

ABSTRACTS FOR SCIENTIFIC PROGRAM:

PAPERS TO BE PRESENTED ORALLY

Experimental Studies on the Gastric Secretion of Sodium Pertechnetate in Rats BY J. ABELS AND A. BARTELINK, Univ. of Groningen, Netherlands, and Univ. of Wisconsin, Madison, Wis. (Session XXVI)

Within 2 hr after parenteral administration of sodium pertechnetate, more than 20% of the radioactivity can be found in the gastric mucosa and in the gastric juice of pylorus ligated rats. The concentration of radioactivity takes place in the superficial cell layer of the whole glandular gastric mucosa and the pertechnetate secretion, which closely resembles iodide secretion, seems to be a specific gastric function. In the present study, we tried to develop a model for measuring this gastric function in rats by determining the excretion of radioactivity in the urine. Pertechnetate is absorbed in the gastrointestinal tract and most of the radioactivity is subsequently present in the urine and feces in about equal amounts. The absorption of pertechnetate can be prevented by feeding a cation exchange resin (Amberlite). This results in excretion of most of the radioactivity in the feces and very little in the urine. To prevent re-absorption of pertechnetate in the stomach, Amberlite was fed to rats who had received pertechnetate parenterally. The urinary excretion of radioactivity in 48 hr amounted to $30.6\% \pm 5.3$ (Av. \pm s.d.) as compared with $52.3\% \pm 8.4$ in control rats who received no Amberlite. In gastrectomized rats, the urinary excretion was $65.4\% \pm 8.2$ and the same value was obtained when the pertechnetate secretion of the stomach had been blocked with perchlorate ($67.3\% \pm 7.4$). In these animals the feeding of Amberlite had no appreciable effect ($63.6\% \pm 5.0$). Total recovery in feces and urine ordinarily was about 70%. These results indicate that after exclusion of pertechnetate from gastric secretion little or no radioactivity enters into the gastrointestinal tract. Partial inhibition of the secretion was reflected by a linear relation between the urine radioactivity and the amount of perchlorate injected until maximal inhibition was reached. It seems likely that the urine radioactivity can be used as a parameter of the gastric secretion of pertechnetate when re-absorption is prevented and possibly as a gastric function test.

Radioactive Agents in the Investigation of Liver-Tumor Circulation BY NORMAN B. ACKERMAN, Boston Univ. Medical Center, Boston, Mass. (Session XXVI)

Many aspects of tumor blood supply including its development, distribution and response to pharmacological agents have not been adequately studied. This subject is of interest not only in relation to the basic science of cancer, but also in the practical therapeutic management of patients with advanced cancers. We have been interested in the circulation of tumors in the liver because of the dual blood supply of the organ and the possibility of controlling circulation to increase perfusion of the tumor with anticancer agents. Radioactive materials were used to study circulatory differences in tumor and normal liver tissue. In initial animal studies, solitary Walker carcinosarcomas were implanted into the left lateral lobe of livers in Sprague-Dawley rats. Four days later 25- μ c injections of RISA were made into either the portal vein or hepatic artery. Animals were sacrificed 1 min later, and relative assessments of radioactivity in tumors and livers were made by radioautography. Tumors were then separated from livers, and radioactivity of both tissues was measured in a well scintillation counter.

The radioautographs indicated more intense radioactivity in the tumors after hepatic-artery injections than after portal-vein injections. This was confirmed in the counting studies. The ratio of liver counts/gm to tumor counts/gm after portal vein injection was 1.41; the ratio after hepatic artery injection was 0.49. Thus under these experimental conditions tumor perfusion was about three times more selective from the hepatic artery. Current studies are assessing differential effects of epinephrine and other vasoactive substances on tumor and normal circulation. Other radioactive agents including ^{99m}Tc and ^{90}Y irradiated microspheres will be used to study tumor circulation, and the results will be compared to the RISA results. Similar studies on patients with liver metastases are also in progress.

Live Color Recording from a 10-Probe Rapid Scanner BY RALPH ADAMS AND HENRY L. JAFFE, Cedars of

Lebanon Hospital, Los Angeles, Calif. (Session VIII)

The authors have developed an instrument for recording scan data from the Dynapix in photographic color during live time.

As usually employed, the Dynapix presents scan data on the screen of a cathode-ray tube as flashes of varying intensity, appearing sequentially in rows and columns at a repetition frequency up to 200/sec. The short grey scale of the Polaroid film does not adequately display the data-gathering capabilities of this instrument, with limited contrast and dynamic range. Furthermore, the repetition frequency is beyond the time-response capability of the color system previously developed by the authors for the conventional scanner.

In our new color version of the instrument, color filters mounted in a wheel between the lens elements of the camera are driven at a continuous 12,000 rpm. The electron beam is pulsed at a constant intensity but by electronically modulated time delay so that an input signal of maximum amplitude delays the flash until the red filter is traversing the lens opening. Signals of lesser amplitude are converted to decreasing time delays, resulting in flashes photographing as corresponding hues of orange, yellow, green, blue and violet. The recording may be either live or played back from magnetic tape. Scans are shown comparing this color system to the usual grey scale.

The authors discuss possible applications of this method of color recording to the problem of reconstructing a color-coded scan following computer processing of scan data from rectilinear scanners or scintillation cameras.

^{113m}In Microcolloid — an Optimal Radiopharmaceutical for Liver and Spleen Scanning BY M. H. ADATEPE AND E. JAMES POTCHEN, Washington Univ. School of Medicine, St. Louis, Mo. (Session XXIII)

^{113m}In, a generator-produced radionuclide, has physical characteristics that are near optimal for rectilinear scanning of deep-seated cold lesions. By changing pH of the eluent, one can convert the indium into colloid particles that will exhibit organ specificity based upon their size. Liver scans are done with the eluent adjusted to pH 3.5 when 70% of the injected activity is found in the liver. Experiments in the rat have shown a homogeneous distribution of radioactivity in the liver reticuloendothelial system. A pH 6 indium complex results in increased splenic labeling, producing excellent clinical spleen scans. The splenic accretion mechanism has not been clearly defined but requires slightly larger particles to increase splenic uptake. Physical chemical studies, animal experiments and clinical experience in 100 patients with liver and spleen scans will be discussed.

Circadian Variation of the T-3 Resin-Uptake Test and Free Thyroxine Concentration BY E. WILLIAM ALLEN AND WALTER DiGIULIO, Univ. of Michigan Medical School, Ann Arbor, Mich. (Session XVII)

The presence or absence of circadian variation in thyroid-function tests is of both physiologic and technical interest. An awareness of these changes is important in interpretation of laboratory tests and has significance in the role of the thyroid as a metabolic regulator. Others have examined the PBI and found no circadian variation in this test. We have examined the T-3 resin-uptake index (*J. Nucl. Med.* 7:372, 1966) and the free (dialyzable) thyroxine levels in 13 convalescing patients at 4-hr intervals over a 48-hr period. All patients were screened to eliminate any thyroid or protein abnormalities, and they maintained their usual ward activities throughout the testing. The mean T-3 resin-uptake index was found to be lowest (1.02) at 12:00 noon and highest (1.06) at 12:00 midnight. Both an analysis of variance and Duncan's multiple range test established this difference to be significant ($p < 0.005$). The level of free thyroxine in these same patients did not demonstrate any significant circadian variation ($p > 1.10$) although the test was statistically less precise than the T-3 resin-uptake index, and small true differences may be obscured. The magnitude of the difference in the T-3 resin-uptake index (12% of the normal range) indicates that the time of day at which the sample is drawn is of little importance in the clinical interpretation of the test. The levels of free thyroxine and a comparison of the T-3 resin uptake index values to the circadian cycle of the total serum protein level suggests that the variation is a reflection of the protein concentration and not due to changes in thyroid-hormone physiology.

Pertechnetate Production from ⁹⁹Mo by Liquid-Liquid Extraction BY M. ANWAR, K. LATHROP, D. ROSS-KELLY AND P. V. HARPER, Argonne Cancer Research Hospital and Univ. of Chicago, Chicago, Ill. (Session XIX)

Various institutions are using ^{99m}Tc for scanning purposes, using commercially available sterile ⁹⁹Mo/^{99m}Tc columns. In these units sterile saline is used to elute pertechnetate which is collected directly into a sterile vial, ready to be used for brain and thyroid scanning. Further manipulation of this eluate for making other technetium preparations presents certain difficulties and renders sterile elution of the pertechnetate useless. Low yields have been reported along with relative danger of ⁹⁹Mo breakthrough and alumina leakage.

^{99m}Tc-pertechnetate may be extracted from ⁹⁹Mo using redistilled methyl-ethyl-ketone with a 90 to 95%

yield. Addition of two to three drops of Superoxol ensures that ^{99m}Tc is in the extractable $^{99m}\text{TcO}_4^-$ form. Sodium molybdate-99 obtained commercially in 25 ml of 5 N sodium hydroxide is transferred by suction into a shielded separatory funnel. Twenty-five milliliters methyl-ethyl-ketone are sucked into the funnel and mixing is achieved by sucking a steady stream of carbon dioxide free air through the mixture for 3 min. After phase separation the lower molybdate layer is returned by gravity to a shielded reservoir for subsequent extractions. The ketone layer is diverted with a two-way stopcock onto a dry alumina column (10 gm) which retains the traces of base and ^{99}Mo . Contamination with ^{99}Mo has been less than $0.003 \mu\text{c}$ for 300 mc. The desired quantity of ketone solution, calibrated for activity, is transferred to a dry sterile vessel and evaporated to dryness with a stream of filtered air. The ^{99m}Tc is then taken in any desired aqueous medium in any volume so that very high specific activity may be obtained.

This process is preferred over eluting the column for several reasons. The direct extraction provides pertechnetate in a form more convenient for further processing into other chemical states. This simplified procedure involves less time, is more economical and gives better yields than the conventional elution process. Most importantly, radiation exposure can be minimized if the extraction unit is properly designed. The working design can be automated for further protection. Since only strong chemical reagents are used, there is no opportunity for bacterial growth and the associated production of pyrogens and bacterial contamination.

Endolymphatic Administration of ^{131}I Ethiodol in the Over-All Treatment of Patients with Malignant Lymphoma BY IRVING M. ARIEL, REUBIN OROPEZA AND DONNA GALEY, Pack Medical Group, New York, N.Y. (Session XXII)

A present concept of treating lymphoma deals with the treatment of all involved lymph nodes. There are some who treat lymph nodes of the supraclavicular area, both axillae, mediastinum, periaortic nodes and pelvic nodes for every type of lymphoma and in every stage, including Stage I. We have adopted a similar principle, but use the endolymphatic route for administering ^{131}I Ethiodol to irradiate the femoral, inguinal, iliac and periaortic lymph nodes. In some instances we also use this route to irradiate the axillary lymph nodes. We then use orthodox radiation therapy for administering the irradiation to the cervical region or the mediastinum.

Seventy-five patients have been treated to date by this modality including those with giant follicular blastoma, lymphosarcoma and reticulum cell sarcoma

and Hodgkin's disease. Doses of from 40 to 80 mc have been administered into the lymphatics of both feet, and doses of irradiation in the pelvic lymph nodes varying from 20,000 to 50,000 rads beta have been obtained. Several patients who had extensive retroperitoneal lymphosarcoma discovered at laparotomy and who were treated by no other methods except the endolymphatic administration of isotopes have remained free of disease for over 4 yr. The results obtained to date are best for those with giant follicular lymphoblastoma and lymphosarcoma and worst for those with reticulum cell sarcoma because this lesion may manifest itself anywhere within the body. The results with Hodgkin's disease vary between the two. The presentation will describe in detail the indications, techniques of administration, dose measurements, results and complications.

Comparison of Brain Scanning Techniques: ^{99m}Tc Using an Anger Camera and ^{74}As Using a Positron Scanner BY A. B. ASHARE, B. BUB, M. S. POTSAID, R. G. OJEMANN, S. ARONOW AND W. H. SWEET, Massachusetts General Hospital, Boston, Mass. (Session XIV)

One hundred and two brain scans were done on 95 randomly selected patients using both ^{74}As with a positron scanner and ^{99m}Tc with an Anger camera. For the ^{99m}Tc scintigrams, eight views of the head were obtained: anterior, posterior, right and left laterals and obliques. The positron scans consisted of a lateral with a simultaneously obtained unbalance scan and an anterior-posterior view.

Fifty studies were read as abnormal by both techniques. Thirty-four tumors and 10 vascular lesions were diagnosed; all of these lesions were confirmed by angiography, pneumoencephalography, electroencephalography and/or surgery.

Twenty-two cases were read as abnormal by only one technique, 11 with the positron scanner and 11 with the Anger camera. Of each of these 11 studies, three were diagnosed by the studies mentioned above as tumors. A left-temporal glioma confirmed by surgery, a metastatic lesion confirmed by arteriography and a left cerebral mass confirmed by arteriography were read as positive on the positron scan but negative on the ^{99m}Tc scintigrams. The three tumors read as abnormal on the ^{99m}Tc scintigram but as normal on the positron scan were a metastatic lesion confirmed by pneumoencephalogram and arteriogram, an unidentified tumor of the fourth ventricle confirmed at surgery and a metastatic lesion confirmed by arteriography.

Of the 30 examinations that were normal by both procedures, one was diagnosed by pneumoencephalography as a tumor and found to be a right temporal lobe astrocytoma (Grade II-III) at surgery.

Results of this study compare the current available techniques and indicate that under certain circumstances double scanning may be of value in the assessment of difficult diagnostic problems. As they are practiced at MGH, both techniques are undergoing revisions; therefore, re-evaluation of this comparison will be necessary. In particular, a hybrid positron scanner will soon replace the single pair of detectors that has been in use here at MGH for the past 15 years.

Two conclusions can be stated: (1) Both techniques are useful for the diagnosis of intracranial lesions, and neither technique is superior to the other. (2) The oblique views of the brain done with the Anger camera provide additional information (a scan illustrating this will be presented).

The presentation will include a comparison of the radiation dose, the counting statistics and resolution distance, the time required for doing each examination and the relative worth of each technique to the clinician. (These studies were supported in part by USPHS Grant No. CA-07368-04 and AEC Grant No. AT(30-1)-3937.)

An Image Recording and Integration System for Dynamic Radioisotope Studies Based on Advanced Television Circuitry BY WILLIAM L. ASHBURN, JOHN C. HARBERT, WILLARD C. WHITEHOUSE AND RAYMOND E. MURPHY, National Institutes of Health, Bethesda, Md. (Session VIII)

The ability of the Anger-type scintillation camera to record sequential images of dynamic functions such as the flow of a radioisotope through the chambers of the heart is well known. Rapid sequence 35-mm cameras (4 frames/sec) have been used to record these events, but they suffer from an inherent deadtime while the film is advanced. Digital magnetic-tape recording from a 1,600-channel multiscaler is possible and allows computer analysis of the recorded data, but the resolution is limited to a 40×40 matrix of picture elements.

The authors have developed a system of image recording which has essentially no deadtime and a mechanism for retrieving analog information simultaneously from any two regions of the image down to a 1×1 -cm area. The system consists of a television camera which is focused on one of the two CRT's of a Nuclear-Chicago Pho-Gamma III scintillation camera or on a "slave" oscilloscope some distance away. The changing image is recorded on video magnetic tape at the standard rate of 30 frames/sec (one frame = two complete interlaced fields). A flash appearing anywhere on the random raster of the CRT is held by the TV camera until it is scanned on a standard

(252 1/2 line field) video raster and then erased immediately. All flashes occurring with any 1/60-sec interval are thereby recorded on the corresponding videotape field. On tape replay each flash is displayed in its correct position and is seen to persist for a constant 1/60 sec. Sequential integrated pictures are possible at any rate up to 60/sec. If an integrated picture of 1/4 sec is desired (i.e., 15 video fields), sequential "stop-action" fields are replayed on a high-resolution TV monitor, and each field is photographed by a Polaroid camera for 1/30 sec without advancing the film (exposed 15 times). A dual "area-of-interest" analog retrieval system is included, the details of which will be discussed.

Measurements of Regional Ventilation and Blood Flow in the Lung Using ^{133}Xe and a Scintillation Camera, BY N. ASPIN, H. LEVISON, T. R. WENG, E. A. FEATHERBY AND A. C. BRYAN, Univ. of Toronto, Institute of Aviation Medicine and Research Institute, Hospital for Sick Children, Toronto, Ontario, Canada. (Session XX)

Indices of blood flow and ventilation per unit alveolus have been measured over 30 areas of the erect right lung using ^{133}Xe and a scintillation camera. With the subject breath-holding at functional residual capacity (FRC) 0.5 mc of ^{133}Xe saline was injected into a peripheral vein. The xenon evolves into the gas phase of a given region of lung in proportion to the blood flow to that region. The subject fills his lungs with air to total lung capacity (TLC) so that all alveoli in the lung are of equal size. While breath-holding at TLC the distribution of radioactivity within the lung was measured with the scintillation camera, and the output stored in a data-handling system. The distribution of a tidal breath at FRC containing 0.75 mc of ^{133}Xe was similarly measured with the subject breath-holding as TLC. A final measurement of regional counting rates over the lung was made after the subject had breathed to equilibrium from a closed-circuit spirometer containing a trace quantity of ^{133}Xe . It was then possible to convert regional counting rates to xenon concentration and to express the results as relative indices of ventilation and flow.

In the lungs of six normal adults and 12 normal children, vertical gravity-dependent gradients in blood flow have been observed at FRC. In addition, lateral perfusion gradients were seen. The adults demonstrated small gradients in ventilation down the lung at FRC while the lungs of the children showed uniform ventilation. Measurements have been made of regional ventilation and blood flow in groups of children with asthma, cystic fibrosis and kyphoscoliosis. The results obtained in these patients will be compared to those obtained in normal children.

Diagnostic Use of ^{85}Sr Scintimetry in Orthopaedics BY
GORON C. H. BAUER, Hospital for Special Surgery,
 New York, N.Y. (Session XXV)

Tracer methods for diagnosis of bone and joint disease are gaining acceptance in clinical routine; it is probable that such methods will eventually form a large share of the work load in clinical laboratories for nuclear medicine. By comparison with the heart, liver and kidney, the skeleton is silent in terms of measurable nontracer parameters of metabolic disorder. However, in terms of tracers the skeleton is remarkably accessible: useful tracers are available for all constituents of bone, and the size, configuration and composition of the skeleton permit precise definition of detection geometry. The equipment needed for radionuclide tracer studies of the skeleton is available in most modern hospitals.

Clinical indications for radionuclide scintimetry of bone metabolism are primarily bone and joint pain in the absence of radiographic or other objective evidence of abnormality. The contribution of scintimetry to diagnosis under such circumstances is primarily topologic; in addition, this technique may contribute in the differential diagnosis of disease. On the basis of 1,500 procedures performed over a 2-yr period in an orthopaedic hospital, indications for ^{85}Sr scintimetry of the spine, the knee and the hip will be reviewed.

Spine — Scintimetry permits detection of cancer metastases and of infectious disease of the spine in the absence of radiographic abnormality. Nonspecific compression fracture, osteoarthritis and Pagetic lesions complicate interpretation of spine scintimetry.

Knee — In rheumatoid arthritis and osteoarthritis ^{85}Sr scintimetry values are higher than normal, diffusely in the former and focal in the latter; a distinction can be made between medial, lateral and patellar type osteoarthritis of the knee. Osteotomy for correction of varus deformity causes return toward normal of the scintimetry pattern along with arrest of the osteoarthritic process. In 25 knees, a subchondral bone lesion usually in the medial femoral condyle was found to be associated with extremely high uptake of ^{85}Sr . In at least one case this abnormality preceded radiographic identification of the lesion. Biopsies suggest these lesions are secondary to osteonecrosis; they may be an important cause of osteoarthritis unassociated with primary cartilage abnormality. Three cases referred because of knee pain had abnormal uptake of ^{85}Sr at a distance from the joint line; they were subsequently diagnosed and successfully treated as osteomalacia.

Hip — Nontraumatic osteonecrosis of the head of femur gives high ^{85}Sr scintimetry values, apparently before the appearance of radiographic abnormality. On the basis of the patterns observed in osteoarthritis

of the knee, ^{85}Sr scintimetry data are being analyzed to provide a classification of osteoarthritis of the hip, which is useful in terms of choice of therapy for this condition.

The radionuclide scintimetry patterns observed in osteoarthritis and osteonecrosis support the concept that regeneration is a more characteristic feature in these conditions than is degeneration. In this sense, tracer methods may also aid therapy in orthopaedic conditions.

Scintillation Scanning of Malignant Melanomas with Radioiodinated Quinoline Derivatives BY **WILLIAM H. BEIERWALTES**, VIJAY VARMA, RAYMOND E. COUNSELL, LIONEL M. LIEBERMAN AND JOSE O. MORALES, Univ. of Michigan Medical Center, Ann Arbor, Mich. (Session XXII)

Chloroquine is known to have a marked affinity for melanin. We studied the tissue concentration of ^{14}C -chloroquine in 52 mice, 16 black and 16 albinos with melanomas, at 24, 48, 72 and 96 hr after injection by liquid scintillation assay of 17 tissues. Dr. Counsell then synthesized an original derivative of chloroquine, 4-(3-dimethylaminopropylamino)-7-iodoquinoline- ^{125}I (hereafter called ^{125}I NM 113), and the tissue distribution of this labeled compound was then compared to that of ^{14}C -chloroquine under similar conditions in 35 mice and six Syrian hamsters with melanomas. For controls, 10 mice and three Syrian hamsters were injected with the same amounts of radioactivity in Na^{125}I and similarly studied.

The highest concentration of ^{14}C was in the eye of the pigmented mouse at 4 days, but no significant concentration occurred in the eye of the albino mouse. The concentration in melanoma was 10 times greater in liver and about 60 times greater in muscle. The concentration of radioactivity fell with time in all tissues except melanoma, eye and skin (double layer in pinna of ear). Similarly, the highest concentration of radioactivity after ^{125}I NM 113 was highest in the eye of the pigmented mouse (but not in albino), 24 times that in liver and 50 times that in kidney at 72 hr. The concentration in melanoma was 5 times that in liver and 10 times that in kidney.

In the Syrian hamsters, concentration of ^{125}I in eyes was 3–7 times that in melanoma, but the concentration in melanoma was 2–7 times that in liver. The malignant melanoma tissues were sharply visualized as a positive image by scintillation scanning with a 5-in.-crystal color photoscanner and a fine-focus collimator. No significant concentrations of ^{125}I occurred in melanin anywhere after Na^{125}I and the thyroid concentration of ^{125}I was 3–40 times greater after Na^{125}I than after ^{125}I NM 113 at 4 days after injection.

Peripheral Glucose Assimilation and Insulin Secretory Capacity in Normals BY COSKUN F. BEKDIK, Boston Univ. Medical Center, Boston, Mass. (Session V)

The rate of peripheral glucose assimilation and the insulin secretory capacity of the pancreas have been studied in normal subjects. To determine the secretory capacity of the pancreas an i.v. glucose tolerance test (GTT) was performed. An oral load of 50 gm glucose was given and a second i.v. GTT was then carried out. The purpose of the oral glucose between two i.v. tests is to evaluate the secretory capacity of the islet cells. The first i.v. test reflects the presently available insulin. The second test should reflect the secretory capacity. If this is so, there should be a greater glucose assimilation rate (K) on the second test because of the large quantity of insulin made available by the oral glucose.

The rate of glucose assimilation in 36 normal subjects was significantly greater during the second i.v. GTT than the first. Expected increase of K between the first and second i.v. GTT showed satisfactory correlation ($r = 0.69$). However, there was no significant difference of the secreted insulin (IRI) measured by radioimmunoassay during the i.v. tests. During the oral GTT prolonged insulinemia and IRI/BS ratios were significantly higher than with i.v. GTT.

The relationship of this ratio to K_2 was significant ($r = 0.65$). The relationship of IRI to BS was more constant during the oral GTT ($r = 0.80$) than during the first ($r = 0.63$) or second ($r = 0.70$) i.v. GTT. During both i.v. situations there was no correlation between K and the IRI/BS ratio.

The data show that:

1. Glucose assimilation rates after i.v. administration are independent of IRI.
2. Increased K_2 is dependent on prolonged insulinemia and high IRI/BS ratio during the previous oral test ($r = 0.65$).
3. This test may be clinically used to measure the insulin secretory capacity and, after oral administration, the rate of peripheral glucose assimilation.

RISA Myeloencephalography in the Differential Diagnosis and Treatment of Hydrocephalus BY ROBERT L. BELL AND WILLIAM G. JONES, V. A. Hospital, Coatesville, Pa. and V. A. Hospital, Wilmington, Del. (Session XXVII)

During the past year we have explored isotope techniques in attempting to evaluate and treat hydrocephalus associated with dementia. Intrathecal radioiodinated ^{131}I human serum albumin has been used to obtain cerebrospinal fluid-flow patterns. These patterns are characteristic for various clinical conditions and are obtained with mechanical scanning at 3-hr, 24-hr and 72-hr intervals. These scans have been correlated with conditions such as presenile dementia

caused by Alzheimer's or Pick's disease. We have evaluated the condition called "hydrocephalus ex vacuo" and have found that we are indeed evaluating a low-pressure hydrocephalus. In the latter situation a ventriculo-atrial shunt has afforded relief of symptomatology. The pattern of the flow of RISA in the serial scans allows a positive diagnosis of this blockade external to the ventricular system and permits a rational treatment with the shunting procedure. Pre- and postoperative studies, in addition to serial scans, have included: serial pre- and postoperative psychological studies, alterations in the neurological examination and cine documentation of improvement.

Study of ^{86}Rb in A Malignancy Metastatic to Liver BY ROBERT L. BELL, Baylor Univ., Houston, Tex. (Session XV)

A single case of leiomyosarcoma originating in the small bowel and metastasizing to the liver was studied with liver scans after intravenous administration of colloidal ^{198}Au and after injection of ^{131}Cs into the hepatic artery. The cesium scan showed a hot spot where the cold spot had been seen on the colloidal-gold liver scan.

Two months later, because of its potential therapeutic utility, 10 mc of $^{86}\text{RbCl}$ were injected into the hepatic artery. Again, a hot spot in the liver was seen where a cold spot was noted on the prior colloidal gold liver scan. The total daily excretion of rubidium into the urine was approximately 3% of the administered dose in the first day and from day 6 until day 18 was approximately 1% of the remaining dose. Eighteen days of study with an externally collimated detecting system showed a disappearance of isotope from tumor, liver and several other organs which agrees with the long biological half-lives noted in the ICRP. The effective half-life in the brain appears to be longer than in most other major organs. Concentrations of rubidium in plasma and red cells over this same period indicated that plasma concentrations increase over the first 3 days and then rapidly decrease until approximately day 6 at which time the plasma concentration curve begins to plateau. Red-cell concentration curves suggest that rubidium is incorporated into red cells by a dual mechanism: by exchange in the blood and by bone-marrow incorporation. A partial autopsy was performed 4½ months later. A total of 18 mc of ^{86}Rb had been injected into the hepatic artery. At autopsy twice as much isotope was found in the leiomyosarcoma in skin, lymph node and liver as was found in normal-liver tissue. It would appear that approximately three times as much ^{86}Rb would concentrate in a normal-sized liver if it were injected via the hepatic artery than if it were injected via a peripheral vein.

Implications for diagnosis as well as therapy via administration of isotope into the hepatic artery are discussed.

225 Brain Scans with Concomitant Cerebral Blood Flow BY ROBERT L. BELL, Baylor University, Houston, Tex. (Session II)

Two hundred and twenty-five consecutive patients with suspect cerebral disease were given ^{99m}Tc intravenously (1 mc/10 lb) and immediately had cerebral blood-flow studies. An oscilloscope image of the anterior view of the head was photographed on Polaroid film. Exposure was 4 sec/film, and exposures were made continuously from 0 to 30 sec. Brain scans were done 30 min later on the Anger camera. Most of these patients subsequently had bilateral angiograms, EEG's, skull x-rays and occasionally pneumoencephalograms. Twenty-eight percent of all the cases had an abnormal flow or abnormal scan or both. The flow studies were able to detect 35 cases of either total occlusion of one internal carotid artery or reduced flow through one middle cerebral artery which went undetected by the scan. Seventeen cases had positive scans and normal cerebral blood-flow studies. In this series, if one compares these categories, it is apparent that by doing scans without cerebral blood flows almost twice as many lesions would be missed as would be detected.

A correlation of the ^{99m}Tc cerebral blood flow studies with bilateral angiograms reveals that 100% of the cases of total occlusion of one internal carotid artery (13 cases) were manifest on both the flow and the angiogram. When the angiogram was positive and the technetium flow was negative, the inability of the flow to detect the lesion was due to either bilateral disease, small aneurysms or abnormalities deep in the mid posterior fossa. Negative angiograms in the face of positive ^{99m}Tc cerebral-flow studies were seen mainly in relatively acute cerebrovascular accidents where the flow showed reduced circulation through the area fed by one middle cerebral artery. Most flow studies showing reduced or slowed flow in middle cerebral artery circulation had negative brain scans.

The flow studies revealed increased flow in five of the six high-grade astrocytomas but were normal in tumors of the posterior fossa and deep midline structures as well as in most of the metastatic carcinomas.

Whole-Body-Survey Scintiscanning for Bone Metastases BY FREDRICK L. BENOIT, JUAN F. TORRES, JR. AND RICHARD E. PETERSON, University Hospitals, Iowa City, Iowa. (Session XXV)

Determination of the extent of skeletal involvement by neoplastic disease is often of paramount importance in planning effective therapy and assessing a valid

prognosis. This study reports the use of a rapid, whole-body isotopic-scanning procedure for obtaining this information.

One-hundred-fifteen patients with tissue-proven neoplastic disease were evaluated for bone involvement. The group was comprised of 37 females and 78 males with a median age of 59 years (range 10-86 years). Each patient was given 1 mc of ^{87m}Sr intravenously and 45 min later a whole-body scintiscan was made with dual opposed 8-in. NaI(Tl) crystals mounted on 199-hole lead collimators which scanned at a speed of 220 in./min. Anterior and posterior photoscan views were recorded simultaneously with a 1:5 reduction in scale so that projection of the entire body fit on 14 × 17-in. x-ray film. The scanning procedure took 45 min for each patient.

