CPA might be useful for scanning the normal and pathological pancreas. This new radiopharmaceutical is also useful for metabolic studies of the drug. Further extensive studies are planned.

REGIONAL CEREBRAL BLOOD FLOW IN ACUTE PHASE OF SUBARACHNOID HEMORRHAGE. Kazuo Uemura, Koichi Yamaguchi and Takashi Kutsuzawa. Research Institute of Brain and Blood Vessels, Akita, Japan.

Understanding of brain circulation in acute phase following subarachnoid hemorrhage (SAH) is important for reasonable treatment of the patients. This investigation was undertaken to analyze the regional cerebral blood flow (rCBF) and regulation of cerebral vessels, particularly in relation to time from hemorrhage.

Fifty-three rCBF studies were carried out on 41 preoperative patients in conjunction with cerebral angiography. The Xe-133 intra-arterial method of measuring rCBF was carried out using a channel 1' detector and small digital computer.

Result: 1) Within 7 days after onset, though arterial spasm was less frequent (15.8%) and mild, hemispheric CBF decreased to 37.6±8.6 ml/100g/min and vasoparalysis was observed frequently. 2) In 3-7 days after onset, it was noteworthy that hemispheric CBF recovered temporarily (42.9±6.7 ml/100g/min). 3) In 1-2 weeks after onset, disturbance of cerebral circulation and arterial spasm became most pronounced. Hemispheric CBF decreased again (34.2±6.5 ml/100g/min). Uneven perfusion was marked. Vasoparalysis was proved on almost all the cases and was spread widely in the brain. After 3 weeks, cerebral circulation was seemed to recover gradually. 4) Decreased CBF was not always accompanied by arterial spasm but it was proved in the patient with marked spasm.

Conclusion: In acute phase of SAH, there is not only a significant decrease of CBF but also considerable change of regional cerebral hemodynamics in relation to time from onset.

BONE SCAN ABNORMALITY PRODUCED BY INTERACTION OF TC-99m DIPHOSPHONATE WITH IRON DEXTRAN (IMFERON). James D. VanAntwerp, Jack N. Hall, Robert E. O'Mara, and Schuyler V. Hiltz. University of Arizona Medical Center and Tucson Medical Center, Tucson, Az.

Accumulation of various bone scanning agents in extra osseous tissue has been reported by numerous investigators. These have included sites both with and without calcification, and in such entities as primary and secondary carcinoma, cerebral infarcts, normal and abnormal breast tissue. Although medical preparations the patient is taking when the bone scan is performed must at times influence the pattern of deposition of the scanning agent, our knowledge in this area is minimal, and to our knowledge has not been previously reported.

We have observed several patients in which a striking pattern of accumulation of Tc-99m diphosphonate and polyphosphate occurred in areas where iron dextran (Imferon) had been administered by intramuscular injection. A markedly unusual, dense, crescentic area of activity following the contour of the iliac crest was seen in the injected hip when scanned 1 to 6 days following the last injection. Repeat scans at 3 and 8 weeks showed clearing of this activity. The pattern of deposition was strikingly similar in each case and may be characteristic.

Tc-99m alone in vivo (human and rabbit) does not combine with Fe-dextran. Silica Gel chromatography supports this finding. Data from work with rabbits shows dextran does not contribute to the deposition of activity. We believe the most probable mechanism of uptake is combination of reduced technetium with ferric hydroxide as it is released from the iron dextran complex. We feel that this study represents an important step in first observing, then identifying and initiating evaluation of the process of interaction of radionuclides with other medical preparations.

COMPARATIVE EVALUATION OF Tc-99m LABELED HEPATO-BILIARY AGENTS WITH I-131 ROSE BENGAL. Ronald L. Van Heertum, Gopal Subramanian, F. Deaver Thomas, John G. McAfee, Robert C. Hall, Linda Heminger and Paul Vescio. Upstate Medical Center, Syracuse, New York

A definite clinical need exists for a Tc-99m labeled hepato-biliary agent possessing biologic properties similar to rose bengal. The purpose of this study is to

evaluate a number of newer Tc-99m hepato-biliary agents and compare them with I-131 rose bengal (RB). Compounds evaluated include: dihydrothioctic acid (DHT), mercaptoisobutyric acid (MBA), pyridoxal arginine (PyA), pyridoxal glutamate (PyG), and pyridoxal leucine (Pyl). Tc-99m pyridoxal amino acid complexes were prepared as follows: a 5-8 ml mixture of Tc-99m (as pertechnetate), 100 mg pyridoxal and 30 mg of the desired amino acid adjusted to pH 8.0 was autoclaved for 15-30 minutes. The labeling yield was quantitated by electrophoresis (greater than 97%). Tc-99m DHT (3M) and MBA (Medi-Physics) were prepared from commercial kits.

Due to the similarity between baboon and human biliary systems, all compounds were evaluated in a baboon model with a T-tube in the common hepatic duct and inflatable occluder cuffs around the distal common bile and cystic ducts. Blood, bile and urine collections of each Tc-99m compound were obtained simultaneously with I-131 rose bengal over a 3 hour period with occluder cuffs inflated. Resultant clearance and excretion data were correlated with imaging studies performed in rabbits and dogs.

All agents evaluated showed significant accumulation in the bile; however, Tc-99m pyridoxal leucine (Pyl) showed significantly more rapid and higher bile concentrations than the other Tc-99m compounds. Pyl approximated rose bengal bile concentrations for the first 60 to 90 minutes. This agent therefore appears promising as a future replacement for I-131 rose bengal.

IRRELEVANCE OF CONVENTIONAL TARGET/NONTARGET RATIO CONCEPT AS APPLIED TO TUMOR DETECTION. Ramesh C. Verma, Melvin J. Silverstein, L. Stephen Graham, and Leslie R. Bennett. University of California Center for the Health Sciences, Los Angeles, Calif.

The present study was designed to measure the conventional target to nontarget ratios. The role of these ratios in predicting the ability to detect tumors on total body scans using Indium-111 bleomycin (InBIm) was evaluated. Counts per gram were calculated on various tissues obtained at surgery from 17 patients -- 5 with carcinoma breast, 5 with metastatic melanoma, and 7 with miscellaneous tumors. Sufficient counts were obtained to give a standard error of less than 1%. On an average, the tumors contained 10, 6, 8, and 3 times more activity as compared to skeletal muscle, blood, fat and skin, respectively. The tissues were obtained from 2 to 16 days (mean 7 days) following administration of InBIm.

It is interesting to note that a few of these tumors (some larger than 1.5 cm) were missed on the scans even though the average tumor versus surrounding tissue ratio was more than 5. Hence, the ability to detect these tumors on InBIm scans cannot literally be deduced from conventional tumor/background ratios as obtained above.

Therefore, to predict the ability to detect any soft tissue tumor in vivo, one should not only know the relative concentration of tracer per unit mass of target and background tissues, but also their relative total volumes and the exact anatomical relationship of each of these. These factors must be taken into consideration and so specified when evaluating tumor localizing radiopharmaceuticals instead of the conventional target/nontarget ratios alone. (Supported by USPHS Grant 5-T01-GM-01920-06.)