Of the 115 patients evaluated, 65 (56.4%) had positive scans for bone involvement by neoplasm. In this group with positive scans, 30 (26%) had x-ray confirmation and 35 (30.4%) had none, signifying an early lesion. In 48 patients (41.7%) both x-ray studies and scans were normal. In 2 cases (1.7%), roentgen bone lesions were present with a normal scan. Alkaline phosphatase levels were recorded in 80 patients and agreed with the scan result on 49 of them. However, 26 patients had abnormal scans (11 also with abnormal x-rays) with normal enzyme levels; five had the reverse findings. The patients with positive scans had the following neoplasms as their primary disease: Hodgkins disease, lymphoma, chondrosarcoma and carcinoma of the prostate, lung, breast, cervix, endometrium, renal pelvis, bladder, testis, stomach and bile duct.

These results suggest that whole-body scintiscanning with ^{87m}Sr may be a more sensitive indicator of skeletal metastatic involvement than roentgen or alkaline phosphatase determinations and may therefore be a valuable diagnostic method for staging cancer, for following the effect of therapy on bone and for allowing a more precise prognosis.

Biological Half-life of ^{75}Se -Selenomethionine in Man BY MOSHE BEN-PORATH, LAWRENCE CASE AND ERVIN KAPLAN, V.A. Hospital, Hines, Ill., Loyola Univ. Stritch School of Medicine and Univ. of Illinois College of Medicine, Chicago, Ill. (Session X)

The biological half-life of ^{75}Se -selenomethionine has been determined in nine normal controls, five patients with malignant lymphomas and five patients with pancreatic insufficiency. They were given 2 μC of ^{75}Se -selenomethionine i.v. and counted during 120 days in a whole-body counter. The disappearance curve in normal subjects has three distinct phases: I of 9.5 hr (12% of dose); II of 8.5 days (9%); and III of 91 days (79%). The curves of patients with pancreatic disease are not significantly different from the

normals. In lymphoma patients, phase II is consistently absent, phase I is similar to the normals (10.5 hr), while phase III is only 49 days, representing 93% of the administered dose. These differences have been found statistically significant. The combined biological half-life for controls is 73 days compared to 45 days for lymphoma patients.

The three phases of the biological half-life in normals may be interpreted in relevance to previously published data from *in vitro* experiments: Phase I—elimination of unbound or nonpeptide-bound ^{75}Se -selenomethionine and in relation to the pancreatic-enteric recycling; Phase II—is of the same order of magnitude as the half-life of serum proteins and may represent incorporation in the relatively rapid metabolizing protein pool. Phase II—incorporation in red cells and structural proteins and other stable protein moieties. The mechanism of the absence of Phase II and the increased turnover rate in the final phase in lymphoma patients is not known but should be of considerable biologic interest.

The measured biological half-life of ^{75}Se -selenomethionine in normals indicates total-body irradiation from a diagnostic dose of 250 μc to be 1.63 rads as calculated by the Quimby method.

The Use of a Tape Recorder in Simultaneous Multi-Isotope Scanning BY MOSHE BEN-PORATH, GLENN CLAYTON AND ERVIN KAPLAN, V.A. Hospital, Hines, Ill., Loyola Univ. Stritch School of Medicine and Univ. of Illinois College of Medicine, Chicago, Ill. (Session VIII)

We have previously described the technique and application of multi-isotope subtract and comparative scanning with multicolor display. In a further modification of this system, the horizontal and vertical movement of the detector head are recorded on tracks one and two of a four-track Picker Magnarecorder. The output signal from the two pulse-height analyzers are recorded on tracks three and four. The tape is replayed with display on a white phosphor cathode-ray tube of a display unit. Tracks three and four information is differentiated by using different color filters between the CRT screen and a Polaroid camera on which the scans are recorded. The information may be played back at different subtract, contrast and intensity levels, permitting optimal display of the distribution of each isotope scanned.

This technique is useful in the interpretation of pancreas scans, in which the pancreas and liver are displayed in different colors. Lesions appearing "cold" on ^{198}Au liver scan may be analyzed for relative ^{75}Se contents.

Using this technique we also have shown that ^{75}Se -selenomethionine appears to be a useful agent for

myocardial scanning. ^{75}Se -selenomethionine concentrates in brain tissue at a higher level than in the accessory structure, permitting the visualization of this organ. Scanning the head for both $^{99\text{m}}\text{Tc}$ and ^{75}Se simultaneously allows color differentiation of the brain from these accessory structures.

In conclusion, using this simple tape-recording technique, significant additional information may be obtained from a multi-isotope scan.

Immediate Assessment of Gamma-Camera Dynamic Studies Using a Small Digital Computer BY R. E. BENTLEY, E. J. POTCHEN AND V. W. GERTH, Washington University, St. Louis, Mo. (Session XXVII)

Dynamic studies with rectilinear radioisotope scanners and with the Anger gamma camera have hitherto been undertaken by depositing data onto magnetic tape. The results have been analyzed at some later time on a large computer. In this paper we describe how a small computer can be connected on line to carry out dynamic studies provided that (1) the number of time intervals is small (~ 20) and (2) the number of separate areas to be resolved is small (~ 64).

A field of investigation not precluded by these restrictions is the measurement of regional changes in cerebral blood flow using the inert-gas washout technique. From a detailed study of the early part of the curve of isotope uptake in patients with and without cerebral vascular disease, we have defined the sampling duration necessary for the application of the Anger-camera imaging process to regional changes in cerebral radioactivity. We now propose to obtain contour plots of calculated mean regional cerebral blood flow within minutes after the intracarotid injection of ^{133}Xe .

The advantages of on-line connection are two fold: (1) to trigger a particular mode of counting on the basis of results currently being obtained and (2) to permit the assessment of results immediately after an investigation so that a particular procedure can be repeated.

Clinical Assessment of Renal Blood Flow with ^{133}Xe BY M. DONALD BLAUFox, ALAN GRUSKIN, MONIQUE KATZ, CHIEN-HSING MENG AND MILTON ELKIN, The Albert Einstein College of Medicine, New York, N.Y. (Session VII)

The use of ^{133}Xe has been developed in the dog as a method for estimating the renal blood flow and its distribution (Thorburn *et al*, *Circulation Res.* 13:290, 1963). Twenty-five patients including five normal subjects and 20 with hydronephrosis, renal artery stenosis, nonfunctioning kidney or the nephrotic syndrome have been studied in an effort to apply this methodology to man. At the time of aortography a radioisotope detector was placed over the kidney to be

studied and 1 mc of ^{133}Xe was injected directly into the renal artery. The washout curve of radioactivity was recorded continuously for 45 min on electromagnetic tape and resultant data was plotted on semi-logarithmic graph paper as the logarithm of the counts/sec against time. In each of the normal patients the curves could be resolved into four components when plotted in this manner. The earliest component of the washout curve was taken to represent the renal cortical blood flow which ranged from 61 to 87% of the total renal blood flow in the normals. Xenon washout studies in those patients with renal cysts and essential hypertension were indistinguishable from the normal subjects. The majority of curves obtained from patients with significant impairment of renal function could be resolved only into three components. In these cases the earliest component was considered to represent a fusion of cortical and cortico-medullary blood flow. To critically test the method eight curves were analyzed independently by two different observers, and the results were compared. The values for cortical and cortico-medullary blood flow were not significantly different in the two analyses by the paired *t* test ($p > 0.5$). Gamma-camera studies performed simultaneously with the externally monitored curve confirmed the relationship between cortical washout of the isotope and the first component of the curve. The ^{133}Xe washout is easily performed and is a potentially useful method for evaluating renal blood flow and its distribution in the human.

Splanchnic Blood-Pool Scanning in Occlusive Disease of the Superior Mesenteric Artery: An Experimental Study BY FREDERICK J. BONTE, ROBERT W. PARKEY AND GEORGE C. CURRY, The Univ. of Texas Medical School, Dallas, Tex. (Session XVI)

Occlusion of the superior mesenteric artery in man, whether by spasm or embolization, and the ischemia that results from this occlusion, produce a syndrome which may progress to bowel necrosis, shock and death. The mortality rate of this syndrome remains alarmingly high because of the inability of physicians to detect it early. The best means of diagnosis is retrograde catheter aortography, but this is a rigorous procedure which should be applied sparingly, and only to those patients in whom a positive diagnosis is apt to be made and in whom immediate surgical intervention would be of decisive, life-saving value. We have attempted to devise a radionuclide blood-pool scintigraphic screening test to select from among those patients who may present with an ischemia-like syndrome and those in whom arteriography should be done for definitive diagnosis.

The rabbit was selected as the experimental animal because of the striking anatomic similarity between its

mesenteric circulation and that of man. Initially, the mechanisms of superior mesenteric artery obstruction in 40 rabbits were explored by means of arteriograms made before and at intervals after ligation of the superior mesenteric artery or one of its major branches. We found that, even with obstruction of the principal superior mesenteric artery trunk, collateral flow developed immediately with excellent perfusion of obstructed segments. With time, however, the collateral subsided, for reasons as yet unknown. Of even more significance were arteriographic findings which suggested that high-capacity shunts opened between mesenteric arteries and the portal venous system shortly after ligation.

With these arteriographic base lines available to us, we then proceeded to study the splanchnic blood pools of 24 rabbits before and after ligation of the superior mesenteric artery using $^{99\text{m}}\text{Tc}$ human serum albumin as a tracer and making serial exposures with a radioisotope camera. Gross defects in the distribution of splanchnic blood may be detected in this fashion, and other findings will be described which are thought to be pertinent to post-ligation shunting of arterial blood.

The study has recently been transferred to man, and the results in a few early patients thought to have a gut ischemia syndrome will be reviewed. We feel that a useful radioisotope test of mesenteric vascular competence can be developed.

System for On-Line Computer Processing of the Radionuclide Scan BY D. W. BROWN AND D. S. GROOME, Univ. of Colorado Medical Center, Denver, Colo. (Session IX)

The resolution of the rectilinear scanner can be improved and valuable quantitative information obtained by processing the data with a digital computer. If this is carried out "on-line", the results are available rapidly and greater flexibility in data collection and analysis can be achieved. Pulses from the pulse-height analyzer of a 5-in. rectilinear scanner with a new method of "electronic noise" suppression installed are accumulated in an 8-bit binary scaler with a 9th overflow bit. A shaft encoder attached to the traverse drive shaft generates a 7-bit binary code showing the exact lateral position of the scanning head. This code generates "process interrupts" in the computer at 0.1 in. or fraction thereof of traverse. These "process interrupts" cause the accumulated count to be transferred to a buffer, the counter to be reset and a 16-bit word, 32K, 3-disk file, 4 μsec computer (IBM 1800) located 210 ft away to read the buffer on a "cycle-stealing" basis, storing the count in its memory and later transferring it to a disk. Patient information is entered, and starting, stopping, etc., is controlled with a remote typewriter-keyboard (IBM 1816). At the

completion of a scan in response to instructions from the 1816 the data are called off the disk, processed statistically and then printed out on the printer in the computer room, plotted on an x-y plotter or transferred to magnetic tape for storage. A new method of statistical processing in which the data are set up as a large system of linear simultaneous equations incorporating a modulation transfer function determined for the particular collimator and isotope and solved to improve resolution will be discussed. The results of the application of this system to patient and phantom studies will be displayed. (This project was supported by AEC Contract AT(11-1)-1472 and U.S. Public Health Research Grant HE-09112.)

^{99m}Tc-Sulfide Scanning in Clinical and Experimental Orthotopic Liver Homotransplantation BY D. W. BROWN, C. G. GROTH, L. BRETTSCHEIDER, D. CORDES, J. D. CLEAVELAND, R. TROW AND T. E. STARZL, Univ. of Colorado Medical Center and Denver V.A. Hospital, Denver, Colo. (Session XIII)

Serial radioisotope liver scans were extremely helpful in the postoperative management of five children subjected to liver homotransplantation. This is due in part to the fact that several of these cases have developed liver abscesses which are strikingly demonstrated by the scan. In addition, changes in the liver size and function are shown. A simple and reliable method of producing colloidal ^{99m}Tc₂S₇ with sodium thiosulfate, potassium perrhenate and gelatin has allowed the use of this material without morbidity. One liver transplant recipient had 15 liver scans in 5 1/2 months without apparent injury. Doses have usually been 800 μc/scan, each of which is estimated to deliver 1 rad to the liver. To evaluate the changes seen in human liver transplantation, serial liver scans have been performed on dogs after hepatic artery ligation, common bile duct ligation and portal caval shunt and in treated and untreated dogs subjected to orthotopic hepatic homotransplantation. In addition, 800 μc of ^{99m}TcS was given twice weekly to a series of control dogs with LiF thermoluminescent dosimeters inserted in their livers. There was no detectable ill effect from these repeated doses. These animal scans were performed with a 3-in. rectilinear scanner connected to a 64 × 64 multichannel analyzer with both oscilloscopic and punch paper-tape output, letting one use a digital computer to compare serial studies. (This project was supported by AEC Contract AT(11-1)-1472, and research grants HE-09112, AM 06334, HE 07735, AM 07772, AM 06283, AI 04152, FR 00051, FR 00069 and FO5-TW-1154.)

Evaluation of Indium Compounds Synthesized for Brain Scanning BY JOHN A. BURDINE, JR., THOMAS A.

WALTZ, FREDERICK A. MATSEN, JR. AND FRED RAPP, Baylor Univ. College of Medicine, Houston, Texas. (Session XXIII)

Two experimental systems were used to determine the affinity which abnormal areas of cerebral cortex have for a series of indium-tagged compounds: (1) radio-frequency-induced focal injuries in the surgically exposed brain of dogs, and (2) primary brain tumors (containing glialelements) produced in hamsters 40-60 days after intracerebral injection of simian virus 7.

The indium-labeled compounds tested included InCl₃ and indium DTPA, EDTA, HEDTA, NTA, tetracycline and citric acid. ^{99m}Tc-pertechnetate was injected simultaneously so that the target-to-brain ratios achieved could be compared.

The results demonstrated injury and tumor-to-brain ratios averaging 10/1 to 25/1. The data showed consistently higher lesion uptake for the indium compounds by a factor of approximately 1.5.

Simple techniques for compound synthesis are described, including appropriate processing for human use. Clinical examples of brain scans will be presented.

Radiopulmonary Cardiography with the Scintillation Camera and ^{99m}Tc-Pertechnetate BY GERALD BURKE, ARLENE HALKO AND DAVID GOLDBERG, Michael Reese Hospital and Medical Center, Chicago, Ill. (Session XVI)

The scintillation camera has been used for dynamic studies of cardiopulmonary blood flow with ^{99m}Tc-pertechnetate. The camera studies have been performed with a modified 70-mm roll film magazine in conjunction with conventional dual-probe radiopulmonary cardiography [RPCG] to permit comparison of visually determined right-heart-to-left-heart transit times with those derived from dual-probe cardiac and pulmonary blood-flow curves. ^{99m}Tc-pertechnetate was injected in a bolus via an antecubital vein with the subject supine. The dual-probe study was performed first using 1 mc of ^{99m}Tc with appropriate positioning of the lung and precordial detectors. For the subsequent scintillation-camera study, 30 mc of ^{99m}Tc was injected with the detector centered over the precordium of the supine patient, using camera exposures of 1 frame/sec (including film advance).

Visualization of the cardiac chambers and cardiopulmonary blood flow achieved with the scintillation camera compares favorably with that obtained on conventional angiocardiology. The technique has been found of value in determining relative cardiac chamber size, detection of intracardiac shunts and demonstration of pericardial effusions.

Determinations of central mean transit time and its

arterial and venous subdivisions from inspection of the scintiphoto sequence yield data entirely analogous to those obtained by the more tedious mathematical analysis of dual-probe RCPG curves in both normal subjects and patients with intracardiac shunts or with confirmed mitral and/or aortic valvular disease. A total of 20 normal subjects and 20 abnormal have been studied in this manner to date. Cardiopulmonary blood-flow visualization and measurement with the scintillation camera is without hazard to the patient and appears to be of significant diagnostic value in a variety of cardiac disorders.

Improved-Resolution Fast-Section Scanner BY B. CASSEN, H. GASS AND PAUL CRANDALL, UCLA School of Medicine, Los Angeles, Calif. (Session IV)

In a cooperative program of fast brain-tumor section scanning with the UCLA neurosurgery group, it appeared that an improvement of geometrical resolution would be of great value to the neurosurgeons in attaining preoperative information relative to the geometrical boundary configurations of a tumor region. Most current brain-tumor scans show the tumor as a blob with very poorly defined boundaries. An appreciable increase in resolution is not easy to attain without other sacrifices. However, postmortem evidence correlated with section scans indicated that any improvement would help. Based on previous experience a greatly improved, under-the-table hydraulically driven fast-section scanner has been constructed using a spherical-cap nest of seven 3-in. crystals with individual collimators all focused at a common focal point. The horizontal resolution is comparable with that of current scanners, and the vertical resolution is not much inferior to the horizontal. The high sensitivity attained by using seven crystals enables high-speed section scanning. Performance characteristics obtained will be illustrated.

Improved, Rapid Method for Free Thyroxine in Serum BY R. R. CAVALIERI, J. N. CASTLE AND G. L. SEARLE, V.A. Hospital, San Francisco, Calif. (Session XVII)

The concentration of free thyroxine (T-4) in the blood is an important determinant of metabolic status and is useful in the diagnosis of abnormal thyroid function. Most methods which measure the fraction of free T-4 in serum involve prolonged dialysis. To permit rapid determination of the free T-4 fraction on a routine basis, we have developed a technique that uses adsorption by Dextran gel (Sephadex). ^{125}I or ^{126}I -labeled L-T-4 (0.02 μgm) is added to 1 ml serum. An aliquot of the mixture is diluted 32-fold with potassium phosphate buffer, pH 7.4. To 3 ml of the diluted mixture is added 0.20-gm Sephadex, G-25 in bead form, using a calibrated spoon. The tube is

agitated on a Vortex mixer for 10 sec, after which the particles of Sephadex are allowed to settle (1/2 min). Following removal of the supernatant, the Sephadex is washed with 3 ml of buffer five times with 5 sec agitation, and three-quarters of the wash-fluid is removed with each wash. Both the Sephadex and an aliquot of the diluted, labeled serum are counted, and the uptake by Sephadex calculated. The results are expressed as a percent of a control value (normal serum pool). Each sample was also assayed by the equilibrium dialysis method of Sterling and Brenner. *Results:* Excellent correlation was found between the results by Sephadex and those by the dialysis method over the entire range of thyroid function, indicating that the Sephadex uptake is directly proportional to the free T-4 fraction. The advantages of this method include: simplicity, rapidity and good reproducibility. There is no interference by radioiodide contaminating labeled T-4, administration of inorganic iodine or x-ray contrast dyes. As will be discussed, the method can also be used to measure indirectly the level of total T-4. From the free T-4 fraction and the total T-4, the free T-4 concentration can be calculated.

Response of Toxic Nodular Goiter to High- and Low-Dose Radioiodine Therapy BY N. DAVID CHARKES AND ROBERT E. CANTOR, Temple Univ. Hospital and Albert Einstein Medical Center, Philadelphia, Pa. (Session XII)

Both high doses (Skillern *et al*, *Arch. Int. Med.* 110:888, 1962) and low doses (Eller *et al*, *Ann. Int. Med.* 52:976, 1960) of radioiodine have been advocated for treatment of toxic nodular goiter. We have studied the responses to ^{131}I therapy of 10 patients with this disorder. Six patients received single doses which deposited 14–20 mc within the nodule(s), and four patients received doses which deposited 3–9 mc. In each case, the diagnosis was confirmed by appropriate radioiodine testing with *l*-triiodothyronine and TSH (Charkes *et al*, *J. Nucl. Med.*, 8:637, 1967). Post-treatment uptakes, scans, stimulation and suppression tests were performed in all patients. In the high-dose group, the nodules were functionally ablated in four of the six patients; the radioiodine uptake of the extranodular tissue was depressed below the normal range following therapy in four, but responded to TSH in three. These findings suggest that post-therapy diminution in uptake of normal tissue is not a result of radiation thyroiditis but is due to functional atrophy from long-continued pituitary suppression by the nodule. None of the nodules was functionally ablated in the low-dose group, and the fall in radioiodine uptake of the nodule following therapy in three of the four patients made further radioiodine therapy more

hazardous by increasing the dose requirement. High doses of radioiodine thus appear to be preferable to low doses in treatment of toxic nodular goiter.

Sequential Strontium Bone Scans in Multiple Myeloma

BY N. DAVID CHARKES AND JOHN DURANT, Temple Univ. Hospital, Philadelphia, Pa. (Session XXV)

Bone pain is a common, indeed a cardinal, symptom of multiple myeloma, yet roentgenograms of painful areas usually disclose only radiolucencies or osteoporosis, which are little different from changes seen in asymptomatic bones. Furthermore, roentgenograms do not reflect changes in the clinical picture resulting from either progressive disease or from the salutary effects of chemotherapy. Studies by ourselves (*Radiol. Clin. North Am.* 3:499, 1965) and others have demonstrated that strontium bone scans may disclose evidence of new bone formation prior to roentgenographic changes. We therefore performed ^{87m}Sr scans of the axial skeleton and pelvis in five patients with multiple myeloma at intervals of 2-3 months for a year. On some occasions ^{85}Sr scans were made instead. Abnormalities were found in four of the five patients, in three cases corresponding to sites of bone pain. In none of these patients were roentgenographic abnormalities noted which differed from changes seen in other bones. In one patient, sequential scans revealed progressively greater involvement of the spine, antedating radiographic evidence of disease by several months. In another patient in clinical remission, the scans remained normal throughout the year. New bone formation therefore appears to be common in multiple myeloma although radiodensities are seen infrequently. The radiostrontium scan, which readily detects osteogenesis, depicts these sites of abnormal activity. The scan correlates closely with the clinical picture and is of value in determining the activity of the disease process.

Stereoscintophotography BY N. DAVID CHARKES,

Temple Univ. Hospital, Philadelphia, Pa. (Session IV)

Stereoscopy is the process whereby two images of an object, taken from different projections, are presented to each eye separately and mentally fused so that the object is reconstructed in three-dimensional form. Levy and Okezie (*J. Nucl. Med.* 4:181, 1963) showed that photoscan images taken at symmetric angles from an imaginary axis through an organ by means of a focusing collimator could also be viewed through a stereoscope and the isotopic deposition reconstructed into a three-dimensional representation of the organ.

We have found that symmetric scintiphotos made by an Anger camera likewise can be mentally fused when

viewed in a stereoscope into a three-dimensional picture of the isotopic content of that organ. We term this process stereoscintophotography.

Any organ or bodily area containing a gamma-emitting radionuclide is theoretically capable of being viewed stereoscopically by this method. We have successfully located brain tumors, thyroid nodules and hepatic metastases with the technique. Angio-stereoscintophotography requires but a brief, continuous infusion of radionuclide. Visualization of deep-seated organs such as the pancreas and placenta is facilitated by stereoscopy.

Preliminary studies have shown that the angle from which the stereo views are taken is not critical; a high counting rate to insure optimal resolution, however, is essential.

The advantages of using the scintiphoto camera for stereo views rather than a rectilinear scanner include: (1) relatively brief exposure time (paired stereo views of brain tumors can be made in 6-7 min with ^{99m}Tc pertechnetate); (2) depth independence (deep-seated organs such as the pancreas are seen in relation to nearby structures); (3) oblique stereo-projections are readily taken (viz., brain scintiphotos); and (4) large-area stereoscintiphotos (viz., torso) are readily made, as in localizing thyroid cancer metastases with therapy doses of ^{131}I .

Radioiodination of Leukocytes by an Electrolytic

Method BY H. F. CHENG AND R. E. PETERSON, University Hospitals, Iowa City, Iowa. (Session III)

Labeling proteins with radioiodine (^{131}I or ^{125}I) has been a widely used procedure. When applied to blood cells, radioiodination by ordinary chemical methods damages cells. To maintain viability of cells, one has to find mild experimental conditions. Rosa *et al* (*Biochim. Biophys. Acta* 86:519, 1964) have added to radioiodination procedures for proteins by developing an electrolytic method. Advantages of that method are: (1) avoidance of using oxidizing agents and (2) mild reaction conditions. We have adapted the electrolytic procedure to labeling rat leukocytes and human lymphocytes with ^{125}I .

The electrolytic cell is made of a 20-ml glass beaker with a cylindrical platinum foil as anode (10 cm²). The cathode is a platinum wire placed in a glass tube with the bottom closed by a cellophane dialysis membrane. Electrolysis is carried out at a constant current with a precision coulometer. (The current ranges are variable continuously from 0 to 100 and in steps upward to 3,000 microamperes with an accuracy of $\pm 0.1\%$.) The anodic compartment is filled with cells in Hank's solution in varying concentrations of KI in saline (0.25 to 25×10^{-4} M KI). The same KI solution in saline is placed in the cathodic compartment. Ten or more

microcuries of ^{125}I is added. Electrolysis has been carried out at 30–300 microamperes. At intervals, samples are taken to measure the radioactivity of the solution, to evaluate cell-bound iodine and for cell-viability tests.

Labeling leukocytes with radioiodine has been found effective, but the problem lies in minimizing the loss of cell viability. We have reached preliminary conditions which iodinated leukocytes without causing cell damage: Cells suspended and gently stirred in Hank's solution in an ice bath were subjected to electrolysis with 100 microamperes for 1 hr. One to 3% of iodide became attached to cells of which over 90% remained viable. Such radioiodinated cells are being used for life span or survival studies. (This investigation was supported by the James Picker Foundation.)

Continuous ^{57}Co B₁₂ Administration Study to Evaluate B₁₂ Absorption in Humans Receiving Colchicine or Cascara Sagrada BY ROBERT B. CHODOS, D. I. WEBB AND W. W. FALON, V.A. Hospital and Upstate Medical Center, Syracuse, N.Y. (Session III)

Previous studies from this laboratory have revealed a reversible malabsorptive effect of oral colchicine, 1.9 to 3.9 mg daily, which includes the reduction of vitamin B₁₂ absorption. The present studies were undertaken to define the mechanism involved in producing this effect. A continuous ^{57}Co vitamin B₁₂ absorption method was used to study B₁₂ absorption in 12 normal obese subjects receiving either colchicine or cascara sagrada. Labeled B₁₂ was given orally followed in 2 hr by 1,000 μg of stable vitamin B₁₂ i.m. during four sequential 4–6-day periods (control, colchicine p.o., control, cascara sagrada p.o.). Urinary ^{57}Co B₁₂ was measured for each 24 hr, and stool activity was determined on pooled collections for each period. In two subjects colchicine was administered to the ileum by tube. The effect of colchicine upon intrinsic factor production was evaluated by an *in vitro* isotopic charcoal assay and by ^{57}Co B₁₂ bioassay in pernicious anemia patients. B₁₂ binding by ileal mucosa in the presence of colchicine was studied by an *in vitro* ^{60}Co B₁₂ guinea pig mucosal system.

Data revealed a reasonably sustained urinary excretion during the control period, a consistent decrease with colchicine, a return to normal during a second control period and no subsequent decrease with cascara. In contrast, pooled stool activity increased with both colchicine and with cascara. Intrinsic factor production and intrinsic factor-B₁₂-mucosa binding were not deleteriously affected by colchicine. Gastric biopsy was normal while jejunal biopsy showed inconsistent mucosal changes.

These studies indicate that colchicine produces ileal

malabsorption of B₁₂ without altering intrinsic factor production or binding function. Cascara-produced catharsis increases fecal recovery of B₁₂ but does not decrease its absorption. In addition, the continuous B₁₂-administration and recovery method provides a useful and practical technique for B₁₂-balance studies, including investigation of variables influencing B₁₂ absorption.

Biologic Turnover and Toxicity of $^{99\text{m}}\text{Tc}$ -S Colloid BY MARVIN B. COHEN, LEONARD SPOLTER, EZRA KLEINER AND DAVID MASUOKA, V.A. Hospital, Sepulveda, Calif. (Session XIX)

The long-term toxicity and biologic turnover of $^{99\text{m}}\text{Tc}$ -S colloid is essentially unknown. Three different preparations of $^{99\text{m}}\text{Tc}$ -S were injected via the tail vein into groups of 25 mature mice. A saline-injected group was used as a control. Twenty percent of each group was sacrificed at day 1 and at intervals thereafter. Rhenium carrier was used in one method of preparation but was not used in the second method which required the use of a column for removal of free pertechnetate. ^{35}S -labeled thiosulfate was incorporated into both preparations for use in turnover studies and radioautography. A third group was injected with $^{99\text{m}}\text{Tc}$ -S prepared with rhenium carrier but not with ^{35}S . This group was used as a secondary control to rule out the possibility of unsuspected radiation damage. Histologic information was obtained by both light and electron microscopy. Biological turnover was measured by counting the liver homogenates. Localization was determined by radioautography. Results will be discussed.

^{198}Au or $^{99\text{m}}\text{Tc}$ -S Colloid and the "False-Positive" Liver Scan BY MARVIN B. COHEN, V.A. Hospital, Sepulveda, Calif. and UCLA Medical Center, Los Angeles, Calif. (Session XIII)

Hepatic photoscanning is primarily used to detect primary or metastatic neoplasms and abscesses. Increased interest is being shown in the "pseudo-tumor" appearance seen in some patients with cirrhosis. Other causes of such "false-positive" liver scans are less well known.

This report will demonstrate several examples of the "pseudo-tumor" formation of cirrhosis including intro-hepatic defects in the presence of normal splenic concentration. Scan findings will be correlated with physiological measurements such as splenic pressure. Examples of extra-hepatic lesions producing large scan defects will also be presented. Advantages and disadvantages of using ^{198}Au and $^{99\text{m}}\text{Tc}$ -S colloid in the evaluation of the "false-positive" liver scan will be discussed. $^{99\text{m}}\text{Tc}$ -S colloid yields the best definition of localized defects, but ^{198}Au appears to give more physiologic information.

Scanning Optimization in Terms of Statistical Criteria

BY T. D. COHEN, P. V. HARPER AND R. N. BECK, Argonne Cancer Research Hospital and Univ. of Chicago, Chicago, Ill. (Session IX)

The concept of a statistical figure of merit has been proposed by several investigators as a criterion for comparing and evaluating radioisotope imaging systems. This concept can be formulated in many different ways in terms of basic scanning parameters (i.e., modulation transfer function, radius of view, collimator sensitivity, counting rate, etc.).

In previous studies, experimental comparison between computed figures of merit and actual scans of test patterns and realistic objects were not extensively investigated. Studies of this kind are presented in the present report illustrating:

1. Image quality when count density and contrast are varied and the figure of merit is constant.
2. Correlation between image quality and figure of merit when collimator resolution and sensitivity are varied to correlate the computed optimal compromise between sensitivity and resolution with what occurs in actual scans.
3. Comparison of sine-wave test patterns with images of realistic objects. An attempt is made to relate the findings to studies of visual perception.

Tissue Vascularity in Positive Brain Scans BY HOWARD

J. COHN AND MANFRED H. SOIDERER, Univ. of Michigan, Ann Arbor, Mich. (Session XXVII)

Alteration of the normal blood-brain barrier is assumed to be responsible for visualization of intracranial lesions on the brain scan. The specific factors are not known. To evaluate the importance of tissue vascularity as a factor, a series of 111 brain scans with histological verification were studied. The tissue vascularity was graded by an independent observer without knowledge of the brain-scan result. The tissue vascularity was then compared with the clinical brain scan readings. Chi square analysis of these data revealed a statistically significant shift which was interpreted as indicating a correlation of the degree of vascularity of the lesion with intensity of visualization on brain scan.

On the other hand, a small group of very highly vascular blood-vessel tumors and malformations did not have a generally high degree of visualization. This suggests that the relative metabolic requirements of the tissue involved is a factor in brain-scan visualization as well as degree of vascularity.

Distribution of ^{113m}In in Labeled Colloids BY LELIO G.

COLOMBETTI, RUSSELL HERMANSON AND DAVID A. GOODWIN, Stanford School of Medicine, Palo Alto, Calif. (Session XXIII)

There is some evidence to suggest that particle size of colloidal material affects the relative uptake by R.E.

cells of the liver, bone marrow and spleen. Colloidal ^{113m}In was prepared with various concentrations of Fe^{+++} carrier in an attempt to increase the size of the colloidal particles. The compounds were prepared using 8 ml of column eluate from the ^{113}Sn - ^{113m}In generator with and without carrier iron. When carrier iron was added, the final concentrations were 50 $\mu\text{g}/\text{ml}$, 250 $\mu\text{g}/\text{ml}$ and 500 $\mu\text{g}/\text{ml}$. It was found that a final concentration of gelatin in the range of 0.05% was sufficient to protect the colloid. The final step was the addition of a fixed amount of phosphate buffer (monosodium and di-sodium phosphate) to bring the final pH to 6.5-6.8. Following i.v. administration of the carrier-free material in mice, liver uptake approached 70-80% of the administered dose and spleen uptake was 1.0-1.5%. With added carrier iron, a marked Tyndall effect was noted in the solution, and splenic uptake increased to 5-6%. Liver uptake remained high (80-90%). In all experiments uptake by the other organs (kidneys, lungs and blood) was very low (less than 1%). The use of phosphate buffer greatly simplifies preparation of the colloid because it makes titration with NaOH unnecessary. Increased splenic uptake which can be obtained with added carrier iron may be useful for visualizations of this organ.

^{47}Ca Absorption in Bile-Duct Ligated Rats BY C.

CONSTANTINIDES, P. KOSTAMIS, K. KEHAYIOGLOU, J. SFONTOURIS AND B. MALAMOS, School of Medicine, University of Athens, "Alexandra" Hospital, Athens, Greece. (Session XI)

In acute obstruction of the biliary tract, calcium absorption is depressed when administered with CaHPO_4 or with calcium phytate as a carrier, but no effect on calcium absorption was found when CaCl_2 was given as a carrier. In chronic obstruction of the biliary tract, calcium absorption was depressed when CaCl_2 was administered as a carrier, but no studies on the effect of CaHPO_4 or calcium phytate in chronic obstruction have been reported so far. In the present study the effect of calcium absorption in acute and chronic obstruction of the biliary tract is discussed using each of the carriers mentioned above separately and together with medium chain triglycerides (MCT).

System for Quality Control of Short-Lived Radiopharmaceuticals BY MARY C. CREWS, JAMES L.

QUINN, III AND NANCY BRYANT, Northwestern Univ. and Chicago Wesley Memorial Hospital, Chicago, Ill. (Session XIX)

Much has been written about the quality control of radiopharmaceutical production but little of it pertains to the special problem of those substances incorporating short-lived radionuclides. It is generally

agreed that any testing of the radiopharmaceutical as injected would have to be "after the fact." At Chicago Wesley Memorial Hospital, we have set up a system for the quality control of radiopharmaceuticals incorporating ^{99m}Tc and ^{113m}In , which involves prior testing of the individual components before use and periodic checks on the methods of preparation as well as the usual "after the fact" testing.

Stock reagents are prepared using the highest available grades of chemicals and sterile pyrogen-free distilled water. These are placed in serum vials, autoclaved, and refrigerated. Each batch is assigned a lot number, and a form is filled out listing the name and formula of the chemical used, the amount, manufacturer, manufacturer's lot number and method of reagent preparation. A sample of each lot is tested bacteriologically, and periodically samples are sent for pyrogen testing. The reagent is not used if these tests are positive.

The method of preparation of each radiopharmaceutical is standardized, and the procedure may be checked by testing the final product. Each time a diagnostic agent is prepared, a lot number is assigned and a form filled out listing the compound, the reagents used, lot number and amount of each component and radioassay data. Each time a generator is eluted a similar form is completed. Pooled samples of all injected radiopharmaceuticals are sent for bacteriologic testing. Periodically these final products are also tested for pyrogenicity. The control forms and test results are kept on file for ready reference.

This system has been in use in our department since May, 1967, and has worked very satisfactorily. Since its use was instituted we have had no cases of bacterial contamination of any radiopharmaceutical. Labels, forms, and the filing system will be illustrated and discussed in detail.

Determination of Thyroxine in Serum by Saturation

Analysis of Thyroxine Binding Proteins BY ALFREDO CUARÓN AND FELIPE GORDON, with technical assistance of NELLY RATTONI AND CARMEN PINEDO, Centro Médico Nacional, Instituto Mexicano del Seguro Social, Mexico City, Mexico. (Session XVII)

A new, rapid and simple method for determining serum thyroxine is introduced which is based on the saturation analysis of the thyroxine (T-4) binding proteins. Two ml of the test sample is deproteinized, and the T-4 that is freed is added with a standard stock serum (2 ml). Then the *in vitro* binding of ^{125}I -triiodothyronine by the proteins of this mixture is estimated by gel-filtration chromatography. The T-4 content of the serum sample is estimated using the standard calibration curve of the binding of ^{125}I -T-3 by the proteins of the standard stock serum obtained using various

concentrations of a T-4 solution. The method is highly specific for T-4 and is unaffected by iodides, MIT, DIT and other iodinated compounds. A good reproducibility was observed by triplicate determinations. The values of T-4 concentration ($\mu\text{g}/100\text{ ml}$) in various groups of subjects were (1) euthyroid subjects: 10.4 ± 2.1 (mean \pm s.d.); (2) hyperthyroidism: 22.7 ± 4.2 ; (3) hypothyroidism: 4.0 ± 2.0 ; (4) nephrosis: 4.7 ± 1.8 and (5) normal pregnancy: 16.4 ± 2.2 . The results, expressed as T-4 iodine were: (1) euthyroid subjects: 6.8 ± 1.4 ; (2) hyperthyroidism: 14.9 ± 2.8 ; (3) hypothyroidism: 2.6 ± 1.3 ; (4) nephrosis: 3.1 ± 1.2 and (5) normal pregnancy: 10.7 ± 1.4 . The values for T-4 iodine had a significant correlation with the values for protein-bound iodine in the same patients. These results proved that this procedure could be used as a routine clinical diagnostic test in place of the PBI estimation, mainly in those cases where iodine contamination is expected.

The Role of Brain Scanning in the Differential Diagnosis of Unilateral Nerve Deafness

BY FRANK H. DELAND AND HENRY N. WAGNER, JR., Johns Hopkins Hospital, Baltimore, Md. (Session I)

Progressive unilateral nerve deafness is less common than conduction deafness but requires early diagnosis for optimum treatment. A common cause is a neoplasm of the eighth cranial nerve. Between 1964 and 1967 12 acoustic neuromas and three meningiomas involving the eighth cranial nerve were removed surgically from 15 patients at the Johns Hopkins Hospital. Brain scans after administration of ^{99m}Tc -pertechnetate were performed in all patients except two with meningiomas. In this series the accuracy of brain scanning exceeded that of other diagnostic procedures. The lesion was demonstrable on the scan in each instance. Retrograde brachial arteriography was positive in only 15% and equivocal in 15%. Pneumoencephalography showed the lesion in 60% of the patients and tomography was positive in 33% and equivocal in 11%.

At surgery the diameters of the lesions ranged from 2.0 to 4.1 cm. There was no relationship between the size of the tumor and the duration of the symptoms prior to diagnosis; however, in three patients with lesions less than 2.4 cm in diameter, no cranial nerves other than the eighth were involved. In the remainder of the patients (10), the tumors were 2.5 cm or larger and involved two or more cranial nerves.

It is concluded that brain scanning plays an important role in the management of patients with unilateral nerve deafness. The sensitivity of the procedure in the detection of acoustic neuromas makes possible early diagnosis, even when only the eighth cranial

nerve is involved. This increases the possibility for successful surgical therapy. (Supported by USPHS Grant GM 10548.)

Distribution of Ventilation BY GERALD L. DENARDO, STUART MCHARDY-YOUNG AND DAVID A. GOODWIN, Stanford School of Medicine, Palo Alto, Calif. (Session XX)

The usual method of using ^{133}Xe to study regional ventilation in the lung is to compare the regional counting rate after a single breath of ^{133}Xe with the counting rate after the alveolar gas has been uniformly labeled with ^{133}Xe . These measurements are made at 500–1,000 cc above functional residual volume and represent the static distribution of ventilation. One of us (Gerald L. DeNardo) previously has made measurements of this type in normal subjects and found a gradient of 1:1.4 from apex to base in the vertical lung but a virtually uniform distribution in the horizontal lung.

We are presently measuring the distribution of ventilation at various levels of inspiration beginning at residual volume and progressing stepwise to maximum inspiration. This technique provides a more dynamic evaluation of lung function because the distribution of ventilation is affected by regional airway resistance. An Anger scintillation camera with a 35-mm camera and a 1,600-location-memory digital computer is used to provide a pictorial and quantitative display of radioisotope distribution. The subject inhales from a spirometer stepwise from residual volume to maximum inspiration while the ^{133}Xe gas is administered in one of two ways: (1) the ^{133}Xe is in the spirometer from which the subject breathes, or (2) the ^{133}Xe in a 2–5-cc bolus of gas is added to the tubing which connects the subject to the nonradioactive air in the spirometer.

With these methods one can illustrate both pictorially and quantitatively the dynamic distribution of ventilation. In the normal vertical lung, the upper zone receives more of the initial portion of inspiration than it does of the later portions. However, the lower and middle zones of the lung receive more ventilation throughout inspiration. The greater the inspiratory volume or the pre-inspiratory volume, the more uniform the distribution. We believe these dynamic methods may be more sensitive than the static method for detecting abnormalities of the distribution of ventilation in pathological conditions such as asthma, bronchitis, chest-wall abnormalities and emphysema.

The Overlap Photoscan Technique BY JAMES T. DODGE, PATRICK A. LYNCH AND MICHAEL D. EDWARDS, Saint Elizabeth Hospital, Yakima, Wash. (Session VIII)

The quality of photoscans obtained with rectilinear-scanning equipment appears limited by the nature of

the imaging system. This problem is due in part to the fact that the area displayed by the light source on the scan is usually much smaller than the area observed by the detector; it is also due to the distracting fluctuations in density caused by the random nature of radioactivity. We determined that a more specific display of the distribution of radioactivity can be achieved by using a light image for the photoscan that corresponded more closely to the width of the area observed by the collimated detector and by overlapping adjacent sweeps of the scan. The overlap photoscan is improved further by an increased information density. The multiple exposure requires a proportionately reduced intensity of the light source to maintain a proper image density. The nondiagnostic density fluctuations appear to be reduced by summing counting rates effected through the multiple exposure aspect of this technique. A longer meaningful scale of contrast appears possible with this technique. The procedure has proven valuable in thyroid scans and work is progressing on the application of the overlap photoscan technique to larger organs.

Improved Recording of Dynamic Scintillation Camera Studies BY C. H. DOUGLAS AND E. SURPRENANT, St. Mary's Long Beach Hospital, Long Beach, Calif. (Session IX)

A major contribution of the Anger scintillation camera is its ability to detect dynamic events. Methods for rapid photography of the scintillation events as they are displayed on the unit's cathode-ray tube (CRT) are useful but present difficulties because exposure and time sequence of the images must be determined before the study. Frequently the data are not optimally recorded.

Video-tape recording of the scintillation-camera output makes it possible to record all the data without concern for film exposure or time sequence. Once recorded, the data may be displayed repeatedly in any convenient manner. However, a direct electronic coupling from the scintillation camera to a tape recorder is costly because it requires a special circuit to make the signals compatible to the recorder and another circuit to display the data on the CRT. Instead, we have devised an optical-coupling system. A vidicon television camera was selected because it can transmit all the light pulses from the CRT to the video tape; this has been confirmed by direct observation. The camera records "high-contrast" images so that light pulses are recorded as bright "spots" on a black background. The video-tape recorder is capable of variable speeds, and the data are displayed on a television monitor. This equipment is commercially available.

This apparatus records all of the data detected by a scintillation camera without significant deterioration

of sensitivity or resolution. After a dynamic study is recorded, the precise section of tape containing the data of interest is identified and then photographed as it is displayed on the monitor. Thus the maximum amount of available counts are integrated into a single image with optimum film exposure. Improved diagnostic accuracy has been achieved in blood-flow studies. The system is currently being adapted to regional pulmonary perfusion and ventilation studies with ^{133}Xe .

This system is economically feasible because it adds to the versatility of the scintillation camera while reducing patient examination time.

Heterogeneous Sample Counting BY ARTHUR F. DRATZ
AND JAMES J. C. COBERLY, V.A. Hospital and
Emory Univ. School of Medicine, Atlanta, Ga.
(Session XIV)

We have devised a more accurate system for the assay of heterogeneously distributed radioactive material at short sample-to-counter distances. The new system compensates for inverse-square and self-absorption errors in three dimensions by using sample rotation and two attenuators, one lateral and one vertical. When these attenuators are properly positioned, the counting rate of a small (1-ml) radioactive source becomes independent of its position within a rotating 375-ml sample volume. The positioning of the attenuators is specific for a single isotope and pulse-height energy range; a simple recalibration is necessary if these are changed. With either ^{59}Fe or ^{131}I counted at their photopeaks errors attributable to the geometric location of a small source at any point within a 375-ml sample volume readily have been reduced to a range of $\pm 1.5\%$. Sensitivity is about 3,000 cpm/ μc ^{59}Fe and 6,000 cpm/ μc ^{131}I .

In this system a 2×2 -in. NaI (Tl) crystal is positioned symmetrically 4 in. from the axis of rotation of the sample. Sufficient water is added to fix the sample volume at 375 ml. The lateral attenuator is a lead brick standing on end. It is inserted laterally as a wedge between the crystal and rotating sample. The vertical attenuator is a bar, 1 in. high and about 4 in. long, made by fastening together two 1/2-in. diameter rods (aluminum for ^{59}Fe , plexiglass for ^{131}I). It is positioned between the crystal and the sample at right angles to the lead wedge.

This counting geometry is being employed for fecal radioassays in quantitative metabolic balance studies. Preliminary experiments with live rats indicate that with minor modifications the basic system can be used in studies involving small animals that require whole-body counting.

Radiation Sensitivity of Mammalian Thyroid Cell Function BY H. J. DWORKIN AND M. CARROLL,

Princess Margaret Hospital and Univ. of Toronto, Toronto, Ontario, Canada. (Session X)

Hypothyroidism following ^{131}I treatment for Graves' disease has been well documented. However, the radiobiology of the mammalian thyroid cell has not been examined under controlled conditions. Reported is an initial experience defining the characteristics of a controlled system of single-cell suspensions of beef thyroid and its response to radiation in terms of function.

Beef thyroids were trypanized in a continuous flow apparatus and the resulting single-cell suspension was filtered and collected in fetal-calf serum. After treatment with DNAase and washing, the cells were exposed to drugs or radiation, and their ability to concentrate ^{131}I on incubation was examined compared to unexposed control cells. The distribution of ^{131}I in the intracellular constituents (MIT, DIT, T-3 and T-4) was examined after paper chromatography.

The cell-to-medium ratio (C/M) of unexposed thyroid cells following 3 hr of incubation with ^{131}I varied from 10 (occasionally lower than 10 but these were discarded as "damaged cells") to 35 but in any one experiment the relative error of replicate determinations was $\pm 5.7\%$. A time-sequence study of C/M showed a rapid cell uptake of ^{131}I in the first hour with a slower component thereafter. In some cases a plateau was not reached by 18 hr.

Cells exposed to 2 mM perchlorate demonstrated a greater reduction in C/M than those exposed to 2 mM iodide.

To examine the specificity of iodine concentration, suspensions of mouse spleen cells were incubated with ^{131}I . The C/M varied from 4 to 9 and 2 mM perchlorate produced no reduction in C/M.

Thyroid-cell suspensions were exposed to 25,000, 50,000 and 100,000 rad (^{60}Co) with no significant reduction in C/M. The lack of radiation sensitivity of the iodine-concentrating mechanism suggests that the radiation effects seen in man are not due to impairment of cell function or disruption of non-replicating cells.

Laminar Scintiscans for Determining Depth of Small Metastases of Thyroid Carcinoma BY C. LOWELL EDWARDS, R. TANIDA AND R. MORA, Oak Ridge Associated Universities, Oak Ridge, Tenn. (Session XII)

The rectilinear scanner can be used to locate radioactivity in metastatic thyroid carcinoma. Locating these lesions assists the surgeon and often allows him to excise the lesion by cutting down directly on it using landmarks made on the skin. Unfortunately the information is only two-dimensional and fails to indicate the depth of the lesion. Furthermore, the fine-focusing collimator gives good resolution only if the focus of

radioactivity is located on the plane of the focal point of the collimator. Otherwise, the image is greatly distorted and may be obscured beyond detection.

A simple technique for assessing depth has proved helpful in precisely locating very small metastatic foci of thyroid carcinoma, especially in the neck where lateral scans are difficult to obtain. After the routine scan is made, the locations of the foci are marked on the patient's skin. Serial small scans are then made over the area in question. The collimator is moved progressively closer to or further from the skin for each scan. The distance between the detector and the skin or some more suitable landmark is carefully measured and recorded. The image obtained at the various levels becomes progressively sharper, smaller and denser as the focal point of the collimator approaches the level of the focus of radioactivity. Likewise, the image gets fuzzier, larger and less intense as the focal point gets further above or below the focus of activity. A careful measurement of the focal distance of the collimator is essential for using this technique.

Radiometric Procedures for *in vitro* Determination of Cholesterol Biosynthesis BY C. D. ESKELSON, H. P. JACOBI, A. L. DUNN AND C. R. CAZEE, V.A. Hospitals, Tucson, Ariz. and Omaha, Neb. (Session V)

This study was designed to evaluate the various factors whose control would lead to a reliable and reproducible system for the *in vitro* determination of the rate of cholesterolgenesis. The need for such a system merits value in the evaluation of endocrine and pharmacologic agents which may affect cholesterol biosynthesis.

Using ^{14}C -acetate or mevalonate together with cofactors and the microsomal plus soluble fractions of liver homogenates adapted from procedures of Bucher and McGarrahan and that of Knauss *et al* (*J. Biol. Chem.* 222:1, 1956, 234:2,835, 1959) cholesterol synthesis can be measured by the *de novo* incorporation of radioactivity in a cholesterol-tomatidine isolate. Methodological procedures and special apparatus designed for manifold sample treatment in conjunction with liquid scintillation counting procedures are described. Results indicated a reliable and reproducible system because the rate of cholesterol-biosynthesis can be obtained in either rat or rabbit liver homogenates. It was observed that for rat liver preparations 85-90% of the *de novo* synthesized cholesterol is recovered from the enzyme system. Cholesterol biosynthesis begins to cease after 1-hr incubation when mevalonate is substrate but not when acetate is substrate. Cholesterolgenesis is linear with time of incubation up to 1 hr, enzyme concentration and substrate concentration. It was observed that liver homogenates from different rats each have different rates of cho-

lesterol biosynthesis and that this variation was not caused by the homogenization procedure. The enzyme system responded characteristically in that the *in vitro* addition of cholesterol did not alter cholesterolgenesis; however, liver homogenates from rats fed cholesterol and from fasting rats have a decreased ability to biosynthesize cholesterol.

Exchangeable Sodium in Man: Comparison of Standard Urinary Method and Metabolic Balance with Whole-Body Counting BY RONALD G. EVENS, LESLIE BAER, JOHN R. GILL, JR. AND FREDERIC C. BARTTER, National Institutes of Health, Bethesda, Md. (Session X)

The determination of exchangeable sodium has been useful in the study of disease. The technique of whole-body counting of clinically useful isotopes has the following advantages: (1) urine and stool collections are not necessary, (2) unexplained losses are avoided, (3) measurement is easier and (4) smaller doses of isotope may be used. Twenty-four-hour exchangeable sodium was calculated by dividing the amount retained after 24 hr in counts per minute of microcuries by the specific activity of serum. Amount of administered dose retained ($25 \mu\text{C } ^{24}\text{Na}$) was determined by two methods: (1) by subtracting total counts excreted in the urine from total counts administered and (2) by whole-body counting. The patient was counted by using an 8×4 -in. NaI(Tl) crystal with fixed geometry in a low-background steel-shielded room. The mean values for 24-hr exchangeable sodium in 55 studies by conventional urine and whole-body counting techniques were similar: 2,374 meq and 2,350 meq, respectively ($P > 0.8$). The mean difference between the two techniques was 24 ± 13 meq (SEM). Twenty-one normals and patients had duplicate determinations of exchangeable sodium performed while on strict balance regimen and during various manipulations to alter sodium balance. The average change in sodium balance was -148 meq calculated from exchangeable-sodium values and -179 meq calculated from metabolic balance. The mean difference between the two techniques was 31 ± 16 meq and was not significant ($P > 0.6$). These results demonstrate that the whole-body-counting method, which may be performed periodically without the use of balance, gives reliable and reproducible data. Such a technique is especially useful in the study of the very sick or psychiatric patient.

Physiological Verification of a Model for Interpretation of the Renogram BY MELVIN H. FARMEANT, SEBASTIAN GENNA, CHARLES SACHS AND BELTON A. BURROWS, Boston Univ. Medical Center, Boston, Mass. (Session IX)

Renographic differences between the kidneys may be

indicative of renal arterial stenosis. To understand the factors that result in renographic differences, observations were made in a series of dogs that lead to a useful model. Dogs were prepared with an adjustable clamp on a renal artery, the ureters were catheterized and a plastic coil that fits into a well counter was inserted between the carotid artery and jugular vein. Dogs were heparinized to maintain flow through the shunt. Either both renal areas or one renal area and the bladder region and the upper chest were externally monitored by matched scintillation probes, and the amounts of each probe and the well counter were recorded on 4-track magnetic tape for subsequent readout through a multiscaler. Standard methods for performing creatinine and para-aminohippurate clearances were used. The upper chest was validated as an appropriate background to simulate the renal areas of a nephrectomized animal, and subsequently upper chest counts were subtracted from renal area counts to yield net kidney curves.

In all cases the integral of the blood-concentration curve was identical to the bladder curve and to the kidney curve before emptying begins. The difference between the integral of blood concentration (renal uptake) and bladder (integrated renal losses) approximate the net kidney curve after loss from the kidney begins. Similarly the difference between renal radioactivity and the integral of blood concentration yields the original integral curve of arterial concentration.

These findings indicate each kidney continuously extracts a fraction of the radioisotope present in the blood; passage through the unobstructed kidney occurs with little mixing of radioisotope in the hydrated state; the kidneys may differ significantly only in the relative times of passage or by mixing in the renal pelvis secondary to unilateral low urine flow rates.

Medical Radioisotope Scanning II. Collimator Point-Response-Function Effects in Optimum Data Processing BY R. A. FARRELL AND R. W. HART, The Johns Hopkins Univ. Applied Physics Laboratory, Silver Spring, Md. (Session IX)

The present theoretical study is concerned with the effects of the shape of the collimator response function on the performance of radioisotope-scanning systems designed to achieve optimum accuracy in imaging the isotope distribution. The methods used are those of statistical communication theory which have been used previously to determine the data-processing procedure which leads to optimum accuracy in imaging. The effects of the shape of the collimator response function on achievable performance is studied analytically, and explicit numerical results are presented for several assumed response functions. The study shows that the form of the collimator response function can have a

very significant effect on the accuracy of imaging the radioisotope distribution. Major emphasis is placed on the comparison of collimators with different forms for their point-response functions, but with equal expected total number of counts. Under this condition, as we might expect, optimum accuracy is achieved in the limit as the width of the response function approaches zero. The theoretical accuracy (in imaging) corresponding to this limit defines a standard for evaluating the performance of nonideal collimators. Practical considerations of collimator design, however, make it impossible to achieve the ideal limit (without sacrificing the expected total number of counts). For this reason, it is of interest to compare the accuracy achievable with collimator response functions having finite width. It is shown that the optimum form of a finite-width collimator depends on the form of the isotope distribution being scanned and that one of the features of a good collimator is that its width should be less than about one-half of the width of the essential structure of the isotope distribution. The optimum accuracy is evaluated for four types of hypothetical collimator response functions. The calculations provide specific illustrations of the significance of the qualitative features mentioned above and provide a quantitative comparison of the effect of various collimator-shape functions on optimum imaging in terms of the dose level of radioisotope.

Studies of Splenic Blood Flow and Function and Spleen Scintiphography Using Heated ^{99m}Tc -Labeled Erythrocytes BY PAUL A. FARRER, PHILIP RUBIN, ALAN E. OESTREICH AND SAMUEL S. CICCIO, Univ. of Rochester School of Medicine and Dentistry, Rochester, N.Y. (Session XVI)

Relatively little precise information is available concerning splenic function and blood flow in pathologic states. We have studied the tagging of erythrocytes with high-specific-activity ^{99m}Tc -pertechnetate and found that a high degree of red-cell labeling can be achieved and that the tracer remains firmly cell-bound after heating at 49.5°C for 20 min. The intravenous administration of heated, labeled RBC's was found to result in selective localization of radioactivity in the spleen, and rapid splenic imaging was possible owing to the high counting rates obtained over the organ. Because preliminary data showed that there is very little *in vivo* dissociation of ^{99m}Tc from red cells during the early time course following intravenous injection in humans, it was decided to explore the possible use of this technique in estimating splenic perfusion function (and size) in normal subjects and patients with splenomegaly.

The time course of regression of erythrocyte and plasma radioactivity following intravenous administra-

tion of ^{99m}Tc -labeled heated and washed RBC's (1 mc total injected radioactivity) were measured in normal subjects and in patients with myeloproliferative/lymphomatous conditions prior to and following radiotherapy or chemotherapy. At the same time, splenic and hepatic accumulation of label were continuously monitored by directional surface counting. Data concerning the rapid early dynamics of splenic perfusion and uptake of radioisotope were derived from rapid sequential gamma-camera scintiphotos.

Splenic accumulation of radioactivity appears to be a bi-exponentially increasing function reaching a maximum asymptotic value by 30 min post-injection. The time to reach half-maximum is about 3 min and the rate of accumulation is greatest in the first 2 min. The effective half-life of ^{99m}Tc in the spleen is about 5 hr, indicating that there is relatively little biological loss of splenic radioactivity. The ratio of RBC-to-plasma radioactivity falls from a maximum of about 20:1 to 2:1 during the first 30 min post-injection, and this fall is attributable to splenic sequestration of labeled cells, organs like liver, thyroid and vascular background showing no concomitant increase in the level of radioactivity. Early, rapid sequential scintiphotographic definition of the spleen shows reasonable correlation with the initial slope and height of the splenic-uptake curve, and it is tentatively concluded that the latter is a useful index of effective splenic perfusion.

Tumor Localization Using Radioactive Metal-Hematoporphyrin Complexes BY R. FAWWAZ, F. FRYE, H. S. WINCHELL AND J. H. LAWRENCE, Donner Laboratory, Univ. of California, Berkeley, Calif. (Session XXII)

Previous investigations have demonstrated localization of hematoporphyrins in many experimental tumors of animals and adenocarcinoma of the cervix and bronchi in man. Similar localization in animal tumors has been demonstrated with metal-hematoporphyrins. However, a previous attempt to localize tumors in man using ^{64}Cr -hematoporphyrin was considered unsuccessful. The present work was devoted to a systematic preparation of a variety of radioactive metal-hematoporphyrin complexes and the study of their *in vivo* distribution and localization in tumors of animals. Hematoporphyrin complexes of ^{62}Zn , ^{203}Hg , ^{52}Mn and ^{58}Co were prepared. When ^{203}Hg -hematoporphyrin was administered intravenously to dogs, it was cleared from the plasma as a two-exponential function. More than 80% of the administered dose was cleared from the plasma by the reticuloendothelial system with a half-life of 2 min and the remaining 20% was slowly cleared with a half-life of 3 hr. When ^{203}Hg -hematoporphyrin was administered to rats with

adenocarcinoma of the breast, to cats with lymphoma and to dogs with adenocarcinoma of the breast, the concentration of the isotope in the tumor tissue was about 20 times higher than that of muscle and of sufficient magnitude to be detected using external imaging devices. However, liver concentration was 7 times higher, spleen and lymph nodes had comparable concentration, and bone marrow and lungs had one-third the concentration of most tumors studied. ^{58}Co -hematoporphyrin was cleared from the plasma of dogs as a single exponential function with a half-life of 3 hr. None of the cobalt-hematoporphyrin was rapidly cleared by reticuloendothelial cells, and its final concentration in the liver was much lower than that obtained with ^{203}Hg -hematoporphyrin. Furthermore, the cobalt compound had significantly higher concentration in lymph nodes than that obtained with the mercury compound. Studies are presently being performed in man to determine localization of the ^{58}Co -hematoporphyrin in tumors.