ROLE OF INDIUM-111 BLEOMYCIN IN PREDICTING MALIGNANCY OF PALPABLE BREAST MASSES. Ramesh C. Verma, Melvin J. Silverstein, Larry D. Greenfield, and Leslie R. Bennett. University of California Center for the Health Sciences, Los Angeles, Calif.

Techniques for preoperative evaluation of the true neoplastic status of lumps in the breast would be of great help to the oncologist. Although not specific, Indium-111 bleomycin (InBIm) has shown very avid uptake in malignant tumors. This study was conducted to evaluate the role of InBIm scintigraphy in prediction of the nature (benign or malignant) of palpable breast masses.

Thirty-one adult female patients with a palpable mass (in one breast only) were studied. Both breasts were scanned soon after and 48 hours following the i.v. administration of 4.5 mCi of InBIm. The scans were interpreted as abnormal if asymmetric increase was noted. Anatomical localization of the lesion was not always possible. Subsequently, all patients underwent a surgical biopsy of their breast masses.

Seventeen of the 31 breast masses proved to be malignant at histopathology. Of these, 13 had abnormal increased uptake demonstrated on scans. The remaining 4 (false negative) were probably not detected because of their small size (1-2 cm range).

In 14 patients with benign disease, no difference was noted between the two sides in 10 patients. However, 4 patients (3 with fibrocystic disease and 1 with a rapidly growing fibroadenoma) had distinct asymmetric abnormal uptake in the breast with the palpable mass.

The true sensitivity (percentage of proven malignant tumors showing abnormal accumulation) was 71% (10/14). With an overall accuracy of 74%, InBIm scintigraphy offers a highly promising noninvasive technique for evaluation (benign vs. malignant) of palpable breast masses. (Supported by USPHS Grant 5-T01-GM-01920-06.)

CORRELATION OF INDIUM-111 BLEOMYCIN BREAST SCANNING WITH OTHER NON-INVASIVE TECHNIQUES. Ramesh C. Verma, Melvin J. Silverstein, Larry D. Greenfield and Leslie R. Bennett. University of California Center for Health Sciences, Los Angeles, California.

The present study was undertaken to evaluate the accuracy of physical examination, mammography and Indium-111 bleomycin (InBIm) scintigraphy in detection of malignant primary tumors of the breast.

Thirty-one patients with clinically palpable mass lesions were carefully examined by a surgeon (M.J.S.) for prediction of malignancy on the basis of palpation findings alone. Subsequently these patients underwent mammography and InBIm scintigraphy. These tests were interpreted by independent observers who had no prior knowledge of the case history. All masses were biopsied and examined histopathologically. Malignancy was present in 17 of these patients whereas 14 proved to be a benign lesion.

Mammography had the highest (83%) accuracy i.e. the number correctly diagnosed/Total number of patients. InBIm scintigraphy was next with 74%, followed by clinical examination with 71%. The specificity (correct predictions of benignancy/Total number with benign lesions) of both InBIm and Mammography was above 70% and that of clinical examination 57%. The sensitivity (percentage of proven malignant tumors correctly diagnosed) of each of the above three modalities was higher than 76%.

Although mammography is superior to InBIm scans for evaluation of such patients, our preliminary work in using these as screening tests (i.e. include nonpalpable lesions also) shows that the specificity of mammography and the sensitivity of InBIm scintigraphy falls leading to a better overall accuracy for InBIm. Scanning with InBIm, therefore, constitutes a worthwhile procedure to evaluate the nature of a mass lesion in the breast.

IN VIVO THROMBOSIS MODEL FOR RADIONUCLIDE EVALUATION. Ramesh C. Verma, Milo M. Webber, Pratiba K. Sansi, and Beth Gleghorn. Center for the Health Sciences, University of California, Los Angeles, Calif.

Basic research on clot-localizing radiopharmaceuticals has been hampered by the absence of a good animal model. Experimental models in general thrombosis research often result in an extensive inflammatory reaction in the region of the clot. Since many radioisotopes are known to accumulate in inflamed tissues, attempts were made to develop an animal model for inducing thrombosis without inflammation of the surrounding tissues.

The marginal ear vein of rabbit was chosen for its easy accessibility to direct examination for evaluation of the clots formed and inflammation, if any.

Local intravenous administration of sclerosing agents and application of electrical current are the most common methods used for inducing thrombosis. Evaluation of these techniques showed that they do not reliably produce thrombi and are usually associated with significant inflammation.

The technique devised by us involves systemic intravenous administration of fresh pooled human serum (to induce a transient hypercoagulable state) with immediate application of external pressure over portion of the vein to achieve stasis. A clot forms within 30 minutes. These clots tend to move and embolize after external pressure is removed. However, carefully induced minimal endothelial damage prior to administration of the serum anchors the clot permanently to the vessel wall.

This technique has yielded adherent clots with essentially no inflammation of the surrounding tissues. This model is currently being used for evaluation of multiple agents reported to accumulate in regions of thrombosis and also to evaluate the basic mechanisms governing such localizations.

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IMAGING OF MULTIPLE MYELOMA WITH Tc-99m LABELLED DIPHOSPHONATE. Heinz W. Wahner, Robert A. Kyle, and John W. Beabout. Mayo Clinic and Mayo Foundation, Rochester, Minn.

The role of bone scintigraphy in diagnosis and follow-up in treated patients with bone involvement by multiple myeloma was evaluated. Because of its slightly different mechanism of action, diphosphonate could give results different from those obtained previously with Sr and F. Roentgenographic skeletal surveys and scintigrams were compared in 25 such patients. They were followed for 2 years with both procedures performed every 6-8 months. For comparison, 99 patients with biopsy-proven prostatic cancer were studied in a similar fashion. The % of total lesions found on roentgenograms and scintigrams follows:

	Prostate	Myeloma
Scan and/or X-ray	100	100
Scan only	65	24
X-ray only	8	49
Total on scan	92	56
Total on X-ray	35	78
On both scan and X-ray	27	37

The general demineralization in myeloma seen on X-ray was not apparent on scintigrams. Lesions found only on scans were in all parts of the skeleton but were most frequent in ribs, pelvis, and sternum. All but one patient with significant bone pain had a positive scan. Prostatic cancer data supported results obtained by others and documented the superiority of the scan. The longitudinal study showed increased number of osteolytic lesions in 8 patients by X-ray and in 3 by scan; the number decreased in 2 and 1, respectively. Osteosclerosis was seen in 6 and further bone loss in 1 patient, all by X-ray only. There was no correlation among bone marrow involvement, myeloma protein production, clinical cause of disease, and positive scintigram. The results of scintigraphy in multiple myeloma are similar to those obtained with Sr and F.

EFFECT OF Tc-99m-Sn BONE SCAN AGENTS ON SUBSEQUENT PERTECHNETATE BRAIN SCANS. Anthony G. Walker, Deaconess Hospital, Milwaukee, Wisconsin.

During routine metastatic evaluations, 40 patients underwent bone imaging, followed one to six days later by a TcO₄ brain scan with 16 KClO₄. In 19 of these studies an alteration in the appearance of the brain scan was observed, with moderate to intense uptake by the large venous sinuses, often associated with considerably increased uptake by the choroid plexus. Occasionally, increased uptake was also noted superficially over the cerebral hemispheres. These changes were of sufficient degree in several cases to render clinical interpretation difficult.