Simple Technique for Organ Scanning using ^{113m}In BY J. F. FILBEE AND SYED IBRAHIM, Halifax Infirmary, Halifax, Nova Scotia, Canada. (Session XXIII)

^{113m}In is increasingly used for organ scanning because of its favorable characteristics: short half-life, excellent counting statistics, ready availability from a commercial generator, low cost and low radiation dose to the patient. ^{113m}In incorporated into a number of compounds for lung, liver, brain and blood-pool scanning have been made possible.

This nuclide is being used in the Halifax Infirmary for a trial period, and a simplified procedure has been developed and successfully used for liver, lung and blood-pool scanning. The procedure involves stabilization of eluant with commercial gelatin at varying pH's. It is found that on autoclaving there may be macroaggregation of gelatin particles and this appears to be highly pH-dependent. At a pH of 2, particles are not formed, leaving a colloid suitable for blood-pool scanning. At 3.5-4, macroaggregates of 10-40 microns in diameter are formed which are suitable for lung scanning, and at pH 7-9, particles suitable for liver scanning are formed.

The dependence of the colloid on the type and source of gelatin will be discussed and indications of possible developments will be described.

Basis for Accurate Scintiphotographic Detection of Subdural Hematoma BY MATHEWS B. FISH, ROBERT L. KOCH, MYRON POLLYCOVE, SEAN O'REILLY AND ARCHIE KHENTIGAN, San Francisco General Hospital and the Univ. of California School of Medicine, San Francisco, Calif. (Session XXVII)

There has always been need for a safe, relatively accurate means of screening for the presence or ab-

sence of subdural hematoma. This stems from the prevalence, usual progressive course and remediable nature of this lesion. Rapid, safe assessment of cranial vascular filling as well as detection of blood-brain-barrier defects can routinely be accomplished by a single antecubital i.v. 10-mc bolus injection of ^{99m}Tc -pertechnetate followed by rapid sequential (sec) and delayed (1 hr) scintiphotography (Anger-type scintillation camera). Such scintiphotographic studies in over 15 patients with eventually proved subdural hematoma revealed blood-brain-barrier defects as evidenced by abnormal accumulation of radioactivity at 1 hr in the majority, but not all, of the lesions. While most exhibited the usual crescentic increase of activity of the affected side, a few showed only slight diffuse increase in the affected hemisphere. Lateral views of the affected side usually exhibited poorly defined large areas of diffuse increase of activity.

Rapid sequential scintiphotography revealed areas of delayed and decreased cranial vascular filling corresponding to the region of the subdural hematoma in the majority of cases. Most importantly, areas of decreased cranial vascular filling were noted in all lesions that did not exhibit abnormal accumulation of radioactivity at 1 hr. Midline shift of anterior cerebral circulation corresponding in direction and degree to that noted on arteriography was noted in some of the rapid sequential scintiphotographic studies.

Since either cranial vascular filling defects or blood-brain-barrier changes were found in all patients, this approach affords a safe, sensitive and reliable means of screening patients suspected of having subdural hematoma prior to cerebral arteriography. The combination of the typical blood-brain-barrier defect and vascular-filling defect noted to be present together in a majority of these patients allows for a degree of differentiation of subdural hematomas from other intracranial processes as well as from extracranial abnormalities resulting from trauma and surgery.

Effect of Route and Load of Administered Phenylalanine on Human *in vivo* Phenylalanine Catabolism BY M. B. FISH, M. POLLYCOVE, J. DEGRAZIA, P. COHEN AND K. FLEURY, San Francisco General Hospital and Univ. of California School of Medicine, San Francisco, Calif. (Session X)

Emphasis on the detection of phenylketonuria (PKU) has resulted in the need for clarification of non-PKU hyperphenylalanemic states as well as the more accurate identification of PKU heterozygotes. Chemical tests to detect heterozygotes result in a 20% overlap of results between PKU-carriers and controls. Thus many areas of human *in vivo* phenylalanine metabolism remain to be defined. In this study, effect of route and load of administered phenylalanine upon

its oxidation was investigated using i.v. and oral tracer amounts of 1- ^{14}C -phenylalanine with varying loads of phenylalanine carrier in normal controls and PKU homozygotes and heterozygotes. The expired $^{14}\text{CO}_2$ specific activity was monitored continuously. The rate of oxidation of ^{14}C -phenylalanine was markedly decreased in the homozygote whether given i.v. or orally. Similar studies in heterozygotes revealed a variable degree of oxidation as compared to normal controls. In all subjects oral administration of the tracer resulted in a 50–100% increase in oxidation as compared to that after i.v. administration. Oral ^{14}C -phenylalanine with a 7-mg/kg body-weight load showed decreased oxidation in all heterozygotes as compared to normals. To further explore the effect of loading upon *in vivo* oxidation and exclude effects of G.I. absorption, normal subjects received i.v. ^{14}C -phenylalanine with increasing amounts of carrier (0–66 mg/kg body weight). Results show a progressive increase in $^{14}\text{CO}_2$ specific activity with increase in carrier up to 35-mg/kg body weight with constant oxidative turnover. At higher carrier doses there was a progressive decrease in oxidation with slowing of oxidative turnover.

These data demonstrate differences in phenylalanine oxidation between controls and PKU heterozygous and homozygous. These differences are affected by route and load of administered phenylalanine. The studies involving increasing i.v. carrier suggest that the enzymatic activity necessary for phenylalanine catabolism is rapidly increased by phenylalanine loading; this approach can estimate the maximal capacity of this enzyme system *in vivo* and may be useful in identifying PKU carriers and other nonclassical hyperphenylalaninemic states.

Combined Diagnostic Approach of Hepatic Scanning and Celiac Angiography in Diagnosis of Liver Disease BY LEONARD M. FREEMAN, ARNOLD DERMAN MONIQUE KATZ AND CHIEN-HSING MENG, Albert Einstein College of Medicine, Bronx, N.Y. (Session XIII)

In the past decade, liver scanning has contributed greatly to the diagnosis and understanding of a number of hepatic disorders such as benign and malignant neoplastic processes (primary and secondary), inflammatory disease, diffuse parenchymal diseases such as cirrhosis and traumatic lesions.

However, the findings as seen on scan are relatively nonspecific. Benign hepatic cysts, abscesses and metastatic disease would all present as single or multiple filling defects. Pseudo-masses in cirrhosis could not accurately be differentiated from a superimposed hepatoma on the basis of scan alone. The end result of a traumatic lesion may be seen on the scan as a filling defect which usually represents the hematoma.

However, the underlying damage causing the bleeding would remain a mystery without further investigation.

Celiac angiography has offered a definitive solution to most of these problems and has in this fashion complemented and clarified the findings seen on the hepatic scan. The better resolution of the radiographic study has on occasion given clearer delineation of lesions that may have been suspected or even entirely missed on the scan. The extent of a disease process is often better appreciated when the results of both the scan and angiogram are available.

Recent advances in hepatic surgery have also created a need for precise anatomic delineation of the vascular supply to the liver. Celiac angiography affords one the opportunity to obtain this extremely valuable and necessary information.

Hepatic scanning is an easily performed innocuous procedure that may be used even in seriously ill patients. Stationary-camera devices have significantly decreased the time required to perform the study. Celiac angiography requires greater skill and more specialized equipment to perform. It has often clarified problems that have existed on the scan and therefore, when used in specific selected situations, has helpfully complemented the radioisotope procedure.

Radioiodinated Synkol as a Tumor Localizing Agent BY

R. D. GANATRA, P. RAMANATHAN, M. C. PATEL, M. N. MEHTA, S. M. SHARMA, R. S. MANI*, O. P. D. NORONHA AND M. BLAU†, Tata Memorial Hospital, Bombay, India. (Session XXII)

Tetrasodium 2-methyl-1:4 naphthaquinol diphosphate (Synkavit) is recognised as a chemical radiosensitizer, and this property is attributed to its specific localization in the malignant cells. Our earlier experiments in developing a radioiodinated derivative of this compound showed that the radioiodine label on this compound was labile. The present work investigates the possibility of using an analog of this compound, known as Synkol (6-hydroxy 2-methyl 1:4 naphthaquinone) as a tumor-localizing agent. The radioiodinated Synkol appeared to be stable in *in vitro* and in *in vivo* experiments. The distribution studies with the labeled compound in mice having spontaneous mammary adenocarcinoma or transplanted fibrosarcoma showed 8% and 5% of the administered dose in tumor at 2 and 24 hr after oral or intraperitoneal administration. It was possible to delineate the tumor in these animals by scanning. In fact, at 24 hr the tumor was the only remaining tissue with a high concentration of the radioisotope. Radioiodinated Synkol was ad-

ministered orally to a series of patients with malignancies at different sites. The scans obtained in these patients will be presented.

Design and Performance of a "Constant-Resolution" Focusing Collimator BY

SEBASTIAN GENNA AND BELTON A. BURROWS, Boston Univ. Medical Center, Boston, Mass. (Session XIV)

The successful use of scanning systems depends on the detailed mapping of the distribution of radioactivity with collimated gamma-ray detectors. Rectilinear scanners produce a two-dimensional representation (i.e., a two-dimensional count-density distribution pattern) of the summation of overlapping images of radioactivity from all depths within the body. Multi-aperture focusing collimators have permitted the use of large detectors without loss of spatial resolving power at the focal point. However, as the solid angle of acceptance is increased, the resolving power at axial regions distant from the focal point deteriorates.

A "constant-resolution" multihole collimator which forms a part of a multidetector scanner has been designed. The design features include: (1) a narrow solid angle of acceptance (i.e., the diameter of the NaI(Tl) detectors is 5 cm and the focal point is 25 cm from the crystal face) and (2) the cross-sectional area of the collimator holes decreases with increasing distance from the collimator axis. Both features serve to reduce the variation of resolution characteristics with depth (i.e., resolving power of the collimators show little variation throughout a depth of approximately 15 cm).

Regional Ventilation-Perfusion Determined by Rapid Scintillation Scanning BY

ALBERT J. GILSON, ASHER MARKS, EDWARD M. SMITH AND WILLIAM M. SMOAK, Univ. of Miami School of Medicine, Miami, Fla. (Session XXI)

A technique has been developed for measuring ventilation-perfusion and its relationship for each 1.2×1.35 -cm area of the lung. ^{133}Xe is used for the ventilation study using a rebreathing system. Scans are rapidly and sequentially performed during the washin, equilibrium and washout phases of ventilation. Following washout of the ^{133}Xe , macroaggregated human albumin with an ^{125}I tag is injected intravenously to define the perfused space. Rectilinear scanning is accomplished using a moving 10-crystal detector assembly (Dynapix). Digital data from each of the 10 channels are recorded on $\frac{1}{2}$ -in., 7-channel magnetic tape for subsequent computer analysis. Digital data from each 1.2×1.35 -cm area of the lung are subsequently reduced by computer analysis of ventilation at equilibrium, perfusion-normalized "ventilation and perfusion" values, ventilation-perfusion comparisons for each of the areas of the lung and a washin-

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washout ratio analog map for each 2.4×2.70 cm region.

The "normalized" equilibration ventilation data are compared to the perfusion values in a "ventilation-perfusion ratio" and printed for each of the anatomic areas. Although this is actually a comparison of the ventilated and perfused spaces rather than a true ventilation-perfusion ratio as defined physiologically, its usefulness in certain clinical situations is apparent.

Analysis of digital data is accomplished on the IBM 7040-1401 computing system at the University of Miami Computing Center. So far our study has been performed on patients with localized bullous disease since this offers an excellent model for correlation and checks on clinical accuracy. The results of the study demonstrate that patients with bullous emphysema differ from the normal controls in the lack of perfusion to the involved area although the bullae do show surprisingly good ventilation after 7 min of ^{133}Xe breathing. The unevenness in delay in ventilation of the involved region is well demonstrated in the wash-in-wash-out ratios.

Quantitative Renal Imaging using $^{113\text{m}}\text{In}$ Chelates and a 1,600-Channel Memory BY DAVID A. GOODWIN, STEPHEN D. MILLER AND GERALD L. DENARDO, V.A. Hospital and Stanford Univ. School of Medicine, Palo Alto, Calif. (Session VI)

Serial, quantitative measurements of regional radioisotope distribution in the dog and human kidney are made following intravenous injection of from 5 to 10 mc $^{113\text{m}}\text{In}$ EDTA. This compound is excreted by the route of glomerular filtration and is prepared according to the method of H. S. Stern *et al.* The Anger scintillation camera is used for detection coupled with a 1,600-channel analyzer for quantitation of the images.

Excellent images of the kidneys are obtained in dogs and humans. Twenty to 30 1-min 35-mm exposures are made, and simultaneous integrated counts and profiles are obtained with the 1,600-channel memory. In the normal human the renal counting rate with 5 mc $^{113\text{m}}\text{In}$ EDTA reaches a maximum of approximately 50,000/min/kidney at 5 min, followed by an exponential-like decline. Renal cortical activity peaks at 2-5 min and falls thereafter to half this value at 20 min. Medullary activity reaches a maximum at 5 min, plateaus, and falls off at 15 min. Appearance of radioactivity begins in the renal pelvis at 7 min and increases to the twelfth minute, falling off at 19 to 20 min. The transit time from first appearance in the kidney to first appearance in the renal pelvis is approximately 7 min. This technique provides a quantitative display of regional distribution of the filtered compound during its passage through the kidney.

Assessment of Erythropoiesis by Ferrokinetics and Radiocolloid Bone-Marrow Scanning BY FRANCIS A. GOSWITZ, C. LOWELL EDWARDS AND HELEN VODOPICK, Oak Ridge Associated Universities, Oak Ridge, Tenn. (Session III)

Ferrokinetic measurements quantitate erythropoiesis accurately but are relatively complex to perform. Radiocolloid bone-marrow scanning cannot quantitate erythropoiesis, but it is a simple procedure that will usually demonstrate the size and distribution of hemopoietic marrow. Patients with various erythropoietic disorders were studied to compare ferrokinetic data and the marrow pattern shown on the scan and to determine whether the scan could be used to assess erythropoiesis or supplement the radio-iron data.

Patients with effective erythropoiesis manifested by an increased plasma iron-turnover rate (PITR) and an increased red-cell utilization of radio-iron (percent ^{59}Fe used) in the ferrokinetic studies had total-body scans that demonstrated normal-to-increased marrow-distribution patterns; thus there was good correlation between the two types of studies. Patients with ineffective erythropoiesis (intramarrow cell death) and with increased PITR and decreased percent ^{59}Fe used had various scan patterns. Those patients with myelofibrosis and ferrokinetic data consistent with ineffective erythropoiesis presented a characteristic scan with almost all the radiocolloid in the liver and spleen, both organs usually large, and none or extremely little of the radioactivity in the bone marrow. Anemic patients with nonproliferative bone-marrow disorders, such as those with infections and those with red-cell hypoplasia, had ferrokinetic data that demonstrated a decreased PITR and decreased ^{59}Fe utilization but scans with a normal to increased pattern. This contrast of data from the two types of study was particularly prominent in patients with infection in whom augmented phagocytic activity caused an increase in the amount of radiocolloid in the bone marrow.

Although the radiocolloid bone-marrow scan cannot yield quantitative data on erythropoiesis, it adds information about disorders of red-cell production when correlated with radio-iron and other hematologic studies.

Pharmacology of Intra-Articularly Injected ^{195}Au -Labeled Myochrysin (Sodium Aurothiomalate) Used as a Diagnostic and Therapeutic Aid in Rheumatoid Arthritis BY NORMAN L. GOTTLIEB AND EDWARD M. SMITH, Univ. of Miami School of Medicine, Miami, Fla. (Session XV)

Based on the work of Lewis and Ziff (*Arthritis Rheum.* 9:682, 1966), we have instituted a study to investigate the pharmacology of intraarticular injection

tions of Myochrysin. This material has been labeled with radioactive ^{195}Au and combined with the non-radioactive pharmaceutical substance. The labeled material has been shown to behave biologically in the same manner as the nonradioactive drug. Subacutely inflamed knees of patients with classical rheumatoid arthritis (as defined by ARA criteria) were injected with a single 50-mg dose of labeled Myochrysin (25 mg of gold). These patients had not received any form of gold therapy in the past, and the only anti-inflammatory medication they were receiving was salicylates. The contralateral knees were used as controls. The rate of disappearance of the radionuclide from the knees and concurrent rate of appearance in samples of blood, urine and synovial fluid were determined. In addition, kidneys and other joints and organs were monitored for their level of radioactivity. Also the spatial distribution of the radioactive gold in the region of the knee at various intervals of time was evaluated using a multicrystal rectilinear scanner (Dynapix). The rate of disappearance of gold from the knee joint was represented by a curve with at least three components; 50–70% disappeared with a half-time of less than 4 hr, 15–25% with a half-time of approximately 1 day and the remaining with a half-time of greater than 20 days. Soon after injection, the radioactive gold could be measured in the blood and it reached a maximum at 4–6 hr. The disappearance curve consisted of one component with a half-time of between 1 and 2 days comprising 30% of the maximum activity and the remaining disappeared with an 8- to 10-day half-time. The kidneys contained between 10 and 20% of the injected activity, which was slowly eliminated. Synovial fluid aspirated from the injected joint contained radioactive gold. When the fluid was allowed to clot, no significant amount of activity was detected in the clot. No significant amounts of gold could be detected in the organs or joints other than the kidney or the injected knee joint.

The Comparison between Sensitivity and Resolution Based on a Clinical Evaluation with the ACRH Brain Scanner BY A. GOTTSCHALK, J. D. ABATIE, J. P. PETASNICK, R. E. POLCYN, R. N. BECK AND D. B. CHARLESTON, Argonne Cancer Research Hospital and Univ. of Chicago, Chicago, Ill. (Session I)

The Argonne Cancer Research Hospital (ACRH) brain scanner uses four collimated detectors arranged in opposing pairs that scan the head concurrently and yield simultaneous lateral or anterior and posterior photoscans recorded with a data-blending system. The high-resolution collimators used in this series have a 7.5-cm focal length, a 1.72-cm diameter of view and a long depth of field (see Beck *et al*, *J. Nucl. Med.* 8:1, 1967). In an effort to determine whether the detec-

tion of focal disease can be improved with better resolution, a series of $^{99\text{m}}\text{Tc}$ -pertechnetate brain scans of 90 autopsy or surgically proven lesions carried out on the ACRH system was analyzed and compared with the results of other workers using a conventional 3-in. scanner (e.g., Witcofski *et al*, *J. Nucl. Med.* 8:187, 1967).

The data showed that *no* increased detection rate resulted from the high-resolution brain scans. In eight of the cases (i.e., 9%), however, the superior resolution made it possible to distinguish significant structure within the lesion. This consisted of a central area of diminished uptake (the "doughnut" sign). Of these eight cases, four were glioblastomas, one was a cystic astrocytoma, two were abscesses and one was metastatic disease.

In one of these cases, the intrinsic structure of the lesion depicted on the scan was the exclusive factor determining the surgical approach to the patient. The high-resolution scan, in general, frequently provides valuable additional information about the precise localization of the lesion in relation to other vital structures (e.g., the relation of a lesion to the sagittal sinus or tentorium) which is of significant benefit in connection with surgical planning.

This series suggests that a rational approach to brain scanning with currently available nuclides would be to do a preliminary rapid screening scan with high-efficiency and low-resolution collimators. In cases of abnormality, the initial studies should be followed with a high-resolution view centered through the lesion. This would permit the neurosurgeon to use all of the relevant information that is available from brain scanning.

Scanning Soft-Tissue Calcification with Radiostrontium-85 BY ROBERT J. GRIEP, U.S. Public Health Service Hospital, Seattle, Wash. (Session XXV)

Radioisotope scanning of bones to detect metastatic and primary neoplasms is a well established diagnostic procedure. The injected radiostrontium (^{85}Sr) is concentrated in all areas of active calcification. Active foci of soft-tissue calcification may have a higher accretion rate than normal bone and can be detected by scintiscanning.

Three unusual cases are presented. One patient had diffuse calcinosis associated with Hodgkin's disease and widespread localized deposits of radioactivity on photoscans. Another patient showed intense radiostrontium concentration in post-surgical myositis ossificans following removal of an osteoid osteoma. A third patient with metastatic carcinoma to bone accumulated $0.1\ \mu\text{c}$ of radiostrontium in each gram of renal stones contained in an infected kidney. The renal pelvis was visualized on the vertebral photoscan.

Marked accumulation of radiostrontium in soft tissue indicates active calcium exchange which may be useful information in evaluating and treating the patient.

Usefulness of Whole-Body Counting for Detecting Carriers of Wilson's Disease BY KEN HAMAMOTO, LADISLAV P. NOVAK, NORMAN P. GOLDSTEIN, W. NEWLON TAUXE, Mayo Clinic and Mayo Foundation, Rochester, Minn. (Session V)

Up to now we have found the most useful test for detecting the carrier state of Wilson's disease to be a complicated 3-day study of ^{64}Cu turnover which requires the analysis of complete urine and stool collections and frequent blood sampling. These studies have suggested that retention studies based on whole-body counting after injection of ^{64}Cu might be useful. Before siblings could be investigated, however, it was necessary to determine turnover in subjects of known zygosity. In this paper, the retention of ^{64}Cu was measured with the whole-body counter, and the reliability of this method was investigated. ^{64}Cu was administered intravenously in a dose of $5\ \mu\text{c}$ to eight patients with Wilson's disease, 15 carriers and nine normal subjects, and the amount of ^{64}Cu retained in the body was determined once or twice a day by whole-body counting for 3 days. The average whole-body retention of ^{64}Cu at 3 days after injection was 97.5% in patients with Wilson's disease, 93.9% in carriers and 87.8% in normal subjects. Biologic half-time of ^{64}Cu , calculated from the whole-body disappearance curve, was 97.0, 39.6 and 17.1 days, respectively. On the basis of these observations, it is evident that determination of the body retention of intravenously injected ^{64}Cu will make it possible to distinguish between heterozygous carriers and homozygous normal persons and may be useful as a screening test.

Preliminary Clinical Studies Using an Image-Integration System BY JOHN C. HARBERT, WILLIAM L. ASHBURN, DEAN T. MASON AND JACK D. DAVIDSON, National Institutes of Health, Bethesda, Md. (Session VIII)

The instrumentation for a new adaptation of the gamma scintillation camera for dynamic radioisotope studies will be described in another paper. Basically, the system transposes the gamma-camera output in random raster to standard video raster. On videotape replay integration of the desired image is made on photographic film. In addition, the replay can be gated by an external physiologic signal such as the simultaneously monitored electrocardiogram or respiratory cycle. These are recorded on the audio portion of the video tape, and allow selected phases of the dynamic process to be integrated. Blood flow can be studied by a separate circuit which delineates small portions of

the field to be analyzed. All recorded flashes occurring within these areas are electronically counted during each 1/60-sec video field, and time-activity curves are derived through a digital-to-analog converter. Cardiac output is determined by defining the pulmonary artery or aorta and monitoring the activity within these areas. Cardiac-output curves can be produced without the interfering background from lung, coronary circulation, left heart chamber, etc. By extension of the same mechanism, any two areas of interest can be simultaneously delineated on replay of the original recording. Of particular interest are differential pulmonary blood flow, cerebral circulation, intracardiac shunts, acquired cardiac valvular defects, renal artery to vein transit times and a variety of other intra-organ time-activity patterns.

Three-Dimensional Display of Scanning Images BY P. V. HARPER, D. B. CHARLESTON, R. N. BECK, N. YASILLO AND B. FROMES, Argonne Cancer Research Hospital and Univ. of Chicago, Chicago, Ill. (Session IV)

The theoretical study on three-dimensional reconstruction of scanning images previously reported has been carried into practical performance on actual scans of phantoms and resolution patterns. Pictures are taken with the Anger camera using a parallel-hole collimator of an object that is rotated in $48\ 7\frac{1}{2}$ -degree steps. The strip of film that is produced has 48 pictures taken from equally spaced directions about the axis of the object. These pictures are then projected by parallel light rays into an image space so that they enter the image from the direction in which the original gamma rays emerged. The image representing isotope concentration is thus made up of regions where the light rays coincide and reinforce in a manner similar to that described by Kuhl, where the image is made up of superimposed linear elements. The principal difference is that all planes are presented simultaneously in continuity, and the image in any desired plane may be displayed with any orientation by inserting a thin sheet of diffusing material into the image space. The resolution of the reconstructed image of the sine-wave resolution pattern is considerably improved over the resolution of any individual view, and in a realistic liver phantom separate lesions are easily displayed with improved definition. We hope that this approach will be useful in selected clinical cases. When appropriately automated, the entire procedure using $^{99\text{m}}\text{Tc}$ in the liver should require no more than 10 to 15 min of over-all scanning time.

Comparison of Quantitative and Photoscanning for Diagnosis of Space-Occupying Lesions in the Brain BY S. HASAN, D. A. WEBER, P. J. KENNY AND J. S.

LAUGHLIN, Memorial Hospital and Sloan-Kettering Institute, New York, N. Y. (Session I)

This is a report of a study to compare the usefulness of quantitative scanning and photoscanning for diagnosis of malignant lesions in the brain. Both quantitative and photoscans have been carried out on over 1,000 patients following intravenous injection of 10 mc of ^{99m}Tc -pertechnetate. This report evaluates those cases with complete follow-up.

A scanner with two opposed detectors was used to obtain two lateral scans, one PA and one AP, routinely on each patient 1/2 hr after injection of the tracer. A premedication dose of 200 mg of potassium perchlorate was given orally 1/2 hr before ^{99m}Tc administration. The number of counts accumulated in each 0.2-in. scan increment was recorded during the scan on punched paper tape for digital and computer-analyzed scans. A regular photoscan was produced simultaneously. The diagnosis of cases was made on the basis of both the quantitative scan and the photoscan.

The individual contribution of both the analog and quantitative scans to the diagnosis was delineated. The cases have included: (1) lymphomas with brain and meningeal involvement; (2) primary and metastatic brain space-occupying lesions; (3) vascular lesions, some of which are due to extension of the malignancy into the major cerebral blood vessels, and cases of subdural hematoma; and (4) bone metastases with and without meningeal extension. Positive or negative confirmation of the scan interpretation was obtained from surgical, pathological or radiographic procedures. Representative cases are presented in this paper.

On the basis of these cases the following specific and general conclusions have been reached:

1. The quantitative scan is more accurate than the photoscan for early detection of cerebral malignancies.
2. The quantitative scan allows easier evaluation of abnormalities due to bone, meningeal or brain lesions.
3. The improved delineation of abnormal areas of increased uptake has resulted in earlier detection of smaller lesions as well as of lesions located at the basal portion of the brain.

Additional advantages seen in the evaluation of response to therapy will also be discussed.

Clinically Useful 3-Dimensional Phantom BY MICHAEL HAYES, UCLA School of Medicine, Los Angeles, Calif. (Session XIV)

Scanner response has often been studied with a point or line source and with single-plane phantoms, and results have been presented in some abstract fashion such as iso-response characteristics, figure of merit or modulation transfer function. Even physicists may disagree as to the accuracy or appropriateness of these methods, and the physician is often unable to derive

the practical information he needs in the solution of clinical scanning problems.

Scanner evaluation has become even more complex with the advent of new rapid gamma-imaging devices. The differences between stationary cameras which use straight-bore cylindrical collimators and conventional scanners with focused collimators cannot be characterized completely by single-plane phantom studies.

A three-dimensional phantom has been devised to compare various instruments. The new phantom consists of hollow or solid rods of three different sizes running diagonally through a tank so that an instrument's imaging capacity may be determined simultaneously at increasing depths with a single scan examination. It is a modification of a phantom originated by G. J. Hine who used a line source running diagonally from top to bottom of a box-shaped container.

Radioactive tubes in the new phantom were scanned in air and in water. Inactive solid rods were scanned in a background of radioactive water. Comparative studies with ^{99m}Tc were made with conventional scanners having 3- and 5-in.-diameter crystal detectors with focused collimators, a 5-in. dual-probe scanner, a 10-probe rectilinear scanner, an Anger camera and a Ter-Pogossian x-ray image-amplifier camera. Similar studies with other scattering media, radionuclides and additional scanning devices are in progress.

Preliminary results indicate that the three-dimensional phantom is superior to point or line sources and to single plane phantoms. It is simpler to use, yet more versatile, than organ phantoms in that an instrument's capacity to image simulated lesions at increasing depths from the surface may be determined by a single scan examination. Furthermore, the physician can readily appreciate differences between instruments by simple scan comparison. More complicated analytical methods are seldom needed for clinical purposes.

Evaluation of Short-Lived Radiopharmaceutical Agents for Sequential and Conventional Kidney Scanning BY MICHAEL HAYES AND NORMAN S. MACDONALD, UCLA School of Medicine, Los Angeles, Calif. (Session VI)

Routine visualization of the kidneys can be accomplished with radiomercurial agents. However, to improve the quality of conventional scans and to study the dynamics of tracer movements within the kidney using rapid, multiprobe scanners or cameras, it is necessary to administer more radioactivity than is desirable from the point of view of radiation exposure to the patient. Therefore several pharmaceutical preparations of the short-lived nuclides ^{99m}Tc and ^{113m}In were evaluated as kidney-scanning agents. These included ^{99m}Tc -Fe-EDTA; ^{99m}Tc -Fe-DTPA; ^{113m}In -

EDTA; ^{99m}Tc -Fe-Glucose; and ^{99m}Tc -Fe-Citrate complexes.