This effect was observed following 7 of 7 bone scans with Tc-99m-Sn-pyrophosphate (PYP), in 12 of 22 with polyphosphate (POP), but in none of 11 studies with disodium etidronate. No alteration in appearance was observed in 12 Tc-99m-D.T.P.A. brain scans following PYP bone scans. The intensity of this uptake was related to (1) the amount of stannous ion administered in the bone scan dose, (2) the interval between administration of TcO₄ and the brain scan, and (3) the interval between the bone and brain scans. No effect was observed when the interval exceeded six days.

These findings indicate that Tc-99m-D.T.P.A. is preferable to TcO₄ when a brain scan follows administration of PYP or POP. The altered behavior of TcO₄ following administration of PYP and POP raises the possibility of other unrecognized interactions in multiple radionuclide studies.

COMPARISON BETWEEN CEA RADIOIMMUNOASSAY, CLINICAL RADIONUCLIDE IMAGING AND RADIOLOGICAL EVALUATION OF METASTASES OF BREAST CARCINOMA. Yen Wang, South Hills Health System and University of Pittsburgh Medical Center, Pittsburgh, Pa.

Recently, CEA radioimmunoassay procedure for the detection of malignant disease processes has been approved by the Food and Drug Administration. Primarily, the test is employed in the evaluation of gastro-intestinal malignant diseases. The usefulness of the test in the follow-up of cancer patients and in the evaluation of the treatment's effectiveness has been reported.

This report compares the CEA titres with the clinical findings, radionuclide imaging, and diagnostic x-ray evaluation of breast carcinoma metastases in 75 patients.

The CEA titre determinations by radioimmunoassay proved 94% accurate in 50 normal volunteers. The titres of 25 known breast carcinoma patients with no evidence of metastases was 92% accurate. The titres of breast carcinoma patients who had evidence of metastases or recurrence was 85.6% accurate overall. The CEA titres in the preceding group of patients demonstrated about 97% correlation with radionuclide scan findings, about 86.6% correlation with roentgenographic findings and about 73.3% correlation with clinical findings.

There is a 15% incidence of false negative results in using CEA titres for the detection of metastases. There is good correlation between CEA titres and patients with no evidence of recurrence or metastases. Therefore, CEA titres may be valuable in the follow-up evaluation of cases of breast carcinoma. Although, initial diagnosis of breast carcinoma cannot be satisfactorily made utilizing the method presently available from Hoffman-La Roche Laboratories.

USEFULNESS OF RADIONUCLIDE VENOGRAM ALONG WITH LUNG SCANNING. Yen Wang, South Hills Health System and University of Pittsburgh Medical Center, Pittsburgh, Pa.

The usefulness of radionuclide venograms of the legs along with lung scanning was evaluated in a group of 108 patients. In an early investigation, a dose of 200 to 300 uCi. of ¹³¹I-MAA was injected through a fine dorsal vein of the affected leg, in later investigations a dose of 0.5 to 1.5 mCi. of ^{99m}Tc-Microspheres was used. The leg, thigh and pelvic regions were monitored and simultaneously recorded using the Dyncamera for a period of 0.5 to 1.0 minute. Each area was monitored repeatedly to determine the degree of retention and delayed accumulation. Approximately 30 minutes post-injection the lung scan was performed. The same technique was repeated for patients who returned for evaluation of resolution of an infarct. The findings in this group of patients were interesting and significant (see attached figures).

1. The combination procedure is valuable in detecting lung infarctions and their possible origin in the lower extremities, (about 60.7% of pulmonary infarct patients).

2. The combination is also useful in detecting the silent infarction and/or silent thrombophlebitis, particularly, noted in about 60.0% of the abnormal venograms in a group of 52 patients. 17 of the 28 patients with positive infarction findings on the lung scan had abnormal venograms, only 6 of the 17 had a clinical history of thrombophlebitis, and the venogram greatly increased the incidence of detection of thrombophlebitis. Another group of 24 patients had normal lung scans and all had abnormal venograms. Clinically only 10 of these 24 patients had a history of thrombophlebitis.

3. The combination procedure should be used for follow up of patients with known infarctions and thrombophlebitis.

METHODS FOR THE RAPID SYNTHESIS AND PURIFICATION OF AMINO ACIDS LABELED WITH CARBON-11¹. Lee C. Washburn, Tan Tan Sun, B. W. Wieland, and R. L. Hayes. Oak Ridge Associated Universities², Oak Ridge, Tenn.

Animal studies using C-14-labeled compounds have demonstrated the potential value of C-11-labeled L-aminocyclopentanecarboxylic acid (ACPC) as a tumor-scanning agent and of C-11-labeled DL-tryptophan as an agent for pancreas scanning. Because of the short half-life of C-11 (20.5 min), techniques for the rapid synthesis and purification of these compounds are required. The analogous C-14-labeled materials have been used in the development of these methods. Both amino acids have been synthesized by modifications of the Strecker amino acid synthesis, starting with cyclopentanone for ACPC and L-acetyl-3-

indoleacetaldehyde semicarbazone (a derivative of the corresponding unstable aldehyde) for DL-tryptophan. Treatment of these starting materials with $(\text{NH}_4)_2\text{CO}_3$, NH_4Cl , and KCN at elevated temperatures and pressures yields the hydantoin, which undergoes basic hydrolysis in a second step to give the amino acid. Yields of 70-80% for ACPC and 10-20% for DL-tryptophan have been obtained using total reaction times of 14 and 22 minutes, respectively. Rapid purification is achieved by means of column chromatography on a cation exchange resin. Since the Strecker amino acid synthesis is quite general, we feel that we have a potential method for the synthesis of many C-11-labeled amino acids which are of interest in nuclear medicine.

¹ This investigation was supported by USPH Research Grant 1 ROI CA 14669-01.

² Under contract with the United States Atomic Energy Commission.

ARTHROSCINTIGRAPHY WITH Tc-99m HSA IN THE DIAGNOSIS OF DISSECTING POPLITEAL CYST. A.E. Watkins, K.P. Poulouse, M. Goodyear and R.C. Reba. Washington Hospital Center and George Washington University, Washington, D.C.

In a patient presenting with acute tender swelling of the calf and/or popliteal fossa, the differential diagnosis of sural thrombophlebitis from dissecting popliteal cyst is difficult, but very important. The easiness and accuracy of arthroscintigraphy following intraarticular injection of I-131 HSA in the diagnosis of popliteal cyst dissection has been established recently.

A total of 15 patients were investigated. Seven patients were already receiving anticoagulants before the isotope procedure. Following intraarticular injection of 3-5 mCi of Tc-99m HSA in a volume of less than 1 ml, scans of the affected extremity were obtained 3 and 24 hours post injection using a 5" crystal rectilinear scanner.

Evidence of popliteal cyst rupture in the scan was seen in 5 patients including one with a negative arthrogram. Of the remaining 10 patients with normal scintigrams, one had a popliteal calf swelling, typical of a ruptured Baker's cyst. Although the arthrogram was also negative in this patient, exploration of the popliteal fossa was undertaken. Surgery did not reveal Baker's cyst but rather a large clot in the popliteal vein. Venograms were done in six patients because of the strong clinical suspicion of thrombophlebitis. There was no disagreement between the venogram and the arthroscintigram results.