More than 40 renograms performed on anesthetized dogs using these agents showed rapid appearance of activity in the kidney, followed by early clearance—the same pattern observed with ^{131}I -labeled iothalamate. Rapid buildup in the urinary bladder was also seen with a second detector. Renal clearances were determined quantitatively by collecting and assaying all urine following injection of a mixture of the agent and ^{125}I -labeled iothalamate, an inulin substitute known to be cleared by glomerular filtration. Clearance of all agents except the citrate complex was the same as that of iothalamate—between 45–55% of the dose by 1 hr. Clearance of ^{99m}Tc administered as the citrate complex was 36–39%. Clearance of uncomplexed pertechnetate ion was <2%. Distribution studies using rabbits showed no significant concentration of the agents in organs other than kidney and bladder. Biological retention of ^{99m}Tc -Fe-EDTA closely paralleled ^{131}I -iothalamate as measured in one human subject with a total-body counter. Rapid sequential scans on dogs following bolus-type injection of the agents demonstrated the various phases of radioisotope transit in the kidney, i.e., appearance in the blood pool, accumulation in kidney parenchyma, followed within 4–5 min by movement of tracer into calyces and renal pelvis. Sufficient activity remained in the kidneys to permit excellent conventional rectilinear scans at 2 hr post dose. Activity in the liver-gall bladder area was detectable at this time but was not sufficient to impair kidney visualization. Rapid sequential kidney scans in surgically induced canine renal artery stenosis and unilateral hydronephrosis demonstrated the value of these agents in the assessment of differential kidney function. All agents except the citrate complex appeared equally effective for kidney scanning and function tests. Any one of them can be substituted for radiomercurial kidney-scanning agents to improve counting statistics and reduce radiation exposure to the patient.

^{113m}In as a Possible Bone Scanning Agent BY R. L. HAYES, B. L. BYRD AND J. E. CARLTON, Oak Ridge Associated Univ., Oak Ridge, Tenn. (Session XI)

Generator-produced ^{113m}In ($T_{1/2}$, 1.7 hr) in the citrate form is diffusely distributed in the rat during the first 3 hr after intravenous administration. This behavior is due to the binding of indium by serum proteins. These indium binding sites can be saturated by the administration of stable indium; any excess indium (^{113}In) then deposits preferentially in the bone and kidneys. Indium in the quantities required is, however, quite toxic. *In vitro* studies have shown that the protein-binding pattern for indium is quite similar

to that for gallium. *In vivo* studies of the effect of gallium on the distribution of ^{113m}In in the rat indicate that gallium can act as a pseudocarrier for indium. With a level of 5 mg Ga/kg the distribution of ^{113m}In in the rat approaches that of ^{68}Ga under similar conditions, indicating that ^{113m}In may find use as a bone-scanning agent. (Under contract with the United States Atomic Energy Commission.)

Perchlorate Washout of Pertechnetate from the Thyroid Gland BY L. HECK, K. LATHROP, A. GOTTSCHALK, P. V. HARPER AND M. FULTZ, Argonne Cancer Research Hospital and Univ. of Chicago, Chicago, Ill. (Session XVII)

Most observers believe that pertechnetate is trapped in the thyroid gland in a manner similar to iodide, but that it is not significantly metabolized. Socolow and Ingbar (*Endocrinology* 80:337, 1967) have recently published data indicating that as much as 70% of administered pertechnetate is organified in the thyroid in rats. Their method of discharging TcO_4^- from the thyroid by ClO_4^- was carried out by incubation *in vitro*. We have undertaken to repeat these experiments *in vivo* to further evaluate whether there is binding of ^{99m}Tc -pertechnetate in the thyroid gland under conditions simulating clinical perchlorate washout measurements.

Groups of 25 rats and mice were given intravenous $^{99m}\text{TcO}_4^-$ followed in 1 hr by i.v. NaClO_4 in doses of 20 and 200 mg/kg. Animals were sacrificed at intervals between 10 and 180 min after NaClO_4 injection. Residual ^{99m}Tc activity in the thyroid at 90–180 min was approximately 5% of the activity in thyroids of control animals sacrificed without perchlorate washout. Thyroid-to-serum ratios and thyroid space in microliters of serum were calculated. In rats the mean T/S ratio was 51.5 in control animals and 3.45 in experimental animals 90 min after perchlorate washout. The mean thyroid space in control animals was 960 μl compared to 50 μl in animals sacrificed 90 min after perchlorate administration. Higher ratios were obtained in mice.

Clinical measurement of perchlorate washout are being performed with a 1,600-channel Nuclear Chicago analyzer with input from an Anger scintillation camera, subtracting adjacent background below the thyroid gland. Initial studies indicate that less than 5% of the initial activity remains in the gland 2 hr after washout with 2 gm of oral perchlorate administered 30 min after 1 mc of ^{99m}Tc .

It would appear that the high values of residual pertechnetate in the thyroid gland reported by Socolow and Ingbar are accounted for by some factors in their *in vitro* method.

The Preparation and Application of a Stabilizer-Free ^{99m}Tc -Sulfide Colloid BY CHARLES K. HELLMAN, JANET QUIRK AND DONALD R. KORST, University of Wisconsin Affiliated Hospitals, Madison General Hospital, Madison, Wis. (Session XIX)

A rapid, simple, stabilizer-free preparation of technetium-sulfide sulfur colloid using standard equipment was developed for reticulo-endothelial (R-E) studies. The preparation uses the radioactivity properties of technetium with its gamma radiation of 0.140 Mev and short half-life of 6 hr. The preparation is simple and can be carried easily in the hospital pharmacy and radioisotope laboratory at very low cost. Colloid preparation time is 10 min plus 8 min incubation and is suitable for use for at least 24 hr. Proper buffering and temperature control in sulfur-colloid development let one omit Dextran or other stabilizers. This freedom from stabilizer adjunct is significant because there have been anaphylactic reactions to Dextran.

Distribution studies of i.v. colloid showed a significant degree of radioactivity uptake by all portions of the reticulo-endothelial system. Spleen scanning, liver scanning and bone-marrow scanning consistently gave high-resolution scans with low doses of radioactivity of 0.5–1.0 mc for spleen and liver scanning and 2.5–4.0 mc for bone-marrow scanning. The colloid labels erythrocyte membranes and is stable to washing. The label appears to be nonenzymatically bound to the cell membrane and does not involve sulfhydryl groups. The process of labeling does not damage the cell in terms of autohemolysis tests. Measures of bone-marrow hypertrophy or expansion is possible with this stabilizer-free colloid. Perhaps there is a correlation of better blood organ (spleen and marrow) R-E-cell uptake with a smaller colloid substance. Advantages appear to be easy preparation in the hospital laboratory at low cost and convenience of availability.

Tumor Scanning with ^{131}I -Human Fibrinogen BY KINICHI HISADA, TATSUNOSUKE HIRAKI, TSUTOMU MISHIMA, RYOZO WATANABE, KAZUMASA YOKOYAMA, SADATAKE KATO, AND TAKAO WAKEBAYASHI, Kanazawa Univ. School of Medicine, Kanazawa, Green Cross Corp., Osaka, and Dainabot Radioisotope Laboratory, Ltd., Tokyo, Japan. (Session XXII)

To detect tumors in man, it is quite obvious that positive delineation of tumors has many advantages over negative delineation. Our first success with ^{131}I -human serum albumin was reported at the 12th Annual Meeting of the Society in 1965 and the results with ^{99m}Tc -human serum albumin, ^{203}Hg -hematoporphyrin- Na_2 salt and ^{131}I -fibrinolytate were then reported at 9th International Cancer Congress in 1966.

Application of radioiodinated fibrinogen to detect malignant tumors clinically by external counting was advocated by the Italian group (G. Monasterio *et al*) in 1964, and the possibility of tumor scanning was suggested. But to our knowledge, further improvement has not been published.

Recently, we found that the degree of tumor affinity of ^{131}I -fibrinogen depends greatly on the condition of labeling fibrinogen. In an experiment with 180 sarcoma-bearing mice, the tumor-to-muscle concentration ratio was 25 at 24 hr after intravenous injection.

0.4–1 mc of the material was administered intravenously to each of the subjects with a variety of malignancies and other conditions resembling malignant tumor. They were scanned after 24 and 48 hr by isosensitive radioisotope scanning mode.

So far positive delineation of the tumorous tissue has been successful in cases with metastatic cervical lymph nodes, iliosacral chondrosarcoma, right diaphragmatic angiosarcoma, liver metastasis of neuroblastoma, lung metastasis of left parotic squamous cell carcinoma and four cases with bronchogenic carcinoma in which ^{131}I -albumin was not helpful for tumor scanning. And it failed to be diagnostic only in two cases with left bronchogenic carcinoma and right metastatic pulmonary carcinoma probably due to the small size of the tumor. On the other hand, no false-positive delineations were observed in benign conditions including a case with benign parotis mixed tumor and two cases with tuberculosis showing coin lesion.

Fluorescent Thyroid Scanning Without the Use of Radioactive Nuclides *in vivo* BY P. B. HOFFER, D. B. CHARLESTON, R. N. BECK AND A. GOTTSCHALK, Argonne Cancer Research Hospital and Univ. of Chicago, Chicago, Ill. (Session XII)

A method has been developed for imaging the thyroid gland using K-shell fluorescence. Although the iodine content of the average thyroid gland is only 0.04% by weight, this quantity is sufficient to act as the target for scanning. No radioactive nuclide is introduced into the patient.

The technique for imaging the thyroid gland incorporates the basic scheme of an x-ray fluorescent spectrometer. ^{241}Am is used as a relatively monochromatic gamma-radiation source (for each 100 alpha disintegrations, ^{241}Am emits 36 gamma rays at 59.6 keV and lesser numbers of gamma and x-rays below 26.4 keV). The detector is a lithium-drifted silicon crystal with energy resolution of 500 eV fwhm at 30 keV. Both the ^{241}Am source and the detector are housed in the same lead collimator block. The scanning subject is placed beneath the block, and the source-

detector housing scans the subject in a rectilinear pattern.

When the 59.6-keV gamma ray from ^{241}Am interacts with a K-shell electron of an iodine atom within the thyroid gland, a characteristic x-ray is produced. The K alpha characteristic x-ray of iodine has an energy of 28.5 keV. This x-ray has a half-value layer in soft tissue of approximately 2 cm. The characteristic x-ray is detected and discriminated from the remainder of the scatter x-rays by the lithium-drifted silicon detector coupled to a single or multichannel analyzer. The information obtained can be recorded directly on film or as a numerical readout for subsequent evaluation. Scans obtained with this system require a radiation dose to the thyroid gland of about 500 mR.

The information obtained with the fluorescent scan is unique. It describes the distribution and relative concentration of stable iodine within the thyroid gland. This information will serve as a valuable adjunct to conventional thyroid scans and studies.

^{169}Yb Diethylenetriaminepentaacetic Acid (^{169}Yb -DTPA): A New Radiopharmaceutical for Brain Scanning BY FAZLE HOSAIN, RICHARD C. REBA AND HENRY N. WAGNER, JR., The Johns Hopkins Medical Institutions, Baltimore, Md. (Session XV)

Because of their short physical half-lives, $^{99\text{m}}\text{Tc}$ and $^{113\text{m}}\text{In}$ have greatly improved radionuclide imaging by providing increased photon yields with decreased patient exposure. However, their short "shelf-life" has made them relatively expensive. We have developed a new radiopharmaceutical that depends on a short effective half-life to limit the radiation dose and that can be prepared at monthly intervals rather than daily. It was found to be stable after several months of storage. The cost per scan with this complex is much lower than $^{113\text{m}}\text{In}$ -DTPA, $^{99\text{m}}\text{TcO}_4^-$ or ^{197}Hg -chlormerodrin.

^{169}Yb has a physical half-life of 31 days and emits several gamma rays of less than 350 keV energy. Trivalent ionic ^{169}Yb was complexed with diethylenetriaminepentaacetic acid (DTPA), the final pH was adjusted between 6 and 7 and then the preparation was made isotonic with sodium chloride solution. Ninety-nine percent of an intravenously injected dose was excreted almost entirely by glomerular filtration in the first 24 hr. The renal clearance of the complex was found to be similar to that of ^{14}C -inulin. The radiation dose to the critical organ (bladder) was comparable to that from equal amounts of $^{113\text{m}}\text{In}$ -DTPA.

In black mice with experimental ependymomas the ratio of the concentrations of the complex in tumor compared to brain was greater than 20:1 shortly after intravenous injection. The complex is therefore being evaluated as a brain-scanning agent. Images com-

parable to those obtained with $^{99\text{m}}\text{TcO}_4^-$ have been obtained in patients with brain tumors.

Internal Absorbed-Dose Calculations for $^{113\text{m}}\text{In}$ BY S. IBRAHIM, Halifax Infirmary, Halifax, Nova Scotia, Canada. (Session XXIII)

The increasing use of $^{113\text{m}}\text{In}$ in organ scanning has resulted from its favorable characteristics, including short-half-life, excellent counting statistics, ready availability from a commercial generator and low body radiation dose. Published studies have indicated that absorbed doses are low, but no thorough study exists. The present work is an attempt to repair this omission.

Internal absorbed-dose calculation will be made for intravenous administration of $^{113\text{m}}\text{In}$. The absorbed dose due to photons of $^{113\text{m}}\text{In}$ will be calculated using the method of Vennart *et al*, utilizing the data given in the report of Committee II of ICRP. The total absorbed dose due to photons and beta-type internal-conversion electrons is calculated using the classical method which uses the average geometrical factor and the absorbed-fraction method which uses the Monte Carlo technique.

\bar{E}_β , the total local energy deposition per disintegration for $^{113\text{m}}\text{In}$ is 134 keV/disintegration. Γ the gamma-ray dose-rate constant is 1.59 $\text{cm}^2\text{-r}/\text{mc-hr}$ for $^{113\text{m}}\text{In}$ of which 16% is contributed by K x-ray components. Their contribution to the value of Σ_γ , the integral dose-rate constant, is also 16%. The gamma component of the total absorbed dose calculated by the classical method underestimates the absorbed dose in all cases except that for kidney by 1.5–13% compared to the absorbed-dose calculations based on the absorbed-fraction method.

Total absorbed-dose estimates to different organs are made when $^{113\text{m}}\text{In}$ is tagged with different compounds for lung scanning, liver scanning, blood-pool scanning and brain scanning.

Kinetics of Seleniated Compounds During Vitamin E Deficiency BY ANDREE IMBACH, LYSETTE TRAHAN AND JOSEPH STERNBERG, Univ. of Montreal, Montreal, Quebec, Canada. (Session X)

During a pancreatic malfunction, a defective absorption of liposoluble vitamin E may occur, and might in its turn provoke a change in the distribution pattern of ^{75}Se -selenomethionine; the close metabolic interrelation between vitamin E and selenium metabolism is well known. This paper presents a study of the kinetics of $^{75}\text{Se-O}_2\text{Na}_2$ and ^{75}Se -selenomethionine in vitamin-E-deficient rats.

Female rats developed histologically detectable lesions characteristic for vitamin E deficiency after 120–150 days of an adequate vitamin E deficient diet; striated muscle degeneration and uterine fibrosis were

more accentuated than liver necrosis. Trace amounts of $^{75}\text{SeO}_3\text{Na}_2$ and ^{75}Se -selenomethionine were injected intravenously, and their kinetics was compared to that of normal controls.

Urinary excretion of selenite is markedly increased in E-deficient animals (45.5% instead of 25.5% of the injected amount in 18 hr); on the other hand, urinary excretion of ^{75}Se -selenomethionine is lower in E-deficient animals (21.9% instead of 31.2%). There is no significant change in the fecal excretion, but there is a slowing down of the rate of lung excretion of selenite in the deficient group.

Plasma selenite level is significantly higher in the deficient group (13.4% vs. 6.6% at 18 hr after injection); the amount of protein-bound ^{75}Se -selenomethionine is significantly higher in the deficient group; at 90 min after injection of the amino-acid practically all the plasma ^{75}Se was protein-bound.

Liver uptake of selenite is markedly higher in deficient animals (48.5% vs. 38.4%); on the other hand, there is less selenite in the striated muscle of the deficient group while red cells, heart muscle and pancreas exhibit similar values in both groups.

Vitamin-E deficiency provokes a marked change in the distribution pattern of ^{75}Se -selenomethionine: the liver has a higher uptake (30.2% vs. 17.6% at 2 hr) and also a slower rate of decrease of the labeled amino acid. The pancreas uptake of ^{75}Se -selenomethionine is markedly higher in the deficient group (9.5%/g vs. 6.4% in controls at 2 hr); also, the amino acid remains longer in the organ of the deficient animal (5.6%/g vs. 2.0%/g at 6 hr).

These data show that vitamin-E deficiency provokes an overall acceleration of protein turnover, reflected in a high plasma uptake and chiefly a high liver and pancreas uptake of ^{75}Se -selenomethionine. If these findings can be extrapolated to humans, they will point to a cause of error in the interpretation of pancreatic scans, in cases of impaired liver function and defective lipid absorption.

Regional Cerebral Blood Flow in Cerebrovascular Accidents and Generalized Cerebral Arteriosclerosis by Means of Rapid Serial 35-mm Scintiphotographs

BY CAROL J. IMBORNONE, WILLIAM LANE AND DAVID A. GOODWIN, V.A. Hospital Stanford School of Medicine, Palo Alto, Calif. (Session XXVII)

Altered cerebral blood flow resulting from generalized cerebral arteriosclerosis has been suggested as a cause of decreased brain function in elderly senile patients. Other investigators have demonstrated delayed "median transit times" of an i.v. bolus of radioactivity in these patients, using low-resolution external detectors. To demonstrate the regional distribution of such a bolus, we made serial 2-sec 35-mm pictures

(anterior view) following i.v. injection of 10 mc of $^{99\text{m}}\text{Tc}$ -pertechnetate, using an Anger gamma scintillation camera. Three groups were studied: (1) eight normal subjects (mean age 59), (2) eight patients with cerebrovascular accidents and hemiplegia (mean age 55) and (3) eight patients with generalized cerebral arteriosclerosis (mean age 70). The time from injection to initial appearance in the cervical segment of the carotid arteries, the time from appearance in the carotid arteries to appearance in the superior sagittal sinus ("transit time") and the time from appearance in the sagittal sinus to disappearance of radioactivity from this structure ("washout time") were measured. The symmetry of distribution of radioactivity during passage of the bolus was observed. $^{99\text{m}}\text{Tc}$ -pertechnetate brain scans were obtained in all cases.

A delayed appearance time $\bar{x} = 12.7 \text{ sec} \pm \text{s.d. } 2.8$ ($p < 0.05$) and a prolonged wash-out time $\bar{x} = 19.9 \text{ sec} \pm \text{s.d. } 4.7$ ($p < 0.005$) were observed in the group with generalized arteriosclerosis. An interesting aspect of our study was the ability to correlate this prolonged washout time with the 35-mm camera pictures, which revealed a retention of activity in the superior sagittal sinus. All the brain scans in this group were normal. In the patients with cerebrovascular accidents, asymmetry in distribution of the bolus consisting of a relative decrease of radioactivity on the obstructed side during the inflow phase was observed in three cases. In one of these cases the brain scan was normal. This technique for studying cerebral blood flow in cerebrovascular disease, provides a useful correlation of the over-all cerebral transit of a bolus of radioactivity with its regional distribution in the vascular system.

Simulation Studies of Radiocardiogram by Analog Computer BY YASUSHI ISHII, KANJI TORIZUKA, MASAICHI FUKASE AND MICHIOYOSHI KUWABARA, Kyoto Univ. School of Medicine, Kyoto, Japan. (Session XVI)

The radiocardiogram is composed of a flow curve from the right and left sides of the heart and probably other organs according to the Stewart dilution principles. Information about the flow and volume in each side of the heart as well as the lung can be retrieved from the radiocardiogram if the original flow curves could be practically separated.

Attempts have been made to construct a rather simple analog model simulating a tracer traversing the circulatory system. Our analog computer model assumes a square-wave input and a series of mixing chambers connected in a cascade fashion with or without a time delay forming a closed circuit. The mixing chambers simulate injection space, right heart, lung, left heart and peripheral circulation. The time delay is necessary to simulate the transport of the bolus

through the lung and body. A radiocardiogram is constructed in the analog computer by iteratively adjusting the variables of each mixing chamber in the order of the course of the bolus. This constructed radiocardiogram is fitted to the one recorded from the patient. The readings of the controls of the computer when adjusted for a perfect fit yield the volumes of the mixing chambers.

Twenty normal subjects were found to have a heart volume of $10.6 \pm 1.4\%$ of total blood volume. The normal pulmonary blood volume was found to be $10.7 \pm 1.8\%$ of the total blood volume. These results are within accepted normal ranges for these volumes. Patients with various cardiovascular diseases could easily be shown to have abnormally large mixing chambers by the analog computer.

Automation of the Thyroid Binding Test BY J. L. IZENSTARK, N. HORWITZ, K. COOK AND A. FORSAITH
William Beaumont Hospital, Royal Oak, Mich. (Session XVII)

The *in vitro* radioiodine binding tests are increasing in popularity because they offer a reliable, rapid, inexpensive screening procedure of thyroid disease without the administration of radioiodine to the patient. There are potential errors inherent in these tests. Pipetting, timing, temperature and calculations represent sources of error which can be controlled by automation. Furthermore, an automatic procedure can free the technician for other duties. The authors have developed a completely automatic system which accepts a serum sample. The sample is processed through the various stages of the test without further attention. The procedure may be interrupted for the introduction of additional samples. The results obtained from the automatic well counter are presented as the thyroid-binding index by an automatic printer calculator. The automatic procedure will be described in this paper.

Pyramidal Lobe in Thyroid Imaging BY J. L. IZENSTARK, A. FORSAITH AND N. HORWITZ, William Beaumont Hospital, Royal Oak, Mich. (Session XII)

The pyramidal lobe of the thyroid has rarely been considered in the literature of thyroid scanning. The incidence of the thyroid pyramidal lobe in operated specimens is stated as 75–80%. Physicians performing thyroid scans certainly do not see this high an incidence. While using a new high-resolution imaging device, the Spintharicon, it seemed apparent that more pyramidal lobes were visualized with this instrument than with the conventional scanner. This paper reports an analysis of 100 cases in which images produced with the spark camera are compared to conventional ^{125}I scans with particular reference to the thyroid pyramidal lobe.

Nondestructive Method of Studying Cerebral Hemispheric Blood Flow BY GEORGE L. JACKSON AND NANCY M. BLOSSER, Harrisburg Hospital, Harrisburg, Pa. (Session II)

There is great interest in studies of cerebral blood flow. Although very accurate, initial techniques had limited clinical value because of the complexity of the preparation and the analytical methods. A simple, reproducible external dynamic counting system has been difficult to produce. One of the limitations of all systems to date has been the inability to eliminate all or most of the contribution from non-neural blood spaces.

Recently the digital autofluoroscope has become available. This instrument with its high-speed tape system is capable of observing a $^{99\text{m}}\text{Tc}$ bolus enter the head. It records this data at preselected accumulation intervals and stores it on magnetic tape with a 30 msec "dumping time." This is replayed later and displayed on the cathode-ray tubes. Cerebral hemispheres and other vascular landmarks are noted. By using a "light wand" which can identify appropriate crystal locations, one hemisphere is "flagged" in one of three zones. The same process is repeated in the contralateral hemisphere in another of the instrument's zones. This results in a mirror-image array. The recorded dynamic study is again replayed with the continuous-strip-chart recorder and integration circuits operating. A graphic display using three pens (one for each integration area) and one pen for totaling results of all of the events "seen" in the crystals is presented for each frame of magnetic-tape data and recorded against a time coordinate. The difference in activity in each hemisphere (a function of blood flow) is thus demonstrated.

We will present results of studies performed in our laboratory. Preliminary data suggests the method is reproducible and correlates with other diagnostic evaluations. Observations on patients with vascular and neoplastic disease will be presented. The author believes that the system will permit quantitative analysis.

Radioautographic Demonstration of Cellular Localization of ^{203}Hg -Chlormerodrin in Various Brain Tumors BY GEORGE L. JACKSON, M. L. CORSON, JANE BAXTER AND NANCY BLOSSER, Harrisburg Hospital, Harrisburg, Pa. (Session XXVII)

This study was designed to contribute to our understanding of the mechanisms which produce an abnormal brain scan. Brain tissue removed from patients whose scan was abnormal was studied by radioautographic techniques. The sections from malignant primary brain tumors, non-neoplastic primary central nervous system tumors (meningioma) and a metastatic nonneural (anaplastic epidermoid carcinoma) brain

tumor have demonstrated that the radioactive mercury is deposited in or on neoplastic cells.

External Monitoring of ^{51}Cr -Labeled Glucose BY ALBERT E. JOHNSON AND FRANK GOLLAN, V.A. Hospital and Univ. of Miami School of Medicine, Miami, Fla. (Session V)

Blood clearance of glucose is an important indicator of metabolic and endocrine functions, and a number of colorimetric methods for the determination of blood glucose are available. Glucose can also be labeled with beta-emitting ^{14}C and ^3H , but the tedious analysis of a great number of blood and urine samples does not offer much advantage over present color measurements. Therefore we have prepared a glucose with a gamma-emitting label by reacting boiling 50% glucose with a carrier-free radiochromic chloride at a pH of 4.5. The labeled glucose fraction is then separated from any unbound chromium by gel filtration. Normal dogs were given an intravenous injection of 20 ml of 50% glucose containing 100 μC of the labeled compound, and radioactivity was monitored over the heart and a shoulder muscle with scintillation detectors. Blood samples were drawn every 10 min and analyzed for chemical glucose and for radioactivity. The slope of disappearance of radioactivity over the heart, shoulder and in the blood was identical with the chemical glucose clearance rate from the plasma for the first hour. Half of the injected radioactivity was excreted in the urine in 90 min. The substitution of external monitoring of a gamma-labeled glucose for the chemical analysis of blood samples may offer considerable advantages in simplicity, time and convenience.

Scintillation Imaging of Arterial Blood Flow in Certain Critical Organs BY P. M. JOHNSON, S. K. HILAL, P. J. CANNON, D. S. SVAHN, J. HAFT AND E. H. WOOD, College of Physicians and Surgeons, Columbia University, New York, N.Y. (Session II)

Organ viability and nutrition are dependent upon an influx of arterial blood and its distribution to the parenchyma. Impaired entry or perfusion of arterial blood may result in stroke, infarction, hypertension or other serious illness. We are investigating arterial perfusion of the brain, kidney and heart and the effect on these organs of various factors induced experimentally or caused by disease. Following intra-arterial injection of a radioactive tracer ($^{99\text{m}}\text{Tc}$ -pertechnetate or ^{133}Xe in saline), the arrival, distribution and efflux of radioactivity in the target organ are recorded and displayed by the Ter-Pogossian-Picker image-intensifier scintillation camera. Although presently limited to the generation of analog information, this instrument is useful for studying these rapid dynamic events be-

cause of its high-speed response. A separate digital ratemeter is used to obtain clearance data. The nature of these investigations and the role of the image-intensifier camera are illustrated by selected material from animal and clinical studies, the latter primarily in patients with abnormal perfusion of the central nervous system.

Liver Scan Evaluation of Amebic Abscess BY G. S. JOHNSTON, T. W. SHEEHY, L. F. PARMLEY, JR. AND H. W. BOYCE, Walter Reed General Hospital, Washington, D.C. (Session XIII)

The diagnosis and location of amebic liver abscess has been greatly enhanced by using radioisotopic scanning techniques. In addition, scintiscanning has made it possible to observe visually the effects of therapy and to estimate the time required for an amebic abscess to heal.

In the present study, the healing time was determined for amebic abscesses treated by different methods. Serial scans performed using colloidal ^{198}Au indicated that liver abscesses treated with chemotherapy alone required 2-12 months to heal. Open surgical drainage and/or needle aspiration of pus in combination with chemotherapy did not appear to shorten the resolution time of an amebic liver abscess when compared with chemotherapy alone.

Sixteen patients with amebic liver abscesses were included in this study and were divided into three groups on the basis of treatment: Group I, five patients whose abscesses were drained surgically; Group II, four patients who were subjected to diagnostic and therapeutic aspiration of their abscesses and Group III, seven patients with amebic abscesses who were treated with emetine, chloroquine and diodoquin. No attempt was made to aspirate their abscesses. The patients in Groups I and II were also given chemotherapy with emetine, chloroquine and diodoquin.

In this series, all but two patients showed excellent resolution of their abscess cavities within 2-4 months of onset of treatment. The mean resolution time for all 16 patients was 3.9 months. The mean resolution time of the three groups was the same with no correlation between size of the abscess and the healing time.

The judicious use of the hepatoscan should permit early diagnosis of amebic liver disease and in conjunction with appropriate medical treatment should obviate or greatly reduce the need for aspiration or surgical treatment.

Prostate Scintiscanning BY G. S. JOHNSTON, J. C. WADE, G. P. MURPHY, E. GOTSHALL AND W. W. SCOTT, Walter Reed General Hospital, Washington, D.C., and Johns Hopkins Hospital, Baltimore, Md. (Session XXIV)

The prostate gland normally contains a relatively

high concentration of zinc and is capable of concentrating administered zinc to a greater degree than surrounding pelvic organs. Much of the zinc concentrated by the prostate is excreted in prostatic fluid. Studies of prostatic zinc dynamics were formed using dogs, monkeys and men with the ultimate aim of human prostatic scintiscanning.

^{65}Zn -chloride, or $^{65\text{m}}\text{Zn}$ -chloride or citrate was administered to 34 dogs, 10 of which were castrated and four of which had surgical prostatic fistulas. Testosterone propionate was used to prepare some dogs for 1-4 days prior to zinc injection. Animals were sacrificed from 5 hr to 6 days following zinc administration. Two rhesus monkeys were studied following intravenous dosing with ^{65}Zn -chloride. *In vitro* prostatic scanning was performed with ^{65}Zn -chloride in dogs.

Delaying sacrifice 24 hr following zinc administration increased prostatic concentration 30%, and a 6-day delay resulted in 400% increase in prostatic ^{65}Zn . Similarly, testosterone preparation increased ^{65}Zn uptake from 120 to 250% over that of untreated dogs. Combining the 6-day delay with testosterone treatment gave a 940% increase in zinc uptake by the prostate. *In vitro* scanning resulted in vaguely outlined prostate scans due to the considerable scatter from the 1.114 Mev gamma of ^{65}Zn . A more suitable isotope was actively sought. In early 1967 ^{65}Zn became available with its 14-hr half-life and 440-kev gamma ray. *In vivo* prostatic scanning using $^{65\text{m}}\text{Zn}$ -chloride and citrate has since been performed on a number of men with resultant good prostatic visualization.