This study suggests that arthroscintigraphy is an accurate procedure for the diagnosis of dissecting popliteal cyst. Thus early diagnosis can prevent inadvertent administration of anticoagulants. Technetium-99m HSA appears to be a suitable substitute for I-131 HSA for arthroscintigraphy. (Supported by USPHS Grant GM 20543)

RADIATION DOSE TO THE LUNGS FROM Xe-133. Evelyn E. Watson, Barbara Y. Howard*, and Roger J. Cloutier. Radiopharmaceutical Internal Dosimetry Information Center, Oak Ridge Associated Universities, Oak Ridge, Tennessee. *University of Virginia School of Medicine, Charlottesville, Virginia.

The radiation dose to the lungs from Xe-133 is directly proportional to the time integral of Xe-133 concentration in the lungs. Because the behavior of Xe-133 used for lung studies varies considerably in different disease states, we have investigated the effect of several biological models on the cumulated concentration of Xe-133 in the lungs. The models studied were based on clinical observations of Xe-133 retention and were of four general types: (1) equal exponential wash-in and wash-out rate constants; (2) unequal exponential wash-in and wash-out rate constants; (3) single compartment wash-in and two-compartment wash-out; and (4) single compartment wash-in and three-compartment wash-out. For multiple compartment wash-out, the fraction of activity associated with each compartment was also varied. The cumulated concentrations for the different models indicate that the radiation dose may be greatly underestimated by assuming the wash-in and wash-out rate constants are equal. Even when the major portion of the Xe-133 is washed out of the lungs rapidly, small amounts (<1%) of the inhaled Xe-133 retained in the lungs would also greatly increase the cumulated concentration and the radiation dose.

ARE ALL GALLIUM CITRATE PREPARATIONS THE SAME? Alan D. Waxman, Tom Kawada, Jan K. Siemsen and Walter Wolf. LAC/USC Medical Center, Los Angeles, California.

Recent studies on brain imaging using gallium-67 citrate have revealed some clinical differences. Using chromatographic techniques, we have analyzed gallium citrate obtained from manufacturers A, B and C as shown on Table 1.

Components	(A)	(B)	(C)
Gallium-67	2 mCi/ml	2 mCi/ml	1 mCi/ml
Sodium citrate	25 mg/ml	2 mg/ml	2.3 mg/ml
Sodium chloride	-----	68 mg/ml	9 mg/ml
Benzyl alcohol	1%	0.9%	None

Chromatography was carried out using silica impregnated glass fiber with 85% methanol in water as the solvent.

Gallium-67 citrate supplied by vendor A clearly differed from B and C in chromatographic mobility. When citrate was added to material of vendor B to bring the final concentration to 25 mg/ml, the chromatographic mobility changed dramatically. Addition of benzyl alcohol had no effect.

At 2 mCi/ml, the present solutions are 8.5×10^{-8} Molar, so that to form the 1:1 gallium citrate complex not more than 1.47×10^5 mg/ml of sodium citrate are needed. The product of vendor B had a citrate concentration of 2 mg/ml, or 10^5 times the concentration of Ga-67 present, assuming no gallium carrier. Thus a 2 mg/ml to 25 mg/ml change in citrate concentration should have little or no effect on the complex or resultant chromatogram. Whether ionic strength, complexation between gallium citrate and some other metal, or some other phenomenon is the basis of our findings remains to be seen. These chromatographic differences reveal a difference in chemistry, which may be carried over into differences in rates of biochemical binding, distribution and localization, and result in clinical differences.

GALLIUM SCANNING OF CRANIAL AND INTRACRANIAL INFECTIONS. A.D. Waxman and J.K. Siemsen, Nuclear Medicine Section, Los Angeles County-University of Southern California Medical Center, Los Angeles, California.

Gallium uptake in inflammatory lesions has been well documented. The use of gallium in the differential diagnosis and detection of cerebral lesions has also been reported. However, these reports have dealt mainly with tumor detection and the differentiation of tumor from infarction. The purpose of this report is to evaluate the detection of cranial and intracranial infections using gallium-67 citrate.

Fifteen patients with documented cranial and intracranial infections were evaluated using standard delayed 4 hour technetium brain scan technique. Comparable gallium-67 citrate brain scans were done 3 hours to 4 days post injection.

In 5 of 5 cases of documented brain abscesses the lesions were clearly demonstrated with gallium. In 2 of these cases the lesions were missed with technetium. A single case of osteomyelitis of the skull was not evident with pertechnetate and polyphosphate but clearly seen with gallium. Three cases of CNS tuberculosis were detected with gallium and technetium. Sinusitis was demonstrated more precisely with gallium than technetium while the detection of meningitis was equally poor for both radionuclides.

We conclude that gallium brain scanning is an important adjunctive study in the evaluation of cranial and intracranial infections.

TECHNETIUM-99m GLUCOHEPTONATE AS A BRAIN SCANNING AGENT: A CRITICAL COMPARISON WITH PERTECHNETATE. Alan D. Waxman, Doina Tanacescu, Jan K. Siemsen and Ralph S. Wolfstein. LAC/USC Medical Center, Los Angeles, Calif. and Cedars-Sinai Medical Center, Los Angeles, California.

Technetium-99m glucoheptonate (GH) has been proposed as a superior brain scanning agent because of its rapid renal blood clearance. The purpose of this study was to compare brain lesion detectability with pertechnetate (Tc04) and GH scanning and to compare early (30 minutes) GH scans to delayed (3-5 hours) GH scans.

42 patients were evaluated with paired delayed Tc04 and GH studies, using 20 mCi of each agent. 57 positive GH scans were evaluated comparing early with delayed studies.

Either scintillation cameras or double headed rectilinear scanners were used, but the same instrument was always employed for both parts of a comparative study. Qualitative estimation of the lesion-to-calvarium concentration ratio served as reference for comparison.

In 8 of 17 cases of documented tumors (47%) and in 2 of 10 cases of infarction the delayed GH scans were superior to the delayed Tc04 scans. One lesion in each group was noted only on the GH study. 22 of 57 (39%) comparisons between early and delayed GH scans showed the late study to be superior. The opposite was not seen. An additional 5 lesions in this group (9%) were seen only on the delayed study.

We conclude that delayed GH scanning is superior to delayed Tc04 scanning and to early GH scanning in producing a higher target-to-nontarget ratio in brain lesions. Early GH scans are significantly inferior in spite of the rapid blood clearance. In this respect, GH is no different than other technetium radiopharmaceuticals used for brain scanning.

RADIONUCLIDE TOMOGRAPHIC SCANNING IN ACUTE MYOCARDIAL INFARCTION (AMI). Paul M. Weber, Donald Van Dyke, Leo V. dos Remedios, and Hal O. Anger. Kaiser-Permanente Medical Center, Oakland, University of California, Berkeley, Calif.