Radioisotopic Assay of Serum Arginase Activity—A Sensitive and Specific Test for Liver Disease BY SHIGEKOTO KAIHARA, NICOLA CARULLI AND HENRY N. WAGNER, JR., The Johns Hopkins Medical Institutions, Baltimore, Md. (Session V)

Assay of serum enzymes is useful in the diagnosis of various diseases, but the lack of organ specificity of these enzymes has been a disadvantage. Arginase is known to be present almost exclusively in the liver which suggested that it might be useful for the specific diagnosis of liver disease. Therefore we developed a new, sensitive method of serum arginase assay and evaluated its role as a test of liver disease.

Arginine-guanido- ^{14}C (0.227 M, specific activity 0.625/mmole; pH 9.5) was incubated with Mn^{++} activated serum for 1 hr at 37° C; the urea- ^{14}C produced was hydrolysed by urease into ammonia and $^{14}\text{CO}_2$, which was measured by a liquid scintillation counter. Arginase activity was expressed as μmole of urea produced in 1 hr by one ml of serum. This method is very sensitive (lower limit of detection: 0.05 μmole) and is not affected by the urea present in serum.

Serum arginase activity was 0.24 ± 0.07 (1 s.d.) $\mu\text{mole/hr}$ in 25 normal subjects. In 14 patients with infectious hepatitis, serum arginase ranged from 0.6 to 6.3 $\mu\text{mole/hr}$, and the values correlated well with transaminase values. In 23 patients with cirrhosis, serum arginase ranged from 0.1 to 1.05 $\mu\text{mole/hr}$ with poor correlation with SGOT. In seven patients with metastatic cancer of the liver, serum arginase levels ranged from 0.6 to 6.5 $\mu\text{mole/hr}$, but SGOT was less affected. In 10 patients with myocardial infarction, serum arginase was only slightly elevated in spite of increased SGOT. In five patients with typhoid fever without signs of liver involvement, serum arginase was elevated although SGOT levels were not. From these results, we conclude that serum arginase is a sensitive as well as a specific test for liver disease.

Tissue Distribution of Toluidine Blue in Dogs BY GURPREM S. KANG AND WALTER DIGIULIO, V.A. Hospital and Univ. of Michigan Medical School, Ann Arbor, Mich. (Session XXIV)

While ^{75}Se -selenomethionine parathyroid scintiscans can localize abnormal parathyroids weighing 1 gm or more, smaller tumors or those located in the mediastinum cannot be regularly visualized. The demonstration (*Surg.* 59:1,101, 1966) that toluidine blue (TB) administered intravenously to dogs resulted in a blue coloration of parathyroids led us to investigate the quantitative distribution of TB in dogs to evaluate the potential value of gamma-emitting analogs of this or similar dyes. TB was extracted from dog tissues by homogenization with alcohol. Recoveries of known quantities of dye added to tissues were better than 90%. Preliminary distribution studies in dogs sacrificed at 1/2-4 hr after the intravenous injection of TB (10 mg/kg) suggested that optimum concentrations were achieved by 2 hr. Eight dogs were given TB by infusion and sacrificed 2 hr later. Parathyroids from these dogs were separated into two pools and TB was extracted. The concentration was 0.05% and 0.09% of the dose/gm of parathyroid tissue, respectively, (90 and 94 μg TB/gm of parathyroid). These uptakes are comparable to the percent uptake of ^{75}Se -selenomethionine by human parathyroid tissue. Concentrations of TB in parathyroids were 10 times that in thyroid, 11 times that in muscle, 63 times that in blood, 11 times that in lung and 1.5 times that in heart. These ratios are more favorable for scanning parathyroids located in the neck or mediastinum than the ratios obtained after intravenous ^{75}Se -selenomethionine. Concentrations of TB in pancreas (average 50.3 $\mu\text{g/gm}$) and in liver (average 3.4 $\mu\text{g/gm}$) suggest that labeled analogs of toluidine blue may also be useful for pancreas scanning.

Depth Discrimination in Scanning by Dual-Channel Color Modulation of Two Probes BY ERVIN KAPLAN AND MOSHE BEN-PORATH, V.A. Hospital, Hines, Ill. (Session VIII)

In a previous report using a single-probe and dual-channel subtract technique, the depth of radioisotope distribution was predicated upon the differential gamma absorption of two isotopes of the same element respectively characterized by low-energy and high-energy gamma emission. The current study has used the color modulation of the output of two facing scintillation probes on either side of a scanned object to determine depth. The two opposing 5-in NaI(Tl)-crystal detectors use the combined attenuation of collimation, distance and gamma absorption of gamma events within an object. The counting rate diminishes as the source of activity occurs at deeper levels. The output of each probe is recorded on individual channels of magnetic-tape recording. The recorded information is displayed on a white phosphor cathode-ray tube. Each channel is photographed on color Polaroid through specific color filters. Each unit of depth is defined by a specific and unique ratio of the two colors, producing a third color and permitting calibration of depth. This system is applicable to an asymmetric "hot" lesion in a symmetrical object or to asymmetric "cold" lesions in a large volume of activity. The method described permits scintigraphic depth discrimination by dual-channel color modulation of two facing detectors and the production in gradation of color of an "Asymmetrogram" without using positron annihilation radiation.

Diagnostic Efficacy of Dual-Channel Pancreas Scanning BY ERVIN KAPLAN, SIDNEY FINK, MOSHE BEN-PORATH AND GLENN D. CLAYTON, V.A. Hospital, Hines, Ill. (Session XXIV)

The simultaneous visualization of the pancreas and the liver by individual pulse-height discrimination of ^{198}Au and ^{75}Se -selenomethionine and color presentation of ^{198}Au in the liver and ^{75}Se minus gold in the pancreas has been previously presented. The diagnostic efficacy of this procedure has been evaluated in 109 patients. Diagnosis arrived at by scanning alone was compared to confirmed diagnosis by other pathognomonic means. In interpreting dual-channel scans in 36 hospital patients with normal pancreatic function, 31 were designated as normal, four as pancreatic insufficiency and one as cirrhosis; in 10 patients with carcinoma of the pancreas, eight were diagnosed and two called normal; in 19 patients with pancreatic insufficiency, 12 were diagnosed, six called normal and one called cirrhosis; in 17 patients with cirrhosis, 10 were diagnosed, four called normal and three called carcinoma; in eight patients with acute recurrent pancreatitis four were called pancreatic insuffi-

ciency and four were called normal. One patient with massive intraperitoneal hematoma was called carcinoma of the pancreas. The criteria for normal diagnosis was clearly visualized pancreas with no defects. Carcinoma of the pancreas showed significant replacement of the pancreas by focal "cold" areas. The spleen was not visualized. Pancreatic insufficiency was characterized by massive extrahepatic, extrapancreatic ^{75}Se concentration. The cirrhotic patients showed patchy liver defects, a visualized spleen and a poor concentration of ^{75}Se in the pancreas.

The dual-channel technique continues to be a useful adjunct in the diagnosis of pancreatic disease. Currently improved readout using multichannel magnetic tape and color Polaroid cathode-ray-tube presentation is being evaluated as it may enhance diagnostic efficacy.

Some Clinical Applications of the Hybrid II Gamma Scanner BY BOWEN KELLER, PAUL A. FARRER, PHILIP RUBIN, T. P. DAVIS AND R. J. MARTONE, Univ. of Rochester School of Medicine and Dentistry, Rochester, N.Y. (Session XIV)

The recently redesigned Hybrid II gamma scanner consists of a 2×2 -in. by 11-in.-long NaI(Tl) scintillation crystal with 2-in.-dia photomultiplier tubes coupled to either end. The crystal and phototubes are sealed in a light-tight low-mass housing, and the entire assembly is placed within a massive lead shield. The upper face of the shield contains a linear, semifocusing collimator. The subject is placed above this collimator and a light-weight wheeled cot, 2 ft wide by 6 ft long.

For each scintillation event that passes the pulse-height analyzer, a light spot is formed on the oscilloscopic screen; the placement of this spot along the vertical is proportional to the logarithm of the ratio of the pulses delivered by the two photomultiplier tubes end-viewing the crystal, hence to the position of the scintillation event. This constitutes the electronic transverse-scanning process and develops one direction of the scan.

To generate the complete area scan, the cot holding the subject is moved by a small variable-speed motor along a horizontal track over the stationary detector. A multiturn potentiometer coupled to the cot delivers a voltage directly proportional to cot position to the horizontal input of the oscilloscope. Because the light spots on the oscilloscope screen are electronically positioned vertically, they are simultaneously shifted horizontally in exact synchronism with the longitudinal motion of the subject. A Polaroid camera focused on the screen integrates all light flashes during the scan and provides the final picture.

Some applications of this instrument to the study of clinical problems, particularly in the quantitation of

regional pulmonary arterial perfusion using ^{125}I -macroaggregated human serum albumin lung scanning, will be presented in some detail.

Radioisotope Scintiangiography of Cerebral Hemisphere Lesions BY JOHN C. KENNADY, ROSS POTTER, FREDRICK CHIN AND LEONARD SWANSON, UCLA School of Medicine and Los Angeles County Harbor General Hospital, Torrance, Calif. (Session II)

The Ter-Pogossian scintillation camera permits continuous visualization of the entire cerebral hemisphere and dynamic examination of the passage of a radioisotope tracer through the cerebral circulation. Data taken from the television monitor is permanently recorded on video tape for playback on Polaroid film as pictures of a single, 1/30th of a second frame or of integrated frames for any desired time interval.

Basic camera studies to determine the parameters for radioisotope dose, anatomical orientation and circulation times were completed in three baboons using ^{133}Xe , $^{99\text{m}}\text{Tc}$ -labeled albumin microaggregates, ($^{99\text{m}}\text{TcAA}$), 1–8 microns in size, and $^{99\text{m}}\text{Tc}$ pertechnetate in a small, high-specific-activity bolus.

Clinical camera studies have been performed on 20 patients with intracranial lesions which were visualized by $^{99\text{m}}\text{Tc}$ brain scanning and/or carotid angiography. Following angiography, ^{133}Xe , $^{99\text{m}}\text{TcAA}$ and $^{99\text{m}}\text{Tc}$ -pertechnetate were sequentially injected via an internal carotid catheter. In the brain-tumor patients, ^{133}Xe and $^{99\text{m}}\text{Tc}$ -pertechnetate rapidly accumulated in the tumor region (2 sec) and remained there for more than 90 and 25 sec, respectively, whereas, they are more rapidly cleared from the adjacent hemisphere. $^{99\text{m}}\text{TcAA}$, which remains intravascular, demonstrates the relative rate of blood flow through the brain tumor. ^{133}Xe shows the greatest and most prolonged radiodensity within the tumors.

In the five head-trauma cases, all three radioisotopes demonstrated relative decreased radiodensity within the surgically proven regions of intracerebral hematoma and cerebral edema compared to the radioactivity seen in the uninvolved brain tissue. These results contrast markedly with the definite increased radiodensity seen in the brain tumors.

Preliminary results would indicate that the camera distinguishes between brain tumors and hematomas in cases not clearly diagnosed by angiography.

Study of Human Brain Tumor Cell Affinity for Specific Radioisotopes BY ROZELLA KNOX, ULRICH BATZDORF AND JOHN C. KENNADY, UCLA School of Medicine, Los Angeles, Calif. (Session XXVII)

Quantitative analysis of $^{99\text{m}}\text{Tc}$ -pertechnetate and of ^{197}Hg uptake by human brain tumor cells grown in tissue culture permits evaluation of possible tumor-cell affinity for these agents.

Once the tumor explant exhibits optimum growth (9–21 days) on a plasma clot or under cellophane in the Rose Culture Chamber, the tissue is measured under phase microscopy and incubated for 18 hr in fresh media containing either 200–300 μc $^{99\text{m}}\text{Tc}$ or 20–35 μc ^{197}Hg . After incubation, the explants are washed five times with isotonic saline, then transferred with clot or cellophane to a dram-vial and assayed for radioactivity in a deep-well counter. Control chambers containing only clot or cellophane are processed simultaneously by the same method to determine the activity adhering to these materials. Percent cellular radioactive uptake is calculated on a quantitative unit basis as the counts per minute (cpm) of the cells minus the control cpm divided by the total cpm of each chamber.

Preliminary results indicate possible cell-type specificity for these radioisotopes. The mean percent uptakes for tumors incubated with $^{99\text{m}}\text{Tc}$ are: ependymomas, 67.3%; choroid papilloma, 82.9%; astrocytomas, 86.5%; glioblastomas, 87.3%; meningiomas, 89.4% and medulloblastomas, 92.3%. The mean uptakes with ^{197}Hg are: ependymoma, 25.2%; choroid papilloma, 44.8% and glioblastoma, 95.3%.

Embryonic human brain cells (8-cm fetus), grown and processed under identical conditions as above, showed a $^{99\text{m}}\text{Tc}$ mean percent uptake of 54.0%. Despite the high metabolic activity of these growing fetal cells, this tissue exhibited a lower uptake than the tumors. This may correlate with the brain-to-tumor radioisotope ratio seen on brain scan. Similarly, results from the choroid papilloma parallel the choroid plexus' greater affinity for $^{99\text{m}}\text{Tc}$ than for ^{197}Hg on scanning. Hence different brain tumors vary in specific radioisotope uptake.

^{67}Ga Metabolism in Rabbits BY P. KOSTAMIS, C. CONSTANTINIDES, D. BINOPOULOS AND B. MALAMOS, School of Medicine, Univ. of Athens, Alexandra Hospital, Athens, Greece. (Session XI)

^{67}Ga is a positron-emitting daughter of ^{68}Ge which has been recently used for brain and bone scanning, positioning and volume measurements. The lack of data in the literature regarding the metabolism of gallium as a whole urged us to perform an extensive study to determine the metabolic pathways of ^{67}Ga in rabbits. After the intravenous administration of a tracer dose of ^{67}Ga , the absorption and excretion rates were determined using a clinical whole-body counter. Plasma clearance and organ distribution were determined with a well-type scintillation counter. The results of the present study are discussed in detail.

Diagnosis of Pericardial Effusion by Radioisotopic Angiography BY JOSEPH P. KRIS, Stanford Univ. School of Medicine, Palo Alto, Calif. (Session XVI)

The technique of radioisotopic angiocardigraphy as carried out in our laboratory (*J. Nucl. Med.* 7:367, 1966) appeared to offer the possibility of rapid and accurate diagnosis of pericardial effusion with minimal risk and discomfort to the patient. Following the intravenous injection of a bolus of 10 mc ^{99m}Tc -pertechnetate, and using an Anger-type scintillation camera positioned over the precordium, one can delineate in sequence the right heart chambers, main pulmonary arteries, lungs, left heart chambers and aorta.

Study of films made with exposures recorded at intervals of 6-8 sec revealed that in normal subjects during the phase of right heart and pulmonary filling the image of the right lung has a straight, horizontal lower border and is contiguous with the right heart image. At this stage, there is a wedge-shaped void in the region of the as yet unfilled left ventricle so that the left lung and heart images are not contiguous. Contiguity of lung images and heart on the left occurs normally later as the left ventricle fills and the bolus enters the aorta. The presence of a pericardial effusion can be revealed quickly by demonstrating failure of contiguity of the lung and heart shadows first on the right side and a few seconds later on the left. The lack of radioactivity in the pericardial sac may still be readily demonstrated as a void around the heart during the next 30 sec, at which time the lungs and heart can yet be distinguished. Thereafter, the effusion is less readily demonstrated, presumably because the isotope in the extracellular and pericardial fluids achieves rapid equilibrium.

The procedure offers several advantages: (1) diagnosis can be made within a few seconds, (2) the patient may be supine, erect or semi-recumbent, (3) if desired, studies can be repeated at daily intervals, thus enabling one to follow the progress of the effusion, (4) administration of drugs to block other organ uptake of isotope is unnecessary and (5) radiation dose to the patient is low.

Rapid Brain Scanner with Self-Contained Computer and CRT Display for both Rectilinear and Transverse Section Viewing BY DAVID E. KUHL AND ROY Q. EDWARDS, Univ. of Pennsylvania School of Medicine, Philadelphia, Pa. (Session IV)

We have designed this instrument especially for rapid brain scanning using ^{99m}Tc pertechnetate. The scanner has four moving detectors and provision for both rectilinear and transverse-section brain scanning. It includes a self-contained computer, integrated digital circuits for compactness and economy and a CRT display for immediate viewing of the completed scan pictures.

Each detector moves back and forth on one side of a square frame about the patient's head. For rectilinear scanning, the patient is translated step-wise through

the detector frame. Repetitive passes of the detectors continue until four complete rectilinear rasters of data have been collected and stored in a magnetic drum beneath the patient's support. For reading, the drum output is displayed directly on the screen of a CRT where proper adjustments in picture contrast can be made by the physician. All four rectilinear views are always exactly at right angles to each other, an optimum orientation that never can be assured when these multiple views are made separately.

For transverse-section scanning, each of the four detectors is moved through one side of the frame; then the entire square frame is rotated through an angle of 15° about the central axis. The process is repeated six times to rotate the square frame through 90° and thereby to cause the four detectors to survey the entire circumference of the head through 360° . An instantaneous transverse section conversion is accomplished using a random-access core store also located under the patient's support. The transverse-section picture is displayed on the CRT screen immediately upon completion of the study.

We expect to use the scanning system as follows: 14 min after the beginning of the study, the physician examines each of the four rectilinear views of the brain in turn on the CRT. He controls a movable transverse line of light on the CRT to identify any region of suspicion on the display. The position of this line corresponds to the longitudinal indexing of the patient so that a subsequent transverse section scan can be accurately keyed to pass through the suspect area. Three additional minutes are then required to complete this transverse section scan. Immediately after this, section data is displayed on the screen for interpretation. The physician then decides whether or not additional sections are required before the patient is moved.

This scanning system is expected to be a practical improvement of the brain study method because it provides a more thorough study using both transverse-section and rectilinear modes, rapid performance, precise orientation of section and rectilinear views to the patient position, efficient transfer of information between physician and machine during studies and economy of design which should encourage wide application. (Supported by USAEC Contract No. AT(30-1)-3175, USPHS Research Grant No. CA-04456 and USPHS Research Career Program Award CA-14,020 from the National Cancer Institute. NYO-3175-42.)

Quantitation of ^{99m}Tc Localization in Stomach and Intestine after Intravenous Administration of $\text{Na}^{99m}\text{TcO}_4$ in Humans BY K. A. LATHROP AND P. V. HARPER, Argonne Cancer Research Hospital and Univ. of Chicago, Chicago, Ill. (Session XXVI)

Quantitation of gastric and intestinal localization of ^{99m}Tc after intravenous administration as NaTcO_4 is of interest for possible diagnostic value, for accurate assessment of absorbed radiation dose and for studying the effect of competing ions such as iodide or perchlorate. Because of the variable size, shape and depth of overlying tissues, these organs are not subject to *in vivo* quantitation by the technique of relating to counts from a known fraction of the radioactivity contained in a flat phantom and an anatomically realistic phantom for each configuration is impractical. However, counts obtained from the subject after ingestion of a known quantity of a nonabsorbable ^{99m}Tc preparation (100–200 μc sulfur-colloid) may be used as standardizing measurements for each case by comparison with a known fraction of the dose counted in any fixed geometry to be used as a counting standard. Several days later when all the colloid radioactivity has disappeared either by fecal elimination or radioactive decay, the subject receives an intravenous injection of pertechnetate and a counting standard identical with that used in standardization is prepared with a known fraction of this dose. Fractions of dose contained in stomach and intestine are determined by relating counts over these areas with appropriate background subtracted to the standard counts corrected to the *in vivo* situation. These measurements are made using a 1,600-channel analyzer in combination with a gamma scintillation camera having less than $\pm 5\%$ variation in uniformity except for the edge-packing effect. Preliminary studies in several subjects indicate: (1) substantial individual variations in localization; (2) marked changes in gastric content in relation to food intake; (3) initial localization in the colon in the region of the splenic flexure which appears due to a secretory mechanism as it is distinct from the later accumulation of ^{99m}Tc beginning at the cecum, subsequently seen throughout the colon and removable by irrigation; and (4) rapid accumulation of radioactivity in the small intestine of individuals whose urinary excretion is low, but little or no accumulation when this is high. Administration of NaClO_4 abolishes gastric localization but has a variable effect on intestinal content. Organ quantitation, combined with total-body-retention studies and with quantitative excreta recovery, yields a clearer understanding of the biological distribution of ^{99m}Tc from NaTcO_4 and of the effects of various modifying agents.

Preparation and Characterization of a ^{99m}Tc -Labeled Antimony Sulfide Colloid BY S. R. LERNER, J. J. SZAFIR, O. L. PIRTLE, JR., AND F. J. PIRCHER, V.A. Hospital, Houston, Tex. (Session XIX)

The problems associated with the preparation of sterile, pyrogen-free radiopharmaceuticals have made

the use of the pre-formed, stable colloid of antimony sulfide described by Garzon *et al* (*J. Appl. Radiation and Isotopes*, 16:613, 1965) an attractive answer to the procurement of a suitable $^{99m}\text{TcO}_4^-$ -carrier colloid for use in scanning the liver and spleen and for inhalation scans of the lungs.

The procedures described by Garzon *et al* have been modified to permit easier control of the colloid preparation and particle size through use of ammonium sulfide. The sterile, pyrogen-free, pre-formed colloid containing PVP is stable for over 6 months and can be adequately sampled and tested for sterility and freedom from pyrogens.

$^{99m}\text{TcO}_4^-$ from a commercial ^{99}Mo generator is added to the pre-formed colloid, the suspension passed through a 1.2 μ Swinny-type Millipore filter and autoclaved for 30 min at 126° to give $^{99m}\text{TcO}_4^-$ -labeled Sb_2S_3 colloid preparation suitable for human use. Paper chromatography of the labeled colloid with 80% methanol-water shows that over 80% of the label is bound to the colloidal Sb_2S_3 and is influenced by its relative insolubility. Less than 20% of the ^{99m}Tc radioactivity moves with the Rf of TcO_4^- .

Labeled Dopamine Concentration in Human Adrenal Medulla and in Neuroblastoma BY LIONEL M. LIEBERMAN, WILLIAM H. BEIERWALTES AND VIJAY VARMA, Univ. of Michigan Medical Center, Ann Arbor, Mich. (Session XXII)

We have reported that ^{14}C -dopamine is concentrated in the dog adrenal medulla more avidly than any other precursor of epinephrine, reaching concentration ratios at 24 hr of 1,000–2,000 times greater than in serum and 100–200 times greater than in liver and kidney.

We report here similar concentrations of labeled dopamine in human neuroblastoma greater than in normal human adrenals in a woman who had a bilateral adrenalectomy for carcinoma of the breast, and no significant concentration in a primary hepatoma in a child or in a neurilemmoma in an adult.

All patients were injected i.v. with 50–97.5 μc of ^{14}C -dopamine (3.3 mg/100 μc) in saline in a volume of 20 ml/100 μc given over a period of 10–20 min with the tissue removed in 1–2 hr. Radioactivity concentrations of specimens of tumor, normal adrenal, fat, muscle and skin, which were routinely removed at surgery, were assayed in a liquid scintillation counter. Disappearance rates of ^{14}C from dopamine in plasma and cumulative urinary excretion were determined. The conversion of ^{14}C -dopamine to N.E. & E. were determined by column chromatography in alumina gel and Dowex 50W.

All muscle, skin and fat from all patients and the neurilemmoma showed ^{14}C radioactivity concentra-

tions of less than 10 cpm/mg. The concentration in left and right adrenal medullas of the patient with breast cancer were 11–24 cpm/mg, respectively. Four aliquots of the neuroblastoma contained 130–237 cpm/mg. The primary hepatoma specimens had a mean counting rate of 19 cpm/mg. None of the radioactivity in the hepatoma was present in the dopamine or N.E. & E. fractions. The neuroblastoma was calculated to contain 1.9% of the injected dose in 32 gm of neuroblastoma. This is greater than the dose of ¹³¹I concentrated in the usual reported carcinomas of the thyroid gland.

Kidney Scanning with Hippuran in the Anuric Transplanted Kidney BY E. LUBIN, Z. LEWITUS, J. ROSENFELD AND M. LEVI, Tel Aviv Univ. School of Medicine, Tel Aviv, Israel. (Session VI)

The rapid identification of the cause of anuria appearing after renal transplantation is fundamental in deciding on the correct therapeutic approach to this serious and frequent condition. Renograms performed with Hippuran ¹³¹I have been reported as useful diagnostic aids for this purpose. We have found the renogram useful in indicating that renal circulation is present in the transplanted kidney, but we think it is an inadequate method of deciding between the possibility of rejection and urethral obstruction as causes of anuria. Every impairment of the kidneys' production or excretion of urine is reflected by a deterioration in the excretion phase of the renogram, the renogram giving no valuable information as to the cause of this deterioration.

The subsequent performance of a renal scan with Hippuran ¹³¹I helps clarify the situation by adding information on the topographical distribution of the Hippuran ¹³¹I in the renal parenchyme. When the cause of the anuria is rejection, the scan shows a homogenous distribution of radioactivity throughout the kidney with no signs of increased concentration at the level of the renal pelvis. The renal pelvis may appear clear of all radioactivity. In cases of urethral obstruction, the renal pelvis appears as the region of maximal concentration, easily recognizable towards the inner border of the kidney. Finally, in cases of intra-abdominal urinary fistula, the Hippuran ¹³¹I is easily recognizable in the tissues surrounding the kidney and/or the urinary bladder.

We have found that Hippuran ¹³¹I scanning of the kidneys is a necessary complement to renography, mainly when dealing with the possibilities of intrarenal or postrenal causes of anuria.

Computer Calculation of Cardiac Output from Radioisotope Dye Dilution Curves BY WILLIAM J. MACINTYRE, DONALD BUTLER, GRETCHEN S. CURTIS AND

MUHAMMAD A. RAZZAK, Case Western Reserve Univ. School of Medicine, Cleveland, Ohio. (Session XVI)

Calculation of the cardiac output from dye-dilution curves may frequently be tedious, time consuming and subject to various inaccuracies of replotting and extrapolation. Both on-line and off-line computers have been used to obtain a more rapid and accurate calculation of the dilution curves when using nonradioactive dyes. Extension of these computing techniques to external recording with radioisotopes, however, introduces several problems not encountered with the single-peak recording characteristic of the nonradioactive measurement.

For the radioisotope method, the computer must be programmed to recognize the difference between double-peaked and single-peaked curves, to differentiate between the second peak of a precordially derived curve and recirculation, to select the optimum section of the curve between the second peak and recirculation in order to calculate the clearance time and to separate statistical fluctuations from actual variations of the dilution curve.

To accomplish these objectives, a program has been written to first identify the final peak (left-heart curve) by examining the trailing edge for a slope change regressively from a value equal to 40% of the counting-rate range between the peak and the equilibrium value. Recirculation is identified as the point of appreciable decrease in the absolute value of the correlation coefficient derived from the logarithmic decrease of the trailing edge. Statistical variation is identified by examining the slopes of three consecutive points so that the error in any single reading is minimized.

Programs written in Fortran II for this measurement have been applied to over 175 determinations, and a comparison of both manual and computer calculations have been accomplished. Satisfactory agreement has been obtained with outputs as low as 1.6 liters/min and as high as 9.0 liters/min. While high counting rates are preferable, valid results have been derived from injections as low as 20 μ c of radioactive material, wherein data points were recorded every second and the peak value of the dilution curve totaled only 118 counts. (Supported by Grant HE-06304 from the National Heart Institute, National Institutes of Health, U.S. Public Health Service.)

Measurement of Extraction Efficiency of Radiohippuran by Renal Artery Injection and Renal Vein Sampling BY WILLIAM J. MACINTYRE, WALTER H. PRITCHARD AND RICHARD W. ECKSTEIN, Case Western Reserve Univ. School of Medicine, Cleveland, Ohio. (Session VII)

To relate the disappearance of radiohippuran from

the circulating blood to arterial renal-blood flow, some assumption must be made as to the fraction extracted during a single passage through the kidney parenchyma. This determination has usually been obtained by sampling the blood from the renal vein during constant infusion of the radioactive or nonradioactive material. This technique determines the average A-V difference but does not provide any information on the time passage of the material through the blood vessels of the kidney.

It has been of interest to our laboratory to ascertain the time course of the passage of hippuran in the kidney circulation and to determine if an appreciable delay occurs that would be consistent with the slower disappearance of hippuran from the blood with time.

This measurement was accomplished by cannulation of the renal vein of dogs and passing the blood through a side scintillation well counter. Separate injections of radiohippuran and radioalbumin were made directly into the renal artery, and the time concentrations were recorded. After passing through the side well counter, the venous blood was collected and assayed to determine what fraction of the injected material was recovered. The trailing edge of the concentration curve was extrapolated, and the Stewart-Hamilton equation was applied to estimate what fraction of the injected material was not collected.

As expected, almost 100% of the radioalbumin was recovered 10 sec after injection. The hippuran passage was considerably slower, and the amount recovered ranged from 9.2% to 48%. In 14 separate determinations on five animals the extraction efficiency for hippuran averaged 75%. Sufficient variation among animals was noted, however, so that it is doubtful that a single average value would be applicable for the individual case. The time delay of the hippuran passage indicated some temporary retention process well in excess of normal transit time of blood through the kidney circulation. (Supported by Grant HE-06304 from the National Heart Institute, National Institutes of Health, U.S. Public Health Service.)

Thyroid Function Studies in Turner's Syndrome and Allied Conditions BY S. MCHARDY-YOUNG, Stanford Medical Center, Palo Alto, Calif., R. E. POLANI, Guy's Hospital Medical School, London, England, AND D. DONIACH, Middlesex Hospital Medical School, London, England. (Session XII)

An increased incidence of thyroiditis and circulating thyroid antibodies has been reported in association with Turner's syndrome, and occasional case reports of Hashimoto's disease and gonadal dysgenesis have appeared in the literature. Results of thyroid-function studies and their relationship to the presence of thyroid antibodies in these cases has not been closely studied.

The results of these studies in 38 patients with and without significant titers of thyroid antibodies and grouped according to their clinical status and chromosomal abnormalities are reported.

Tanned red-cell agglutination and complement fixation were used to measure thyroglobulin and microsomal antibodies respectively. Serum PBI, T_3 -resin uptake, free thyroxine factor and iodine uptake before and after TSH were measured.

No significant difference could be found between those patients with and without significant titers of thyroid antibodies in respect of PBI level, T_3 resin uptake, free thyroxine factor or iodine uptake. However, the two groups differed significantly in their response to TSH. The 4-hr iodine uptake following TSH was greater than 35% in all cases without antibodies except one; by contrast only four of the 11 patients with high titers of antibodies had a response greater than 35%, and in a further four the response was either absent or extremely poor.

Williams *et al* (1964) demonstrated a higher incidence of thyroiditis and thyroid antibodies in patients with gonadal dysgenesis. We have confirmed these findings. Our present studies suggest that any alteration in thyroid function or iodine metabolism in these patients is similar to that seen in chronic focal thyroiditis or Hashimoto's disease in as far as the mean value and range for PBI, T_3 resin uptake, free thyroxine factor and iodine uptake are normal, but that the response to exogenous TSH stimulation is impaired in cases with significant titers of thyroid antibodies.

Evaluation of ^{75}Se -Selenomethionine as a Tool for Hematologic Investigation BY PATRICIA A. MCINTYRE, BRUCE EVATT, URSULA SCHEFFEL AND BARBARA HODKINSON, The Johns Hopkins Medical Institutions, Baltimore, Md. (Session III)

Simpler and more accurate methods were devised to use ^{75}Se -selenomethionine as a cohort label for the formed elements of the blood in man, rabbits, mongrel dogs and the C3H/He strain of inbred mice.

As reported by others, after intravenous injection of ^{75}Se -methionine (150 $\mu\text{C}/70$ kg) radioactivity appears in erythrocytes, platelets and leucocytes. Meticulous care was taken in washing the separated cells to avoid variable contamination by serum proteins which had a much greater specific activity than the cellular elements.

The rate of incorporation of selenomethionine into erythrocytes and the survival of the labeled cells in man were comparable to those obtained with ^{15}N -glycine but not with ^{51}Cr or ^{59}Fe -labeled erythrocytes. Curves obtained by sacrificing mice at varied times after isotope injection were comparable to those obtained by serial sampling of individual men or dogs.

Enhanced incorporation of ^{75}Se -selenomethionine reflected increased rate of erythropoiesis in hemorrhaged rabbits.

Leucokinetics were investigated in man. Reproducible curves were obtained when the % dose incorporated was measured in terms of milligrams of protein of harvested wbc. In 5 normal males, peak radioactivity occurred 5-7 days later and returned to baseline by 21 days.

Reproducible platelet curves were also obtained in these species. Circulating platelets did not accumulate the label. Peak radioactivity occurred on the following days: man 7-10; rabbits 3, dogs 4-6, mice 2-4.

A rapid simplified method was devised for harvesting platelets for determination of radioactivity.

^{75}Se -selenomethionine provides a valuable tool for the investigation of a wide variety of hematologic disorders.

Scanning of Transplanted Kidneys BY WILLIAM S. MAXFIELD, JULIO E. FIGUEROA AND ROBERT BIRCHALL, Ochsner Clinic and Ochsner Foundation Hospital, New Orleans, La. (Session VI)

Scintillation scanning of the transplanted kidney has been a useful adjunct to the renogram in following the course of the patient after kidney transplant. The renogram and scan can be helpful in determining acceptance or rejection of the kidney transplant. The scan is particularly useful in picking up abnormalities such as breakdown of the ureteral anastomosis and decreased blood flow to the kidney. Examples of these problems will be presented from our experience with scanning of 12 kidney transplants.

Autonomous Function in Sporadic Multinodular Goiter BY J. MARTIN MILLER, BERNICE KAWAS AND MELVIN A. BLOCK, Henry Ford Hospital, Detroit, Mich. (Session XVII)

Sporadic goiter has long been considered to be one precursor of hyperthyroidism from an autonomous thyroid. To evaluate this hypothesis, 70 euthyroid patients with an estimated 50-300-gm multinodular goiter were given a minimum suppression test of 75 μC of T-3 for 5 days and second-24-hr radioiodine uptake and scintigram were done. In 40 nongoitrous controls the average initial uptake was 27%. After suppression the mean was 5% with no individual value above 10%. In 24 of the goitrous patients the average fell from 26 to 5% and to below 10% in each. Appreciable autonomy was demonstrated in the goiters of 46 patients. Two had areas of localized function, and the scintigram after TSH revealed considerable suppressed tissue. The 24-hr uptake in four suppressed to < 10% but retained function localized to one or two nodules not previously visible. Forty did not suppress below

12% and in six of these the scintigram recorded a change in the distribution of the radioiodine. Eight of the 40 received the standard suppression, and the uptake decreased by < 5%. Thirty-two received 300 μC of T-4 or its equivalent for 3-8 weeks instead of or in addition to the standard test.

Fifty-two non-Graves' hyperthyroid patients with large multinodular goiters were scanned, 36 during the 5-year period of suppression testing. On five scintigrams uptake of radioiodine was predominantly in a single nodule and TSH demonstrated the suppressed tissue. On 47 it was diffuse and patchy and in only two of 13 tested with TSH did the scintigram pattern change. Two patients made the transition from eu- to hyperthyroidism while under observation. Single- or double-isotope autoradiography confirmed the validity of the scanning operations and the diagnosis in 19 patients. The emergence of diffuse and less often of localized autonomy in sporadic goiter would seem documented as a prelude to hyperthyroidism. The 65% incidence of this autonomy in euthyroid patients would make suppression tests a prerequisite to thyroid hormone therapy.

Diagnosis of Intracranial Cyst by Means of Brain Scanning BY FRED S. MISHKIN, AND JOHN TRUKSA, Indiana Univ. Medical Center, Indianapolis, Ind. (Session I)

Most reports concerning brain scans deal with areas of increased activity. We have found that large cysts cause areas of decreased activity on the brain scan. While arachnoid and porencephalic cysts are uncommon causes of brain compression and excessive head growth in infancy, their diagnosis is important because they may act as slowly growing lesions requiring early surgical treatment. Development of radiopharmaceuticals which more clearly define normal anatomical structures on the brain scan allows recognition of large cysts by the effect they have on normal structures, as well as their decreased activity.

A vertex view is helpful in demonstrating asymmetric enlargement of the head. In four of six cases this view revealed a shift of the sagittal sinus away from the expanding intracranial lesion. By demonstrating this shift, it became obvious that the apparently increased activity on the anterior, posterior and lateral views represented compressed normal cerebral tissue rather than neoplasm or other abnormality with increased accumulation of the radionuclide.

In six cases we have seen during the past year, the scan correctly suggested the diagnosis of intracranial cyst.

Placental Localization by Scanning with $^{113\text{m}}\text{In}$ BY FRED MISHKIN, ISAAC C. REESE, JAMES HUDDLESTON,

JAMES CARTER AND PHILIP DUBOIS, Indiana Univ. Medical Center, Indianapolis, Ind. (Session XXIV)

^{113}In prepared with gelatin and NaCl as stabilizers at pH 4 has properties which make it a superior agent for placental localization. The short 1.7-hr half-life and lack of particulate emission result in relatively low radiation dose. The pure 390-keV gamma has adequate penetrability so that a low-lying posterior placenta can be detected by a posterior scan without significant absorption or distortion of the photon image by the maternal spine. The radiopharmaceutical does not accumulate in the bladder, and there is no confusing uptake in the pelvis. The stability of the compound allows terminal autoclaving, and preparation is quite simple. The relatively high number of photons administered makes scanning time reasonably short, about 40 min for four views.

We administer 4 mc of the ^{113}In -gelatin preparation and begin scanning immediately with a commercially available dual 8-in.-crystal rectilinear scanner. With this dose, radiation to the fetus is less than that received with a plain abdominal film. In our first 15 studies we have encountered two cases of inferior vena cava syndrome and therefore prefer to do the study with the patient prone if possible.

Scanning has been carried out to aid in amniocentesis in patients with rH incompatibility and to exclude placenta previa when bleeding occurs in the third trimester. In seven instances in which the location of the placenta has been confirmed by exploration of the uterus, the location predicted by the scan was exactly correct. These cases include a low-lying posterior placenta previa and a case of twins.

Radioisotope Imaging in Three Dimensions BY GERD MUEHLEHNER, Nuclear-Chicago Corp., Des Plaines, Ill. (Session IV)

To obtain an image in three dimensions a limited number of views of an object are taken from different directions. The information contained in these views is used in a computer program which calculates the radioisotope distribution in the form of a $40 \times 40 \times 40$ matrix. Slices of variable thickness through this matrix can be viewed on a CRT.

The principle of the method is that of transverse-section scanning with the difference that views from different directions are not merely superimposed but use is made of the fact that the point response function is known to a first approximation. The resultant section views therefore do not contain information from neighboring planes as in rectilinear or "longitudinal" section scanning; resolution and contrast are superior to normal transverse section scans.

The results of tests will be presented in which a head phantom was used. The phantom contained a uniform

background and two high activity areas. Target-to-nontarget ratios from 25:1 to 2.5:1 were used. Even low-activity targets were clearly displayed using a clinically acceptable amount of radiation and a counting time of 1 min per picture (8 min total counting time). For the phantom used, a target-to-nontarget ratio of 5:1 results in a contrast ratio of 2:1 in any single picture. By using the technique described the contrast ratio is increased to 3:1 in a section view.

Labeled SrCO_3 Aggregates for Organ Scanning BY WILLIAM G. MYERS AND WILLIAM W. HUNTER, JR., Ohio State Univ. Health Center, Columbus, Ohio. (Session XXII)

Short-lived radionuclides used with rapid imaging systems such as Hal Anger's gamma-ray or positron scintillation cameras may provide the advantages of decreased radiation exposure, improved statistics, frequent repeatability and patient comfort.

Carbonate and strontium are present in serum normally. The solubility of SrCO_3 is only about 1–2 mg/100 ml of water at room temperature, and aggregates of SrCO_3 particles form promptly *in vitro* when the constituent ions are mixed in adequate concentrations. Simple procedures have evolved for preparing aggregates reproducibly in each of several diameters for various potential applications in nuclear medicine.

These aggregates have been labeled either with 2.8-hr $^{87\text{m}}\text{Sr}$ (388-keV gamma-ray) that is milked from our 80-hr "cow" in our clinical laboratory; or with 20.3-min $^{11\text{C}}$ ($^{+}\beta$ -isotope) generated in our cyclotron. Advantageous physical properties of 70-min $^{86\text{m}}\text{Sr}$ (231-keV gamma-ray) might be exploited also.

For lung scanning, 4–12-micron dia, smoothly rounded SrCO_3 aggregates are used. More than 80% fall within the 6–8-micron range.

Scintillation-camera scanning of dog lungs immediately after intravenous injection of about 500,000 $^{87\text{m}}\text{SrCO}_3$ aggregates has demonstrated small experimental peripheral thromboemboli with excellent resolution. Lack of circulating radioactivity indicates efficient labeling. Clearance of radioactivity from lungs with 9-hr half-time results concomitantly in accumulation in liver but not in bone or bladder.

Small 0.5-micron-diameter particles also can be made readily that might find applications for reticulo-endothelial scanning; and large individual aggregates or uniform clumps of small aggregates have been prepared for studies of peripheral circulation.

Inherent potential advantages of these labeled SrCO_3 aggregates include: small radiation exposure; nonantigenicity; uniform sizes; excellent scanning resolution; good statistics; and dependability of preparation by technical personnel. (Supported by the Julius Stone Fund for Research in Medical Biophysics

and by funds appropriated for cancer research by The Ohio Legislature.)

Total-Body Nitrogen, Protein and Phosphorus by In Vivo Fast-Neutron Activation Analysis BY TERUO NAGAI, ISAO FUJII AND HARUO MUTO, National Institute of Radiological Sciences, Chiba and Toshiba Central Research Lab, Kawasaki, Japan. (Session XI)

In this report an *in vivo* fast-neutron activation analysis for measuring the total-body contents of nitrogen, protein and phosphorus in mice is discussed.

A group of ddY mice was irradiated with 14-Mev fast neutrons from a Cockcroft-Walton generator ("ACTIVAC" constructed by Tokyo Shibaura Electronic Co., Ltd.). The average neutron flux was approximately 10^9 n/cm²/sec. The induced gamma radiation was measured with a Ge(Li) semiconductor detector with an active volume of 22 cm³. A 10-min irradiation of each mouse gave reasonable counting rates. Pulses from the detector were analyzed with a 800-channel pulse-height analyzer. The gamma spectra were analyzed by computer processing (smoothing, background subtraction, peak sorting and normalization). ¹³N formed by the n, 2n reaction on ¹⁴N in the body was measured by counting the annihilation photons. Polyethylene phantoms containing a series of known concentration of NH₄NO₃ solution were irradiated under exactly the same condition and used to calibrate the detector. The gamma spectra from the irradiated mice showed two prominent peaks at 0.51 and 1.78 Mev. The peak at 1.78 Mev is attributed to ²⁸Al produced by the n, α reaction on ³¹P.

To determine contributions from other gamma emitters produced by fast-neutron reactions in the body, phantoms containing various elements (H, O, C, Cl, Na, K, Ca, Mg, Cu and P) were irradiated and the gamma spectra were analyzed. The gamma spectrum from the phosphorus phantom showed two peaks at 1.78 and 0.51 Mev. The first of these peaks is attributed to ²⁸Al produced by the n, α reaction, and the peak at 0.51 Mev is attributed to annihilation radiation due to ³⁰P produced by the n, 2n reaction which gives an activity sufficiently like ¹³N to be confused with it. Therefore, to quantify ¹³N radioactivity in the body of mice it was necessary to subtract the contribution from ³⁰P. Contributions from other positron emitters such as ^{38m}K produced by fast-neutron reactions in the body were negligible.

The nitrogen, protein and phosphorus contents of the mice, human plasma protein and bovine pure albumin solution were determined by chemical analysis, and the results were compared with the results obtained by neutron activation. The activation analysis gave valid results.

Clinical value of this 14-Mev fast-neutron activation analysis and possible uses of ¹³N or ³⁰P- labeled organic compounds as tracers in the biomedical field will be discussed. The computer processing was done with the help of Tamon Inoue of Toshiba Central Research Lab.

Interval Determination in Radioisotope Scanning BY R. NASH AND A. B. BRILL, Vanderbilt Univ., Nashville, Tenn. (Session IX)

The most common technique for displaying radioisotope scan data is the intensity-modulated planar display. This presentation suffers from the disadvantage that human judgment is needed to sense intensity changes and to detect any changes from what constitutes normal appearance. An alternative procedure which avoids the need for visual sensing of amplitude changes is to present the output of the scanner in the form of a contour map. This permits the physician to devote his attention to pattern interpretation and relieves him of the task of sensing amplitude changes. Thus there are clear advantages associated with the contour presentation vis-à-vis the intensity modulated photograph.

Given that one wishes to use the contour interval presentation, several questions of substantial import must be answered. What separation should exist between contour lines? Should uniform separations be employed. These questions will be answered using the concepts of statistical decision theory. It will be shown that the resolving area of the scanner, the standard deviation of the detector output and the emission properties of the volume being scanned must be considered in combination if the best choice is to be made.

Results of the application of these ideas to the construction of contour diagrams for brain scans will be presented. It will be shown how one may take the output data from a brain scan and prepare the best possible contour diagrams. In the opinion of the authors, several distinct practical advantages accrue if the data is presented in this manner. One's attention may be directed to the interpretation of the output data, and small intensity changes may be more easily sensed and evaluated. These desirable attributes which the contour diagram form of presentation possesses make it a data-display technique of substantial import. (This work was supported in part by AEC Contract AT (40-1)-2401.)

Data Storage, Processing and Display System for Radionuclide Imaging BY T. K. NATARAJAN, DILIP MEHTA AND HENRY N. WAGNER, JR., The Johns Hopkins Medical Institutions, Baltimore, Md. (Session XIV)

Present imaging systems have limited data-storage

capabilities and most do not permit data processing while the physician simultaneously views the image. We have designed and constructed a system that permits storage of integrated pulses arising from radio-nuclide scanners, data processing and display of the activity distribution by means of a three-color kinescope. Each of eight colors—black, white, yellow, green, cyan, blue, magenta and red, in that order—corresponds to fractional increases in counting rate from the lowest to the highest. For example, black portrays counting rates from 0 to 1/8 of the maximum while red delineates the areas of maximum counting rate. Provision is made to permit subtraction of a fixed counting rate before data display in color. Various amounts of background subtraction can be made while the observer views the resultant image. The original data stored on incremental magnetic tape are not destroyed during this process. Integration of counts is done over the period required for the scanner to travel 1/8 of an inch. The field of view always contains 10,000 image cells over a 12 × 12-in. area which can be displayed at 60 times/sec to produce a flicker-free image on the kinescope. With reduction in the size of the area under study, the 10,000 cells can be used to construct images of smaller size but with improved resolution. The system is being improved to permit storage, processing and presentation of multiple views. Computations can be made relating areas observed on multiple views.

Organ Imaging with Ektacolor Paper BY MAURICE NATARO, O. R. CZERWONKA AND B. R. LARKE, V. A. Hospital, Louisville, Ky. (Session VIII)

The purpose of this study was to review the various color-scanning methods currently available and to develop a color attachment that could be used on most rectilinear scanners. Cost, simplicity, better colors and full-scale size in relation to black-and-white photoscans was of primary concern in developing this Ektacolor scanning device.

An Ektacolor scan attachment has been commercially designed and used successfully on a rectilinear scanner for producing color scans in six colors on 14 × 17-in. Ektacolor paper.

The completely electronic Ektacolor scan attachment uses three filtered-light sources corresponding to the three basic emulsion color layers on Ektacolor professional paper. By electronically controlling the three basic colors individually and in combination with each other to correspond to small increments of rate-meter response, three additional colors are obtained making a total of six colors produced on Ektacolor paper simultaneously with the black-and-white scan.

The paper to be presented will include the following:

1. A brief description of the Ektacolor scan attachment in the rectilinear scanner.
2. The processing procedure for Ektacolor professional paper.
3. Examples of Ektacolor scans, together with black and white scans of most of the major organs.
4. A comparative cost analysis of Ektacolor vs. black and white.

In summary, a new concept of producing photoscans on Ektacolor professional paper has been successfully completed and described. For those interested in more detailed information, a scientific exhibit will be on display at the meeting.

Some Effects of Scalp and Skull on External Measurements of Brain Isotope BY WILLIAM H. OLDENDORF AND YOUSUICHI IISAKA, Univ. of California, Los Angeles, Calif. (Session II)

This paper discusses the interference of scalp and skull with external measurements of gamma emitters in brain. Data to be presented were obtained by post-mortem measurements of human wet skull and by soft-tissue radiography of human heads to estimate human scalp volumes. Additional animal studies in rabbits established isotope distributions in skin, brain and blood.

The skull minerals create an electron-dense shield which becomes more effective against lower-energy photons because of photoelectric absorption. The broad-beam absorption of wet human skull was measured using isotopes emitting various gamma energies. Below 100 kev the absorption curve rises steeply so that ¹³²Xe radiation is about 25% absorbed and ¹²⁵I about 70% absorbed. The scalp interferes with brain measurements by interposing between source and detector a layer of tissue containing much higher levels of isotope per gram of tissue than brain. This influence of skin is much more prominent for brain than in clinical scanning of other organs because the brain contains so little isotope that the scalp content becomes a significant source of count.

Animal studies of scalp-to-brain ratios of ¹³¹I-RIHSA and ^{99m}Tc were made and compared with other tissues. Radiographic-anatomic estimates of scalp-tissue volume covering human cerebral cortex indicated a mean volume of 230 cc. The scalp-to-brain ratio of ^{99m}Tc-pertechnetate a few minutes after injection was about 17 and of ¹³¹I-RIHSA about 3. This probably reflects the higher diffusibility of ^{99m}Tc through skin capillaries and its more rapid equilibration between skin extracellular space and plasma. The contribution of scalp to the total cranial count will be discussed. The scalp-to-brain ratios should be considered when establishing figures of merit for brain-

scanning agents and determining optimum time after isotope administration for brain scanning.

⁴²K and ⁶⁷Cu for Medical Applications BY H. A. O'BRIEN AND H. B. HUPF, Oak Ridge National Laboratory, Oak Ridge, Tenn. (Session XV)

The Isotope Development Center of ORNL has been assisting medical and biological research groups by providing small quantities of some uncommon radionuclides for experimental evaluation. Many of these commercially unavailable radionuclides are produced by fast-neutron (n,p) reactions which generally have small production cross sections and often require the use of isotopically enriched target material. ⁴²K and ⁶⁷Cu are two examples of this type of production.

⁴²K (T_{1/2} 12.4 hr, 1.52-Mev gamma) has been used in nuclear medicine to locate tumors, tag red blood cells and study blood flow. Its relatively short half-life and high gamma-ray emission have limited its usefulness for metabolism studies. ⁴²K (T_{1/2} 228 hr, 0.371, 0.591-Mev gammas) is more suitable for metabolic and clinical studies because of its longer half-life and lower-energy gamma emission.

Targets of 63.6% isotopically enriched ⁴²CaCO₃ were irradiated in the Oak Ridge Research Reactor (ORR) to produce ⁴²K by the ⁴²Ca(n,p)⁴²K reaction. The carrier-free product was separated from the target by ion exchange, and the target was recovered for re-use. An average yield of 39 μc of ⁴²K/mg calcium target was obtained, giving an average fission-neutron spectrum cross section of 1.5 mb.

Carrier-free ⁶⁷Cu (T_{1/2} 61 hr, 0.182-Mev gamma) which has a half-life about five times longer than ⁶⁴Cu, is being used in a cooperative research effort at the Mayo Clinic to study the metabolism of copper in patients with Wilson's disease and in normals. Extrapolations of the metabolic behavior of copper based on ⁶⁴Cu studies are inconsistent with preliminary results obtained from ⁶⁷Cu studies.

⁶⁷Cu is produced in the ORR by the ⁶⁷Zn(n,p)⁶⁷Cu reaction using isotopically enriched ⁶⁷ZnO. An average yield of 30 μc/mg ⁶⁷Zn was obtained giving a fission-neutron spectrum cross section of 0.86 mb.

¹⁷⁷Lu and ^{176m}Lu as Potential Agents for Skeletal Imaging BY ROBERT E. O'MARA, JOHN G. MCAFEE AND GOPAL SUBRAMANIAN, State Univ. Hospital of the Upstate Medical Center, Syracuse, N.Y. (Session XV)

Almost all radionuclides that have been used for skeletal imaging so far are high-energy gamma-emitters, such as ⁴⁷Ca, ⁸⁵Sr, ^{87m}Sr, ¹⁸F and ⁶⁸Ga. These agents are not particularly suited for the Anger camera, because of the difficulties of effective collimation and low counting efficiency with a crystal only 1/2 in.

in thickness. Even with rectilinear scanners the efficiency of detection is lower than for weaker gamma emissions because collimators with greater depth and thicker septa must be used for good resolution.

Two bone-seeking radionuclides of lutetium have relatively weak gamma emissions and can be produced easily and economically in a reactor.

The first, ^{176m}Lu, has a half-life of 3.7 hr and a monoenergetic gamma emission of 88 kev. An administered dose of 10 mc of this material is proposed for rectilinear scanning. The second nuclide, ¹⁷⁷Lu, has a physical half-life of 6.6 days and a principal gamma emission of 208 kev. An administered dose of 1 mc is proposed for Anger-camera studies. Neither nuclide is "ideal" for a physical standpoint, because both are beta-gamma emitters and the ratio of external photons per disintegration is relatively low (0.25 for ^{176m}Lu and 0.11 for ¹⁷⁷Lu).

The toxicity of soluble lutetium is low to intermediate compared with other metals. Anticoagulant and hemolysis effects observed with larger pharmaceutical doses are not observed with tracer doses.

Durbin demonstrated previously that the heavier lanthanons in the carrier-free state deposited primarily in bone. Current studies in rabbits revealed that reactor-produced lutetium with minimal amounts of carrier localized in the reticuloendothelial system because of "radiocolloid" formation.

When complexed with chelating agents with high-stability constants such as EDTA lutetium was promptly excreted in the urine without reticuloendothelial or skeletal localization. When complexed with HEDTA or NTA, however, approximately 50% of the administered dose localized in the skeleton, and the remainder promptly cleared from the plasma by the kidneys. Although satisfactory skeletal images were obtained 2 hr after administration, the highest bone-to-soft-tissue concentration ratios were achieved at 24-48 hr with ¹⁷⁷Lu.

In experimental animals images obtained with ^{176m}Lu by scanning and with ¹⁷⁷Lu by camera were superior to those performed with other bone-seeking radionuclides.

Combined Inhalation and Perfusion Scanning as an Aide in the Evaluation of Pulmonary Tuberculosis BY FELIX J. PIRCHER, THOMAS C. BLACK AND S. R. LERNER, V.A. Hospital, Houston, Tex. (Session XXI)

Lopez-Majano and co-workers reported that perfusion scans of the lungs proved useful in the evaluation of pulmonary tuberculosis, especially in determining the extent of the disease and the relative involvement of the two lungs, in planning surgical resections and in observing the course of the disease.

Since December 1966, we have studied patients with pulmonary tuberculosis by inhalation as well as perfusion scans using the following technique: 10–15 cc of antimony sulfide colloid in a 0.03% solution labeled with 4 mc of ^{99m}Tc is gradually injected into an ultrasonic nebulizer. The aerosol is inhaled with or without the assistance of a respirator depending upon how dyspneic a patient is. Within 1 hr after the inhalation the patient's chest is scanned. While remaining in the same position the scan is repeated after the injection of MAA particles labeled with ^{131}I . Both scans are then compared with one another for the total area of densities and for the distribution of density deficits. Our observations confirm those of Lopez-Majano. In addition, however, we have found that areas with perfusion deficits also show ventilation deficits. Some of these areas are associated with changes in the chest x-ray, usually of fibrotic or exudative nature, while others are not. The latter are probably due to emphysema. In an appreciable number of cases, the ventilation deficits were more extensive and most often of the diffuse distal type. It was also noticed that turbulent precipitations were quite common in larger airways indicating areas of distortion of the normal ditochomic pattern. Consequently, the inhalation scans often resembled in appearance those from patients with chronic bronchitis and asthma. It thus appears that in patients with pulmonary tuberculosis, emphysema and bronchial obstruction are not uncommon and can be recognized readily by a combined examination with an inhalation and a perfusion scan.

Limitations of Quantitating Regional Pulmonary Perfusion by Lung Scanning by NORMAN D. POE, UCLA School of Medicine, Los Angeles, Calif. (Session XXVI)

To determine the limitations of quantitative lung scanning in regions corresponding to subdivisions of the human lung, measurements of relative regional flow in dogs determined from lung scans were compared to the anatomical distribution of radionuclide found by direct counting of individual excised lobes.

Previously demonstrated principles of quantitative scanning have shown that the total counts obtained by scanning any shape organ can, after suitable calibration, measure the total activity in that organ regardless of the type of collimator used. However, quantitation of subdivisions is difficult because it is usually not possible to separate the counts arising from any specific area alone. Even with a focusing collimator, activity outside the focal plane will contribute counts when individual subdivisions are not well separated.

Using ^{131}I albumin macroaggregates, *in vivo* and *in vitro* estimates of flow were made following postural changes in 20 dogs and unilateral bronchial obstruc-

tion in 10. Blood flow to the relatively ischemic lung was usually overestimated posteriorly and underestimated anteriorly by scanning. However, if the relative percentages determined from both views are averaged, the scan results correlate well with the *in vitro* findings. It was possible with postural change to qualitatively show regional shifts in perfusion within a single lung by scanning, but attempts to quantify these changes anatomically were unsuccessful.

Quantitation of relative differences in blood flow between the two lungs can be achieved by lung scanning in both man and animals if the flow changes are homogeneous. With multiview scanning, lobar and most segmental perfusion defects can be localized, but the flow differences can not be quantitated because present scanning equipment lacks three-dimensional data readout. However, with serial scan examinations, semiquantitative measurement of perfusion changes in small regions of the lung is possible.

Significance of Early and Delayed Inhalation Lung-scan Examinations by NORMAN D. POE, EARL K. DORE, ALFRED GREENBERG, GEORGE V. TAPLIN AND R. L. YANDA, Memorial Hospital, Long Beach and Olive View Hospital, Olive View, Calif. (Session XX)

Inhalation lung scanning was explored initially as a means of estimating regional pulmonary ventilation, but variable and unpredictable amounts of aerosol deposition in the major bronchi frequently posed problems of interpretation. Further studies with ^{198}Au aerosols produced by an ultrasonic nebulizer show that material deposited in the lower respiratory tract clears in a biphasic manner. The first phase is rapid (<12 hr) and represents aerosol removal from the conducting airways by the ciliary escalator mechanism. The second phase is slow (>24 hr) and mainly represents clearance of aerosol deposited distal to the ciliated epithelium in the alveoli.

Excessive deposition in the major bronchi is found in normal subjects during rapid, shallow respiration and in certain patients with obstructive bronchopulmonary disease. It is especially marked in severe pulmonary emphysema presumably due to collapse of the major bronchi during expiration. It occurs at sites of experimental partial bronchial obstruction and in smaller bronchi in patients with bronchiectasis. Clearance of these abnormal deposits is rapid.

In normal humans and intubated dogs breathing in a slow, uniform manner, usually only alveolar deposition is apparent. The distributions of retained aerosol and a single breath of ^{133}Xe are proportional and therefore the alveolar concentration of aerosol is an index of ventilation. Reduced to absent ventilation can be demonstrated in most forms of parenchymal

lung disease and bronchial obstruction. However, ischemic lesions produced by arterial occlusion usually remain ventilated. This provides a practical technique for differentiating pulmonary embolism from other causes of regional pulmonary ischemia.

In clinical application, scans made within the first hour following aerosol inhalation are satisfactory for localization of ventilation disturbances in a majority of cases. However, with obstructive diseases the airway abnormalities may obscure the alveolar deposition pattern and delayed scans are required to evaluate regional ventilation.

Liver Scan Artifacts BY R. E. POLCYN, JAMES L. QUINN, III AND A. GOTTSCHALK, Argonne Cancer Research Hospital, Univ. of Chicago and Northwestern Univ. Chicago, Ill. (Session XIII)

Although it is conceded that the "normal" liver scan may conceal a variety of small lesions, most clinicians have confidence in a liver scan that is distinctly positive. Over the past few years, we have collected several liver scans with an abnormal configuration caused by nonhepatic structures. These artifacts have been produced by metallic objects in the patient's clothing, restraining devices used to immobilize the patient, subcutaneous infiltration of the scanning agent into the antecubital fossa, axillary collection of colloidal material presumed secondary to extravasation in infants, extraneous adipose tissue (e.g., pendulous breasts) and rigid upper extremities. Each of these artifacts made the diagnosis uncertain until the nature of the problem was recognized. It is our hope that by sharing this experience with others, the potential diagnostic errors that these cases represent may be avoided.