Because most radiopharmaceuticals known to concentrate in infarcted myocardium also concentrate in normal surrounding tissues, e.g., bone, liver, we attempted to distinguish uptake in infarcted from normal tissue by longitudinal tomography. Ninety sequential patients admitted to the Coronary Care Unit, 42 controls referred for bone scanning, and selected patients with other cardiovascular diseases were imaged with the Anger tomoscanner 1 hr or more after injection of one of several compounds, e.g., Tc-99m pyrophosphate (PYP), diphosphonate (EHDP), glucoheptonate, or F-18. The presence of infarction was evaluated by standard epidemiologic criteria. All 32 patients with definite AMI had positive myocardial tomoscans though in two uptake was minimal. Tomoscans were positive in several patients with cardiovascular disease without AMI; two with old infarcts, one each with crescendo angina, left ventricular aneurysm, and acute pericarditis. No scans from alcoholic cardiomyopathy were positive. Several studies negative with EHDP were positive with PYP; F-18 failed to concentrate visibly in infarcted myocardium. Longitudinal tomographic scanning effectively detects increased myocardial labeling and separates this activity from that in adjacent tissues. Since 20% of control subjects show weak uptake in the cardiac region 1 hr but not 3 hr after injection, delayed imaging is recommended. The subgroup of patients with positive scans without AMI are being further studied.

TRANSPLACENTAL TRANSFER OF GA-67. Audrey V. Wegst, Ralph G. Robinson, and Richard C. Riley. University of Kansas Medical Center, Kansas City, Kans.

Diagnostic Nuclear Medicine procedures are discouraged in pregnant women. This is due in part to the lack of precise radiation exposure data to the fetus at specific gestational ages, which makes estimation of risk/benefit ratios difficult. In order to accumulate the necessary biological data for such a fetal dose calculation, it is necessary to know the maternal radioactivity distribution, the placental accumulation, the fetal content and distribution, as well as the effective half-life. We are modeling the kinetics of each major radiopharmaceutical during pregnancy in animal systems and report herein our results only with gallium-67, though wherever possible our studies were done with dual isotopes.

We studied pregnant rats at 13, 15, 17, 19, and 21 days gestation and pregnant rabbits at 14, 19, 24, and 29 days gestation. The mother was injected with Ga-67, killed 2 or 6 hours after injection, and the maternal organs along with the fetal material and placentas were removed for counting. The rabbits were given Se-75 with the Ga-67 and the 2 isotopes separated by decay of the Ga-67. The percent of injected dose per gram and per organ or fetus was calculated.

Less than 0.1% of the injected dose per gram of fetus was found in the rat and less than 0.02% per gram in the rabbit fetuses, which precluded fetal distribution studies. The placental uptake in the rat increased from 2.7% per gram at 15 days gestation to 6.8% per gram at 21 days, 6 hours after injection. The rat uterine uptake is approximately 1% per gram throughout pregnancy.

If this data can be extrapolated to humans, the fetal self-irradiation from a maternal injection of Ga-67 is insignificant and could be calculated by considering only the contribution from maternal and placental tissues.

VOLTAGE FLUCTUATION AS CAUSE FOR IMAGE DEGRADATION IN SCINTILLATION CAMERA. Jerome M. Weinraub, Klaus W. Buzzi, and Gerald A.L. Irwin. Nassau County Medical Center, East Meadow, N.Y.

Rapid line voltage changes are a common cause for degradation of scintiphoto image quality. These voltage irregularities result from voltage variations in the supply to the building and from inconstant demand within the building. In our institution this problem became so severe that reliable scintillation camera function was impaired. Our camera, a Searle Radiographics Pho/Gamma HP, needed to be re-peaked at least hourly to preserve image quality. Image size also fluctuated widely with voltage changes. To improve performance, a Sola 3000 Voltamp Harmonic Neutralized voltage compensating transformer was installed and our two scintillation cameras, two microdot imagers, and one computer were coupled to it. Image quality was subsequently improved, image size was stabilized and the voltage peak did not drift. The use of voltage compensating transformers would then seem to be a relatively easy and inexpensive answer to a problem that promises to become worse with the energy crisis.

TECHNETIUM-99m POLYPHOSPHATE IN DIFFERENTIAL DIAGNOSIS OF BREAST MASSES. Jerome M. Weinraub, Robert Rosenberg, and Gerald A.L. Irwin. Nassau County Medical Center, East Meadow, N.Y.

Frequent reports have been made of breast masses concentrating technetium phosphate compounds. Twenty eight female patients, age 27 to 84, presenting with breast masses, were injected with Tc-99m polyphosphate. Serial flow pictures were obtained, followed by static camera views of both breasts at 15 to 30 minutes. Interpretation was made without any clinical supporting data, and afterward correlation was made with mammography and/or pathology reports. No specific differences were discerned between benign and malignant masses on the flow study. The static studies showed malignant masses had two distinct characteristics: they were more vivid than benign masses, and had more clearly defined borders. Of the 30 patients, 12 had proven malignancy of which the static scans defined 11. There were no false positive readings. The malignancy not revealed by the breast scan was a very rapidly growing inflammatory carcinoma. All benign masses were correctly identified. The use of Technetium-99m Polyphosphate appears to be useful in differentiating benign from malignant breast masses.

RADIOISOTOPIC TECHNIQUES IN THE DEMONSTRATION OF EXPERIMENTAL AND CLINICAL HYDROSYRINGOMELIA PATHOGENESIS. H. Wellman, P. Hall, J. Kalsbeck, and S. Lewis, Indiana University Medical Center, Indianapolis, Ind.

Hydrosyringomyelia as it develops in children with myelomeningoceles, originally thought to have its pathogenesis in ischemia, can be shown experimentally to result from disordered ventricular hydrodynamics. Clinically, diagnosis of this entity is very hazardous with contrast media. Thus, Tc-99m albumin (0.5 mCi) ventriculography was developed in 12 dogs in whom Kaolin hydromyelia was experimentally induced. Subsequent "decompressing" dilatation of the central spinal canal (CSC) results in a shunt between the ventricular system via lumbosacral spinal subarachnoid space (SAS) which could be demonstrated 6-30 hours post Kaolin injection. Three normal control dogs demonstrated no activity below the mid cervical regions. Proof of CSC filling was manifest in the narrower width of the CSC than the SAS and also in root sleeve filling when the SAS was separately injected. In 2 animals separate serial aliquots of CSF post ventricular injection confirmed much earlier appearance of activity in the CSC and much later in the SAS. Syringes were demonstrable with

scintimaging as a chronic effect. The techniques have been applied with success clinically to diagnose the presence of hydromyelia in children with myelomeningoceles.

CANINE MYOCARDIAL INFARCT SCINTIMAGING WITH DMSA COMPARED TO OTHER REPORTED Tc-99m(Sn) COMPOUNDS. H. Wellman and D. Schauwecker, Indiana University Medical Center, Indianapolis, Ind.

At least three reported Tc-99m(Sn) compounds are reported for myocardial infarct (MI) scintimaging: tetracycline (TCN), pyrophosphate (PYP), and glucoheptonate (GLUH). TCN localization is slow (24H) and PYP has high MI/normal tissue but a drawback of concentration in overlying bone. GLUH is reported to have lesser concentration in MI tissue than PYP. Dimercaptosuccinic acid (DMSA) mimics the action of organic mercurials, which localize in infarcted tissue and this study intercompares DMSA to the above. Serial control cardiac scintimages over a 20 H period in three dogs for each compound were compared with the series for 20 H. after ligating their distal left anterior descending coronary artery. At 20 H. post ligation, a final injection of the agents and subsequent scintimages assessed the visualization of the older evolving MI for four hours and thereafter the dog was sacrificed, with subsequent coronary angiography, scintimaging of the excised heart, and tissue studies. Computer analyses of MI uptake were compared with tissue data. TCN was clearly inferior. With PYP scintimaging, small MIs could easily be missed even though tissue ratios are highest. A panel of observers judged DMSA and GLUH about equivalent in demonstrating MIs, although GLUH tissue ratios were higher. In vivo computer "tissue dissection" appears to more accurately reflect scintimaging conditions than classical tissue ratios.

A NEW SCANNING SYSTEM FOR USE WITH THE SCINTILLATION CAMERA. D.L. WIESELER and A.S. ZIMMERMAN. St. Francis Hospital of Lynwood, Lynwood, Calif.

A novel method for total body scanning with a scintillation camera has been developed and evaluated in a clinical situation. A twelve inch long by five inch wide collimator is used, with holes converging in one direction but diverging in the other. The resulting field of view is a line, with best focus at a distance of three inches from the collimator face and with a length of eighteen inches at this distance. The X-deflection of the camera's CRT is disconnected so that activity is displayed as a narrow line on the phosphor.

A motor driven table-top moves the patient under the collimator, perpendicular to the line of view, while a motor driven cassette moves X-ray film in front of the CRT, perpendicular to the line response. The patient and film move in a ratio of five to one, regardless of the speed or direction of travel. In this manner a six foot long by eighteen inch wide field may be displayed on a sheet of X-ray film in one pass. The method has an inherent plane of best focus, similar to that of a rectilinear scanner.

An important feature is that there no modifications to the camera and any camera may be used. The table is mobile and may be used for static imaging as well.

The system described is ideal for total body scanning and for many other studies which benefit from a larger field of view.

CARBON-11 AMINONITRILES. M. B. Winstead, P.J. Widner, J. L. Means, M. A. Engstrom, G. E. Graham, A. Khentigan, T. H. Lin, J. F. Lamb, and H. S. Winchell. Bucknell University, Lewisburg, Pa. and Medi-Physics, Inc., Emeryville, Ca.

This study describes the preparation and scintigraphic evaluation of the distribution pattern in dogs of structurally related aminonitriles labeled with carbon-11. C-11

HCN was collected in water containing carrier NaCN following 22 MeV proton bombardment of 99% N₂ - 1% H₂ gas mixture for 1 hr. Ten C-11 α -N-alkylaminophenylacetonitriles and nine C-11 α -N-arylaminophenylacetonitriles were prepared from C-11 NaCN and the corresponding Schiff base. All compounds showed initial blood pool distribution with accumulation of activity in brain, heart, lung, liver, and kidney. Prolonged retention of activity in the blood pool was observed with α -N-methyl-, ethyl-, propyl-, isopropyl-, butyl-, isobutyl-, sec-butyl-, and tert-butylaminophenylacetonitrile. Several aminonitriles showed pronounced accumulation of activity in brain, including α -anilino- and α -p-chloroanilinophenylacetonitrile, and, to a lesser extent, α -p-toluidino- and α -p-anisidinophenylacetonitrile, and α -anilino-p-tolylacetonitrile. The extent and rapidity of such accumulation suggests remarkably high extraction efficiency of these compounds by the brain. These aminonitriles, in addition to α -anilino-p-chlorophenyl- and α -anilino-p-anisylacetonitrile, showed marked accumulation of activity in lungs and liver with excretion of activity in bile. α -p-Anisidinophenylacetonitrile showed significant retention of activity in heart. In general, the more polar the compound the greater the accumulation of activity in kidney with excretion in urine, whereas activity of less polar compounds accumulated largely in liver with excretion in bile. These results provide some correlation between chemical structure and distribution pattern of the compounds studied and suggest the diagnostic utility of some of these compounds for organ visualization and for measuring regional brain blood flow.

RENAL VISUALIZATION DURING TECHNETIUM-99m DIPHOSPHONATE BONE SCANNING IN PATIENTS WITH SYMPTOMATIC PAGET'S DISEASE. Peter F. Winter and Philip M. Johnson. College of Physicians and Surgeons, Columbia University, New York, N.Y.

The significance of the relative intensity of renal activity in bone scans in symptomatic Paget's disease was evaluated in 26 patients referred for treatment of this disease. Prior to treatment, each patient underwent biochemical evaluation and skeletal radiography. Bone scanning was routinely performed 3 hours after administration of Tc-99m diphosphonate, 15 mCi.

The intensity of renal activity was classed as Normal (equal to or greater than that in uninvolved vertebrae) or Poor (significantly less than that in normal vertebrae). Underlying renal disease was excluded by appropriate means. The hypothesis tested was that the intensity of renal activity was inversely related to the extent and/or activity of Paget's disease. For this purpose, 3 measures of disease activity and/or extent were evaluated: the serum alkaline phosphatase level, the 24 hour urinary hydroxyproline excretion and the percent of radiographic skeletal involvement, determined by standard methods.

Seventeen patients exhibited Poor renal activity; in this group the mean values of the serum alkaline phosphatase level, 24 hour urinary hydroxyproline excretion and percent of skeletal involvement were significantly higher than in the group of 9 patients with Normal renal activity ($p < 0.05$, 0.025 + 0.025 respectively).

These findings indicate that the bone:renal tracer concentration ratio shifts toward bone in extensive and/or active osteoblastic skeletal disease. We are currently investigating methods to refine these determinations by data processing methods.

RADIOPHARMACOKINETICS OF 5-FLUOROURACIL. Walter Wolf, Jeffrey A. Berman and Jashovam Shanl. Radio pharmacy Program, University of Southern California, Los Angeles, Calif.

Determination of the optimal dose of chemotherapeutic agents remains a key problem in pharmacology, especially when the agent is highly toxic. The use of γ -emitting radionuclides for *in vivo* drug distribution and kinetics can be accomplished using the techniques of nuclear medicine.

5-Fluorouracil (5FU) is a well established antineoplastic agent, but only around 28% of patients respond to the "standard" dose. 5FU can be labeled with ¹⁸F, a short lived positron emitter. A study was conducted of the kinetics of 2-¹⁴C-5FU to determine if the time frame available was adequate to obtain significant information.

Mice bearing sarcoma 180 were administered 2-¹⁴C-5FU and sacrificed 10, 15, 30, 70 and 120 mi-

minutes post administration. The agent was used both with or without carrier and administered either I.V. or *per os*. Tissue distribution was studied using whole body autoradiography and the target organs were kidney, liver, bladder and tumor, with one fraction undergoing rapid urinary clearance. Significant tumor localization was observed at 30 and 70 minutes; tumor localization is highest following I.V. administration.

Experiments using ^{18}F -5FU for the study of the rate of *in vivo* distribution and localization are in progress, using either a scanner or a camera with computer interphase. It is expected that both the radiopharmacokinetics and this surveillance monitoring will enhance and optimize chemotherapeutic effectiveness of this and other anti-neoplastic drugs.

RADIOASSAY OF TOTAL IRON-BINDING CAPACITY OF THE SERUM (TIBC). Hideo Yamada, and Hiroshi Saito.
Nagoya University Hospital, Nagoya, Japan.

The radioassay method of TIBC by eliminating serum iron from transferrin with resin and citric acid was developed by Saito, and a resin strip was introduced for the simplification of the procedure, as for determining unsaturated iron-binding capacity (UIBC). The radioassay TIBC was compared with the value by immunodiffusion, colorimetry, and radioassayed UIBC plus serum iron (SI). These TIBC values were in good agreement each other, and the best accuracy was obtained by radioassay due to the elimination of iron contamination, and simplicity.

The highest TIBC value was 522 $\mu\text{g}/100\text{ ml}$ in a patient with iron deficiency anemia, and the highest mean TIBC was 418 ± 41 (mean \pm standard deviation) of iron deficiency anemia group. Mean TIBC of normal males and females were 316 ± 30 , and 356 ± 39 respectively. The lowest value, comparable to the case of congenital atransferrinemia, was 54 due to severe protein loss at the rate of 41%/day. There found 25 cases out of 550 tests having TIBC lower than 200: 4 cases of aplastic anemia, 3 cases of erythroleukemia, Hodgkin's disease, and uterine cancer, 2 cases of hereditary spherocytosis, and a case of liver cancer, lung cancer, chordoma, renal failure, malabsorption syndrome, cerebral embolism, hemosiderosis, and protein losing enteropathy. Among the 25 low TIBC cases 11 cases were malignancies.

The comparative study of TIBC with UIBC and SI proved the usefulness of this *in vitro* test.

LEUCOCYTE LABELING FOR ABSCESS DETECTION. M. G. Yeates, J. Sarchilli, P.D. Vescio, R.J. Blair and J. G. McAfee.
Upstate Medical Center, Syracuse, New York.

This study was designed to assess whether the preincubation of blood with various radiopharmaceuticals would improve abscess detection as has been reported with Ga-67 citrate.

Pyogenic abscesses were produced in the rabbit by implanting a gelatin capsule containing feces into the anterior abdominal wall. A sterile chemical abscess was also produced in each rabbit by injecting turpentine into the rabbit's thigh. In 2 groups of rabbits, 30 ml of blood was withdrawn and incubated with Ga-67 citrate or In-111 chloride. The blood was then centrifuged, the plasma discarded and the labeled cellular fraction reinjected. Two other groups of rabbits received intravenous Ga-67 citrate or In-111 chloride without any preincubation. Radioassay was performed after the completion of Anger camera imaging at 24 hours post injection.

Abscess concentration using the labeled cellular fraction was significantly higher than that achieved by direct IV injection ($p < .005$). Ga-67 citrate, whether administered as the labeled cellular fraction or by direct intravenous injection, achieved higher abscess concentration than In-111 chloride ($p < .05$). Pyogenic abscesses achieved higher concentration than chemical abscesses in all groups ($p < .005$). On imaging, the chemical abscesses were more clearly demonstrated than the pyogenic abscesses because of lower background.

Incubation of human whole blood with two antimalarial analogues, I-125 Acridine and I-125 Quinoline, resulted in relatively high labeling of the cellular fraction as determined by cell separation with methyl cellulose and gravity sedimentation. These agents are being further evaluated in the rabbit abscess model described above.

MULTI-RADIONUCLIDE STUDIES OF FILLING DEFECTS IN LIVER AND SPLEEN OF PATIENTS WITH CANCER. Samuel D.J. Yeh, Robert D. Leeper and Richard S. Benua.
Memorial Hospital & Cornell Medical College, N.Y.N.Y.

The purpose of this study was to find if multi-radionuclide scanning would improve the diagnostic specificity of liver and spleen scans. ^{67}Ga citrate, ^{111}In bleomycin or $^{113\text{m}}\text{InCl}_3$ were chosen to further study the nature of focal defects in $^{99\text{m}}\text{Tc}$ sulfur colloid scans. Patients were chosen from the 45% positive cases from a total of 6,000 liver scans performed in the past two years.

Increased ^{67}Ga uptake was found in 32 of 43 patients with hepatoma (75%) and in 90% of cases when well differentiated. Failure to demonstrate increased uptake was found most often in bile duct Ca or tumor with atypical histology.

Fourteen of 17 patients (82%) with colon cancer had cold areas in both colloid and ^{67}Ga scans. In patients with focal liver and spleen defects, increased ^{67}Ga uptake was found among all 17 with RCS (12 in liver, 3 in spleen, 2 in adjacent areas), 83% of 12 with LSA, 84% of 25 with Hodgkin's and 55% of 11 with melanoma. Increased ^{67}Ga uptake in the cold areas was usually not seen in other types of malignancy.

Increased ^{111}In bleomycin uptake in cold areas was demonstrated in all 6 cases of hepatoma, and in several patients with RCS, Hodgkin's disease, and malignant melanoma but not in the metastases from other malignancy. Increased iodide uptake was found in the liver metastases from thyroid cancer and decreased blood pool in colon cancer.

It is concluded that multi-radionuclide studies may increase the specificity of liver scan diagnosis and provide important clues about the nature of these lesions.

HIGH RESOLUTION OPTIMAL COLLIMATORS FOR 70 to 167 keV GAMMA RAYS. Haim Zaklad, Stephen E. Derenzo, Thomas Budinger.
Lawrence Berkeley Laboratory, Berkeley, Calif.

The improvement of spatial resolution for emission imaging in nuclear medicine for isotopes such as Tc-99m and Tl-201 requires not only an improved detector (such as the germanium or liquid xenon cameras under development) but also improved techniques in the design and construction of optimal collimators having a very large number of fine channels.

An optimal collimator to be used in conjunction with the multi-wire liquid xenon gamma camera (resolution 3 mm FWHM) was constructed from corrugated lead sheets to yield 150 triangular channels per square cm (septum thickness 0.15 mm; channel length 12 mm). Leakages due to the imperfect mating of the lead sheets have been eliminated by suitable shaping of adjoining sheets. Images *in vivo* using the above camera-collimator combination demonstrate 4 mm FWHM at a distance of 5 cm from the front face of the collimator.

The effect of various channel shapes on the geometrical transmission and its two-dimensional point spread functions are discussed. For equal average FWHM, the circle, square, hexagonal and triangular channels have relative geometrical transmissions of 1, 1.01, 1.10 and 1.37 respectively. For equal rms the relative transmissions are 1, 1.0, 1.10, and 0.88 respectively. The geometrical point spread function of the triangle is relatively narrow with a broad tail.

Examples of optimal collimators are tabulated for 70, 140 and 167 keV, resolutions from 2 mm to 10 mm FWHM, and imaging distances from 5 cm to 15 cm. The results are compared with two commercially available collimators and show that collimators optimized for specific resolutions and depths can yield some improvements in transmission (e.g. 30% at 5 cm).

We conclude that optimal collimators for high resolution imaging (better than 4 mm FWHM) must and can be easily constructed to alleviate the burden of the losses in geometrical transmission.

RADIOCHEMICAL PURITY AND STABILITY OF COMMERCIAL Tc-99m-Sn-DIPHOSPHONATE KITS USING A NEW CHROMATOGRAPHY TECHNIQUE. A. Michael Zimmer and Richard A. Holmes. The Medical College of Wisconsin, Milwaukee, Wisconsin

The radiochemical purity of four commercially available technetium-99m diphosphonate (Tc-DiP) kits was determined using a chromatography technique that differentiated technetium-99m pertechnetate, Tc-DiP, and hydrolyzed reduced technetium-99m. The chromatographic procedure involved spotting the radiopharmaceutical on Gelman instant thin layer chromatography-silica gel (ITIC-SG), developing the strip in acetone, air drying, and re-developing the chromatography strip in normal saline. The Tc-DiP kits included: Osteoscan (Proctor and Gamble); HEDSPA (Union Carbide); Diphosphonate (Diagnostic Isotopes) and MPI Bone Scintigraphin (Medi-Physics). Each kit was

prepared daily on successive days by adding either methyl ethyl ketone (MEK) extracted technetium-99m (Medi-Physics) or technetium-99m generator eluate (Hallinckrodt). The stability of the Tc-DiP kits was also determined hourly for as long as 5 hours after preparation.

The radiochemical purity for three commercial Tc-DiP kits was consistently greater than 95 percent. The other kit failed to achieve 95 percent purity using pertechnetate eluted from a generator and 85 percent purity using MEK extracted pertechnetate. More daily consistent radiochemical purities were achieved with MEK extracted technetium-99m, however, higher daily radiochemical purities were obtained with generator produced technetium-99m.

The entire chromatographic procedure took less than 15 minutes to perform. No significant degradation to skeletal image quality was observed when the Tc-HR concentration was less than 5 percent.

TECHNOLOGISTS' SCIENTIFIC PROGRAM

The following papers have been accepted for the Technologists' Scientific Program. Complete abstracts may be found in the June issue of the JOURNAL OF NUCLEAR MEDICINE TECHNOLOGY.

RADIONUCLIDE TECHNOLOGY IN THE DIAGNOSIS AND MANAGEMENT OF THE TRAUMATIZED PATIENT. Larry E. Alt, Barbara Koch, Kenneth B. Miller, Kathy A. Virant, and B.C. Berg. St. Francis Hospital and Peoria School of Medicine, University of Illinois, Peoria, Ill.

CONVENIENT, INEXPENSIVE TRAPPING OF RADIOXENON. Norma S. Anderton, Gary Myers, and Paul H. Murphy. St. Luke's Episcopal-Texas Children's Hospitals, Houston, Tex.

MULTI-PURPOSE DOUBLE-BARREL SYRINGE: AN AID IN THE ADMINISTRATION OF RADIOPHARMACEUTICALS. Sheldon J. Ashley. Flushing Hospital and Medical Center, Flushing, N.Y.

IODINE-125-DIGOXIN RADIOIMMUNOASSAY: KIT COMPARISON. D.J. Battaglia, C.F. Burkhead, M.L. Cianci, and O.B. Hunter, Jr. Oscar B. Hunter Memorial Laboratory, Washington, D.C.

PDS 3 COMPUTERIZED RADIOIMMUNOASSAY: MODIFICATIONS. D.J. Battaglia, M.L. Cianci, C.F. Burkhead, and O.B. Hunter, Jr. Oscar B. Hunter Memorial Laboratory, Washington, D.C.

TECHNETIUM-99m-ALBUMIN WALL MOTION STUDY FOR LEFT VENTRICULAR WALL MOTION. E. Botvinick, C. Boyce, L. Bunz, and D. Shames. University of California, San Francisco, Calif.

A TECHNICAL COMPARISON OF SCANNER AND CAMERA IMAGING SYSTEMS USING THE MODULATION TRANSFER FUNCTION (MTF) AS A FUNCTION OF DEPTH. Michael R. Budge. Toronto Institute of Medical Technology (Toronto General Hospital), Toronto, Ontario, Canada

HUMAN PANCREATIC IMAGING WITH ¹³N-L-ALANINE. C.C. Chang, J. Takahashi, H.H. Neely, and D.D. Bobinet. Veterans Administration Hospital, Sepulveda, Calif., and UCLA Biomedical Cyclotron Facility, Los Angeles, Calif.

RAPID DETERMINATION OF FREE PERTECHNETATE IN LABELED RADIOPHARMACEUTICALS. Lelio G. Colombetti, Steven Pinsky, Stephen Marlien, and Angel Quaiot. Michael Reese Hospital and Medical Center, Chicago, Ill.

THE ANGER RECTILINEAR TOMOGRAPHIC SCANNER. Bridget H. Czerwinski and Margaret H. Comer. Rush-Presbyterian St. Luke's Medical Center, Chicago, Ill.

CHEMICAL DETERMINANTS OF ACCURACY IN THE RADIO-ASSAY FOR SERUM FOLATE. Diane Forrest and Timothy Shea. Harvard Medical School and Peter Bent Brigham Hospital, Boston, Mass.

A COMPARISON OF WEEKLY AND BIWEEKLY GENERATOR SYSTEMS WITH RESPECT TO RADIATION SAFETY. Anne W. Hempel and Christopher B. Martin. Roseville Community Hospital, Roseville, Calif.

REGIONAL SCANNING METHODOLOGY USING AN OVERHEAD SCINTILLATION CAMERA. Charles A. Henry, Michael F. Barnes, Edward G. Bell, David F. Mahon, William White, Jay R. Wolff, and Ronald E. Turcotte. Crouse-Irving Memorial Hospital, Syracuse, N.Y.

A TANTALUM SYRINGE SHIELD FOR ^{99m}Tc INJECTIONS. J. Howley, H. Tipton, A. Jones, M. Dickinson, M. Green, and G. Johnston. National Institutes of Health, Bethesda, Md.

EVALUATION OF SCINTILLATION CAMERA COLLIMATORS FOR IMAGING WITH ²⁰¹Tl. Eugene Kilanowski, Ernest Garcia, and August Miale. Jackson Memorial Hospital, University of Miami School of Medicine, Miami, Fla.

MINIDIGITAL COMPUTER ANALYSIS FOR IN VITRO LABORATORY. Ilsup Kim, A. Sidney Johnston, Hunter Mermall, and Steven Pinsky. Michael Reese Medical Center, Chicago, Ill.

RADIOIMMUNOASSAY OF DIGOXIN: WHICH METHOD? Louise Larraga, Donald E. Tow, Carolyn A. Diets, Paul F. Godin, and John S. Belko. Veterans Administration Hospital, West Roxbury, Mass.

FUNCTIONAL IMAGES OF THE LEFT VENTRICLE. Michael T. LeFree, Dennis L. Kuch, and Peter P. Steele. Veterans Administration Hospital, Denver, Colo.

A QUALITY CONTROL PROCEDURE FOR PIPETTING SYSTEMS. Janet M. Marks, A. Michael Zimmer, Edward A. Silverstein, and Richard A. Holmes. Milwaukee County Medical Complex, Milwaukee, Wisc.

FREE TECHNETIUM IN PREPARATIONS OF ^{99m}Tc-DIPHOSPHONATE (HEDSPA) FOR BONE IMAGING. Michael V. McCormick, Michael D. Sinclair, and Heinz W. Wahner. Mayo Clinic and Mayo Foundation, Rochester, Minn.