Application of Spark Chambers in Nuclear Medicine BY MALCOLM R. POWELL AND DAVID C. PRICE, Univ. of California Medical Center, San Francisco, Calif., AND LEON KAUFMAN, DICK A. MACK AND VICTOR PEREZ-MENDEZ, Lawrence Radiation Laboratory, Berkeley, Calif. (Session XIV)

Medical applications of spark chambers have been limited by the low efficiency of these devices in detecting gamma energies useful in nuclear medicine. Newer developments in spark-chamber technology as applied to nuclear medicine will be reviewed to demonstrate possibilities for using spark chambers in counting and in imaging the distribution of radioisotopes with gamma energies as high as those of ^{47}Ca and ^{59}Fe . Spark chambers offer calculated detection efficiencies of 3-10%, depending on the gamma energy considered, and they can accept counting rates above 10,000 cpm with high spatial resolution. Spark chambers are relatively inexpensive to construct, may be constructed in

large sizes without great increase of cost and the data provided is digital. Plans for specific medical applications will be described including results with some initial experiments.

Consecutive Determination of the Cardiac Output and Renal Blood Flow by External Monitoring of Radioactive Isotopes BY MUHAMMAD A. RAZZAK, ROBERT E. BOTTI, WILLIAM J. MACINTYRE AND WALTER H. PRITCHARD, Case Western Reserve Univ. School of Medicine, Cleveland, Ohio. (Session XVIII)

Estimation of the cardiac output and renal blood flow is of great value in the proper understanding and accurate evaluation of certain cardiorenal disorders. The available nonradioactive techniques are troublesome, time consuming and inconvenient to the patient. To obviate some of these difficulties, cardiac output (CO) was determined by external monitoring of the isotope dilution curve following the intravenous injection of 30 μc of radioiodinated human serum albumin. This was followed by external recording of the disappearance of 50 μc of radiohippuran to estimate the renal blood flow (RBF). The data were obtained through a pair of printing scalers activated at 1-sec intervals for CO and at 10 sec for RBF determination.

Using this procedure in 15 normal individuals, the cardiac index was found to be 3.36 ± 0.35 l/min/m², whereas the RBF amounted to 629 ± 70 ml/min/m². The renal blood flow as fraction of the cardiac output (RBF/CO) proved to be $18.8\% \pm 2.5$.

The data from the 64 patients included in the present study were variable and dependent on their disease entities. All possible combinations of CO and RBF values were encountered, giving either normal, diminished or increased ratios of RBF to CO.

The primary advantage of this procedure is that it has enabled determination of both CO and RBF within 40 min, with accuracy equal to the more laborious and time consuming nonradioactive techniques. Another advantage is that the procedure is nontraumatic and repeated determinations can be performed with the acutely ill or surgically recovering patient remaining in his own bed. Taking these advantages into consideration, this method has been used in the follow-up of 12 cases of acute myocardial infarction and 16 patients after cardiac surgery with the first measurement as early as 2 hr postoperatively. (Supported by Grant HE-06304 from the National Heart Institute, National Institutes of Health, USPHS.)

Chelates of Diethyltriaminopentaacetic Acid (DTPA) for Visualization of Renal Structure and Function BY RICHARD C. REBA, FAZLE HOSAIN AND HENRY N. WAGNER, JR., The Johns Hopkins Medical Institutions, Baltimore, Md. (Session VI)

We recently reported the use of ^{113m}In DTPA for measuring glomerular filtration rate and for renal scanning. The short effective half-life allows administration of millicurie quantities of radioactivity which makes possible increased precision in clearance studies and better images. The radionuclide ^{169}Yb is useful in the form of a chelate because its rapid biological excretion permits administration of millicurie doses despite the physical half-life of 31 days. Measurement of ^{169}Yb DTPA and ^{14}C -inulin clearance ratios indicated that the ytterbium chelate was excreted almost entirely by glomerular filtration. The principal advantages of the ^{169}Yb -labeled chelate over the indium chelate is its slower rate of radioactive decay. This decreases the cost, makes it possible to prepare the material at monthly rather than daily intervals and permits more rigorous quality control. The multiple gamma-photon energies of ^{169}Yb are less desirable than the monoenergetic gamma rays of ^{113m}In or ^{99m}Tc for external detection.

When the ^{113m}In or ^{169}Yb chelates are used with the scintillation camera, we can visualize both renal structure and function. Rapid intravenous injection of 5–15 mc of the radiopharmaceutical is followed by serial camera images. An exposure from 0–20 sec after the injection outlines the blood flow to each kidney and vascular abnormalities. An exposure 1–4 min after injection delineates renal mass. Exposures after 5 min portray the urine flow from each kidney. The use of these chelates lets one measure several functions with a single agent and obviates the need to use multiple agents as proposed by Powell *et al.*

Approaches to the Problem of Noise in ^{99m}Tc Liver Scans BY M. REDDY, P. V. HARPER, A. GOTTSCHALK AND R. POLCYN, Argonne Cancer Research Hospital and The Univ. of Chicago, Chicago, Ill. (Session XIII)

An estimated 20% of the clinical liver scans made with 3 mc of ^{99m}Tc sulfur colloid and the Anger camera at the University of Chicago Hospitals are mottled enough to make diagnosis of lesions less than 2.5 cm in diameter extremely inaccurate. The reliable visualization, however, of cold lesions as small as 1 cm in diameter in a realistic liver phantom, has given rise to the idea that the system has not yet reached the limits of its resolving power in the clinical situation and has occasioned a reinvestigation of traditional factors that could be responsible for degradation of scan quality.

Evidence accumulated from mice and rabbits suggests that there is an irregular distribution of ^{99m}Tc colloid in the liver which depends upon both normal liver architecture and nonhomogeneous uptake of the colloid. Some simple statistical calculations based on the fact that the real message of interest in the scan is

the difference in counts between two adjacent areas have been made showing that the reliability of the scan varies considerably over its surface and is especially poor near the edges.

As a result of these studies and in furtherance of them, a new protocol for clinical scans has been devised. This requires 10^6 rather than 4×10^6 counts/view, with an increased dose of 6 mc to permit breath holding. Follow-up collected from the new protocol indicates improved accuracy in the small-tumor range. Studies are being conducted to determine if the decrease in scan mottle is consonant with the increase in statistical accuracy. These should be of aid in deciding the extent to which the hepatic mottle is physiological or pathological.

^{85}Sr Scans in the Diagnosis of Devascularized Bone BY J. B. REDEKOP, B. R. WALSKE, R. S. HOGE, E. C. BRODIE AND J. C. TOWNE, V.A. Hospital, Tucson, Ariz. (Session XXV)

There is a need for a good early diagnostic method for determining the status of the femoral head in fractures of the femoral neck. Other than radiological findings, attempts have been made to use ^{32}P phosphate uptake and tetracycline fluorescence in bone as early indicators of the devascularization processes. Since bone-seeking nuclides are transported by the intact circulatory system, an interruption of such a supply, as may occur in subcapital fracture of the femoral neck, should reduce the transport and consequent uptake of the nuclide to the region of interest.

Two groups of 12 mongrel dogs were subjected to experimental bone fractures under appropriate anesthesia. In one group, an intracapsular fracture was made just distal to the femoral head in the subcapital region with concomitant interruption of the posterior retinacular vessels as evidence by visual observations. The opposite side of each animal served as a control. In some cases a sham operation was performed. In the other group of dogs using similar procedures an extracapsular fracture in the subtrochanteric region was carried out. No interruption of the blood supply to the femoral head occurs in this process. After closing the wound, $2.86 \mu\text{C}$ $^{85}\text{Sr}/\text{kg}$ was given intravenously, and x-rays taken to visualize the fractured area. Dogs were maintained on demerol. After 72 hr the pelvic and femoral areas were scanned in the anesthetized preparation. In some animals the femoral heads were removed after sacrifice and rescanned.

Results indicated that in nearly all intracapsular fractures less radioactivity was detected in the femoral-head region of the fracture when compared to the opposite area of the dog. Scanning of the femoral heads *in vitro* showed similar results. In six dogs the fracture line was detected as an interruption in the

continuity of radioactivity in the scan. With extracapsular fractures an occasional increase of radioactivity was seen in the general area of the fracture, but this was attributed to a reacting hyperemia in the fractured region.

^{113m}In as a Routine Scanning Agent in Turkey BY FEVZI RENDA, ALI TAN ISITMAN, MUNIR TELATAR AND HOWARD S. STERN, Univ. of Ankara Medical School, Ankara, Turkey. (Session XXIII)

The problems arising in nuclear medicine laboratories which are located far from nuclear reactors and radiopharmaceutical suppliers are obviously evident to those associated with the field. With the advent of the new radionuclide generator systems, these problems have been partially solved. At the Institute of Radiobiology, University of Ankara Medical School, Ankara, Turkey, the logistic problem has been circumvented by using $^{99}\text{Mo}/^{99m}\text{Tc}$ and $^{113}\text{Sn}/^{113m}\text{In}$ generator systems to synthesize short-lived radiolabeled drugs for routine diagnostic scanning.

Although ^{99m}Tc is still one of the optimum radionuclides for scanning various organs, the physical half-life of the $^{99}\text{Mo}/^{99m}\text{Tc}$ generator system requires weekly receipt of the isotope source. In Turkey geographical and economic considerations have led us to prefer the $^{113}\text{Sn}/^{113m}\text{In}$ generator system. The advantages of this parent-daughter equilibrium pair have been reported earlier by other investigators.

It is a recognized fact that to fully use generator-produced radionuclides an adequate radiochemistry laboratory is absolutely necessary to rapidly prepare specific radiopharmaceutical compounds. Insofar as such a laboratory was recently established at our Institute, we are now preparing both ^{99m}Tc and ^{113m}In labeled compounds for various routine organ scanning. The use of ^{113m}In was begun in July 1967, and, presently, brain, lung, liver, spleen and blood pool (heart and placenta) scans are being performed routinely with this newly developed radioisotope by preparing specific compounds previously described by Stern and his co-workers.

Our limited experience with ^{113m}In labeled radiopharmaceuticals consists of more than 200 brain scans, 50 liver scans, 60 spleen scans and 50 blood pool scans. Various examples demonstrating the results of this experience will be discussed. It is noteworthy that during our studies with $^{113m}\text{In}\text{-Fe}(\text{OH})_3$ suspensions for lung scanning, we have made what we consider an important observation. Whenever the preparation was nonuniform (contained a near equal mixture of large and small particles), although capillary blockade was seen in the lungs, the smaller particles were phagocytized by the RES of the liver and spleen. Therefore, three different organs (lungs, liver and spleen) can be

simultaneously visualized by one injection of a single radiolabeled compound. This finding has enabled us to better visualize the subdiaphragmatic space-occupying lesions such as tumors, cysts and abscesses of which the latter two are more frequently encountered in Turkey.

Inhalation Perfusion Tracer Studies in Pediatric Chest Disease BY ARVIN E. ROBINSON AND JACK K. GOODRICH, Duke Univ. Medical Center, Durham, N.C. (Session XXI)

The inability to evaluate pulmonary function in the pediatric patient has been a major obstacle in estimating the extent and reversibility of such chronic pediatric problems as bronchial asthma and cystic fibrosis. The pulmonary physiologist is strongly dependent on the child's learning ability, cooperation, strength, fears and size in performing routine pulmonary-function studies. Applying these studies to children requires specially trained personnel and special equipment with low resistance and small dead space.

Recent advances in instrumentation and shorter-lived radionuclides have allowed for refined techniques in visualizing and quantifying pulmonary function in nuclear medicine. These procedures are easily adapted to the pediatric patient, even on an outpatient basis, at permissible radiation exposure levels.

We have instituted routine ventilation and perfusion pulmonary studies on children with chronic pulmonary disease using the Anger scintillation camera. We are primarily concerned with the extent and degree of pulmonary embarrassment and the effects of local therapy on bronchial asthma and cystic fibrosis.

Following ultrasonic nebulization of ^{99m}Tc -labeled albumin, anterior and posterior scintiphotos are obtained with the entire thorax included within view of the $11 \times 1/2$ -in. scintillation crystal. Nebulization is performed by mask or mouthpiece with a two-way valve adapter for collecting the exhaled tracer into a closed exhaust system. The image is divided vertically to allow scaler quantification of radionuclide distribution throughout each lung field with the stomach shielded by $1/16$ in. of lead. The lungs can be sectioned into quadrants by careful external shielding. The initial inhalation study is followed by similar views after intravenous administration of a calculated dose of ^{125}I -labeled macroaggregated albumin. The entire procedure can be performed in 1 hr. A 10-min. nebulization period precedes the imaging period of 5 min/view. The perfusion study requires a 10-min counting period for satisfactory imaging and statistics. Very little patient cooperation is required, and there is no discomfort.

Ultrasonic nebulization distributes particles ranging

under 1 micron size for deposition on respiratory bronchial mucosa with a minimal effort on the part of the patient. The energy of ^{99m}Tc allows for good counting statistics and imaging over a short period of time. Administration is performed in a separate area, and no appreciable body absorption of radioactivity is present to obscure quantification of ventilatory ability.

Early procedures using these techniques have produced findings similar to those previously described for adults. Partial bronchial obstructions, recognized by focal "hot spots" with diminished peripheral ventilation are readily discovered and are therefore amenable to local therapeutic measures of pulmonary lavage and bronchoscopy prior to bacterial invasion. Peripheral areas of bronchospasm are also similarly represented. Ventilatory deficits without decreased perfusion are expected to represent reversible regions of alveolar-capillary block which can be quantitated on the basis of total lung uptake or capacity.

These procedures fill a significant gap in the armamentarium readily available to the pediatrician and pulmonary physiologist. They reveal another significant contribution to the pediatric patient by newer advances in nuclear medicine.

Comparison of Diagnostic Accuracy of Arteriography with Liver and Pancreas Scans BY A. RODRIGUEZ-ANTUNEZ AND R. ALFIDI, Cleveland Hospital, Cleveland, Ohio. (Session XXIV)

Celiac arteriography was performed in about 60 cases in which liver scans were carried out. The liver scan was performed with radioactive ^{198}Au and a 3-in. crystal scanner. Analysis of these cases reveals that the number of false-positives was slightly higher in liver scanning than in arteriography. On the other hand, liver scanning had a definite advantage over arteriographic diagnosis of a tumor, cirrhosis or cysts.

In about 70 cases in which pancreatic scans were done, celiac arteriography was performed. No significant difference in the diagnostic accuracy of one method over the other was seen.

It is our conclusion that liver scanning seems to be superior to arteriography in diagnostic accuracy of liver disease and that pancreatic scanning is preferable to celiac arteriography in the diagnosis of pancreatic disease because having the same degree of accuracy, it is easier to perform.

Detection of Secondary Tumors of Bone Using ^{18}F and ^{85}Sr in Conjunction with the Anger Positron and Gamma Cameras and Mark II Whole-Body Scanner BY PETER RONAL, H. S. WINCHELL AND H. O. ANGER, Donner Laboratory, Univ. of California, Berkeley, Calif. (Session XXV)

Previous investigators have demonstrated the use-

fulness of ^{85}Sr in the detection of bony metastases even in the presence of negative skeletal x-rays. The strontium isotopes behave in a similar fashion to calcium and measure the accretion rate of bone crystal in areas of osteoblastic activity. The fluoride ion is deposited in bone by a process of exchange. Van Dyke has shown that it is taken up so rapidly that it is distributed according to regional skeletal blood flow. Thus the deposition of strontium isotopes primarily measures osteoblastic activity while fluoride deposition is a measure of regional blood flow.

In the present investigation simultaneous studies of ^{18}F and ^{85}Sr were performed in patients with known secondary tumors of bone. The distribution of these radioisotopes in bone was determined with the Anger positron and gamma cameras and the Anger Mark II whole-body scanner.

The best results from the point of view of both accuracy and rapidity were obtained with ^{18}F and the positron camera. This combination rarely missed a lesion and detected many previously unsuspected ones. 11-22-min scans with the whole-body scanner were very valuable in pointing out areas for closer study with the positron camera. It was found essential to take both anterior and posterior views with the scanner because each of these views would often miss lesions located close to the opposite body surface.

The presence of most lesions could be detected with the whole-body scanner alone, suggesting the potential usefulness of this device in routine evaluation of large populations for bone lesions.

Visualization of lesions containing ^{85}Sr (gamma-ray energy 514 kev) with the gamma camera was poor as the maximum gamma-ray design energy of available multichannel collimators was 445 kev. In the ^{85}Sr studies, therefore, the whole-body scanner with its high-energy capability was the instrument of choice.

Occasional lesions were detected with ^{18}F and not with ^{85}Sr and vice versa, suggesting that increased blood flow and increased osteoblastic activity are not necessarily concomitant phenomena in these lesions and that adequate assessment requires the use of both isotopes.

Whole-Body Scanning of ^{59}Fe in Evaluation of Body Distribution of Erythropoietic Marrow and as an Adjunct to Iron Kinetic Studies BY PETER RONAL, H. S. WINCHELL AND JOHN H. LAWRENCE, Donner Laboratory, Univ. of California, Berkeley, Calif. (Session III)

Previous investigations by Van Dyke in this laboratory have demonstrated the usefulness of ^{59}Fe and the Anger positron camera in evaluating the body distribution of erythropoietic marrow. Unfortunately neither ^{59}Fe nor the Anger positron camera are available in

other centers at the present time. Further the Anger gamma camera which is now in operation in many centers is unsuitable for imaging the readily available ^{59}Fe , while rectilinear scanning with ^{59}Fe is limited by the time involved in scanning the entire body. A simple rapid-imaging whole-body scanner built by Anger in this laboratory has been found valuable in mapping marrow distribution and in providing useful supplemental information in the course of ^{59}Fe kinetics studies.

The distribution of erythropoietic marrow is readily determined by performing an 11-min whole-body scan 24 hr after the intravenous administration of 20 μC of ^{59}Fe . Uptake of ^{59}Fe is normally seen in this scan in the vertebrae, pelvis, proximal femora and proximal humeri only. Extension of erythropoietic marrow into the distal femora, proximal tibiae, ankles and distal humeri such as occurs in hemolytic anemia is revealed by the presence of ^{59}Fe activity in these sites in the 24-hr scan. When there is a loss of central marrow as in myelofibrosis, there is decreased ^{59}Fe activity in vertebrae and pelvis in the 24-hr scan. In the presence of myeloid metaplasia there is an initial accumulation of radioiron in the spleen and occasionally liver is seen in the 24-hr scan followed by a secondary loss of radioactivity from these sites as ^{59}Fe containing red cells are released into the circulation. This secondary fall is detected by a repeat scan 2 weeks after ^{59}Fe administration. Normal marrow also displays this secondary ^{59}Fe release, and hangup of ^{59}Fe in the marrow suggests intramedullary hemolysis. When iron-storage disease such as hemochromatosis is present, initial deposition of iron in the liver occurs without secondary release. A delayed accumulation of radioiron in the spleen detected in the 2-week scan indicates splenic sequestration of red cells. While whole-body scanning does not provide quantitative data on ^{59}Fe distribution, it serves as a valuable check on the accuracy of external-monitoring activity curves which are critically dependent on probe positioning and zero-time extrapolation. Such dependence occasionally results in ambiguities which can be resolved with the total-body scan.

Demonstration of Posterior Fossa Tumors in Children
 BY L. D. SAMUELS, Children's Hospital, Columbus, Ohio. (Session I)

In contrast with adults, the majority of children's brain tumors are located in the posterior fossa, an area usually difficult to visualize on routine $^{99\text{m}}\text{Tc}$ brain scans because of the well-developed overlying occipital muscles. Pre-teenage children have less muscle mass in this area, so that posterior views of the posterior fossa are possible if the head is flexed forward about 30 degrees. This positioning shifts the relative position of

the venous vascular pattern and "opens up" the posterior fossa to visibility. Two hundred $^{99\text{m}}\text{Tc}$ -pertechnetate brain scans have been performed with this technique. It has been possible to demonstrate not only cerebellar tumors but also tumors of the 4th ventricle and brain stem which have pushed upward into the posterior fossa. False positive scans have been more of a problem than false negative scans, probably because of variations in normal anatomy which produce asymmetries of posterior fossa configuration. Despite these occasional variations, any significant asymmetry in a scan obtained in a straight posterior view has been interpreted as suspicious, with contrast ventriculography and angiography ordered in these cases and with surgical exploration undertaken in selected patients.

Details of this technique will be described, examples of positive and negative results will be shown and analysis of the usefulness of the method of diagnosis will be presented.

Estimation of Spleen Size in Sickle Cell Anemia with $^{99\text{m}}\text{Tc}$ Sulfide Colloid BY L. D. SAMUELS AND W. A. NEWTON, JR., The Children's Hospital, Columbus, Ohio. (Session XIX)

$^{99\text{m}}\text{Tc}$ sulfide colloid is a radioisotope which by virtue of its particle size has selective uptake in the reticulo-endothelial (R-E) system. As such, it has been used to obtain liver scans but may also be useful in obtaining rectilinear scans of the spleen. We have evaluated the use of $^{99\text{m}}\text{Tc}$ sulfide colloid in children for obtaining combined anterior-posterior liver-spleen scans in a variety of clinical problems and have found it to be the agent of choice in our hands for visualizing both organs since it gives an index of relative R-E cell activity in liver and spleen and at the same time describes size and configuration.

The estimation of true organ size from a single rectilinear scan has recently been reported for kidneys. The series to be reported here will attempt this technique for estimating spleen size in a group of 50 children with sickle cell anemia with or without known enlargement of their spleens. From 0.25 to 0.5 mc of $^{99\text{m}}\text{Tc}$ sulfide colloid were injected i.v. and posterior scans were performed 1 hr later. This technique appears to offer real promise for evaluating size and relative R-E activity of the spleen. (The radioisotope used in these studies was contributed as Colloscan by Abbott Laboratories.)

Perfusion Lung Scans in Bullous Lesions of the Lung
 BY BERTRAM J. L. SAUERBRUNN, HAROLD WEISS, MELVIN M. SCHIFF AND PETER C. LUCHSINGER, V.A. Hospital, Washington, D.C. (Session XXI)

In the patient with a bullous lesion of the lung, it is important for the clinician to ascertain whether diffuse obstructive emphysema exists as part of the under-

lying pathologic process. In our study of this problem, the use of the perfusion lung-scan pattern was evaluated as a diagnostic laboratory aid and correlated with other parameters of investigation.

Ten patients were given 300 μc of ^{131}I macroaggregated albumin and scanned in the prone and supine position. Each patient had a complete clinical evaluation, chest roentgenograph, a battery of pulmonary ventilatory studies, blood-gas determinations, diffusing capacity and pulmonary angiography. Clinical severity of symptoms ranged from 1+–4+.

Scan patterns could generally be classified in 2 groups: Pattern A—one or more localized “cold defects” with good perfusion in other areas. Pattern B—patchy “salt-and-pepper” type defects in one or more areas with or without evidence of absolute “cold defects.”

Pattern A was associated with patients who had bullous disease without associated generalized emphysema. Depending on the amount of bullous involvement, the degree of impairment of pulmonary function and ventilatory tests ranged from minimal to moderately severe. Blood gases and diffusing capacity were normal. Angiography confirmed good perfusion in the areas uninvolved with bullae.

Pattern B was seen in diffuse obstructive emphysema. Marked abnormality of ventilatory tests and abnormal diffusing capacity was noted. Alteration of blood gases was also evident. Angiography was abnormal showing a “winter tree” pattern of pulmonary vessels and poor perfusion in the capillary phase.

It would appear from this preliminary study that lung-scan patterns can be correlated to some extent with the degree and type of pathophysiologic abnormality in disorders of the lung associated with bullae and may prove helpful to the physician in his clinical appraisal of the patient.

Measurement of the Absolute Uptake of Radioiodine by the Thyroid BY A. G. SCHULTZ AND F. D. ROLLO, Johns Hopkins Medical Institutions, Baltimore, Md. (Session XVII)

Previously a method has been proposed for estimating the absolute uptake of an organ by measuring the ratio of the counts obtained with a flat-field collimator at two prescribed distances from the subject. On the basis of calibration measurements made with a special phantom, this ratio provides an estimate of the effective depth of the organ below the collimator reference positions. Another calibration is made which relates the counting rate at the near reference position to the absolute activity as a function of the effective depth. Combined with the initial estimate of depth, the latter calibration lets one convert the counting rate at the

near position to an absolute estimate of the organ activity.

To a first approximation, the method is independent of variations in the depth of the organ, the distance between the detector and the thyroid, scattering and attenuation. The techniques widely used at present for estimating activity within the thyroid using a standard phantom (such as the ORINS phantom) take into account these effects only in so far as the subjects match the phantom with regard to shape of the neck and—more significantly—depth of the gland. The method proposed automatically corrects for depth effects.

Repeated experiments using unknown activity in phantom thyroid gives accurate estimates of the absolute activity over a wide range of depths. For a series of measurements, the mean value is within 2% and the conversion is within 5%. Preliminary clinical trials are being run to provide comparison between this method and the standard phantom method in estimating absolute thyroid uptake. The spectrum of thyroid depth is also being studied and the results will be compared with data.

Effects of Mercurials on Erythrocytes BY BERNARD SHAPIRO, GEORGE KOLLMANN AND DAVID MARTIN, Albert Einstein Medical Center, Philadelphia, Pa. (Session III)

The use of radioactive mercury-labeled mercurials in brain, kidney and spleen scanning raises certain questions as to the reactions of mercurials with erythrocytes. To study these reactions, human bank blood erythrocytes suspended in saline were treated with four different ^{203}Hg -labeled mercurials: (1) mercurihydroxypropane (MHP), (2) chlormerodrin, (3) p-chloromercuribenzoate (PCMB) and (4) p-chloromercuribenzene sulfonic acid (PCMBS). All four mercurials are bound to the cell surface and enter the cells at different rates. Mercurial uptake measurements were compared with cell damage as indicated by increased K loss and Na accumulation of the cells suspended in saline at 4°C. MHP, which entered the cells more rapidly than the other mercurials, had the greatest effect on K-Na exchange. Chlormerodrin entered the cells more slowly, but produced an equal effect on K-Na exchange. PCMB, while behaving like chlormerodrin in cell entry showed the least effect on K-Na exchange. PCMBS, which hardly entered the cells at all, but was bound to the surface, showed effects on K-Na exchange greater than PCMB. All the mercurials entering erythrocytes became bound to hemoglobin. They may initially react with intracellular reduced glutathione (GSH) but the hemoglobin sulfhydryl groups effectively remove the mercurial from the glutathione. ^{51}Cr -tagged rabbit erythrocytes

were treated with the four mercurials, and partial distribution was studied after reinjection into the rabbits. Treatment of the cells at 10% hematocrit with at least 0.001 M mercurial was necessary to change the distribution in the spleen and liver. At this concentration, chlormerodrin hemolyzed the cells and the other three caused about equal percent sequestration in spleen and liver. Alteration of the cell surface by mercurial appears to be all that is needed for effect on K-Na exchange and splenic sequestration.

Improved Technique to Denature Red Cells for Spleen Scanning BY S. M. SHARMA, M. C. PATEL, P. RAMANATHAN, R. D. GANATRA, M. BLAU*, Tata Memorial Hospital, Bombay, India. (Session III)

The two standard techniques to denature the red cells for scanning the spleen are heat treatment of the ⁵¹Cr-tagged red cells and ²⁰³Hg- or ¹⁹⁷Hg-labeled BMHP. The former has the disadvantage of being time consuming, and the latter has the disadvantage of delivering more radiation dose to the kidneys. In addition, ²⁰³Hg- or ¹⁹⁷Hg-labeled BMHP is more expensive than ⁵¹Cr-labeled Na₂CrO₄ and it is not readily available in many countries.

It has been reported that red-cell survival is severely impaired if the usual 1:4 proportion of ACD-to-blood is exceeded. The reduced survival is presumably due to some injury to the red cells by excess amount of ACD. This paper presents the organ-distribution data in rats and dogs 4 and 24 hr after an i.v. injection of ⁵¹Cr tagged autologous red cells treated with concentrated ACD mixture (four times the usual concentration). Animals sacrificed at 24 hr showed the highest concentration of administered activity (about 65%) in the spleen with very low concentrations in liver, kidneys and circulating blood. Similar studies were carried out by adding 1 mg of stable Na₂CrO₄ after ⁵¹Cr labeling of red cells in concentrated ACD solution was completed. The organ distribution data in rats showed 75% of the administered activity in the spleen at 24 hr. The circulating activity and concentration in other organs was low. Comparative data with heat-treated red cells is also presented.

Work is in progress to apply the technique to scanning the spleen of patients.

Absorbed-Dose Estimates for Radiopharmaceuticals Used for Bone Scanning BY EDWARD M. SMITH, JOHN G. MCAFEE, JAMES M. MOZLEY AND WILLIAM M. SMOAK, III, Univ. of Miami School of Medicine, Miami, Fla., and Upstate Medical Center, State Univ. of New York, Syracuse, N.Y. (Session XXV)

The objective of this paper is to critically evaluate the interrelationship of the radiopharmaceuticals, ra-

dionuclides and organ visualization instrumentation on the resultant absorbed dose to a patient having a bone scan versus the clinical information obtained from the study. The radionuclides to be considered in this evaluation are ⁴⁷Ca, ¹⁸F, ⁶⁸Ga, ^{176m}Lu, ¹⁷⁷Lu, ⁸⁵Sr, ^{85m}Sr and ^{87m}Sr. Several of these radionuclides will be considered in chelated as well as ionic form. The nuclear characteristics of these radionuclides will be presented giving special attention to the number of unconverted photons per disintegration, the photon energy and the distribution of energy of the particulate radiations. Also considered will be the blood disappearance curve and the bone-uptake curve for these radiopharmaceuticals. A simple bone model will be used to calculate absorbed dose to the bone using the recent Monte Carlo calculations of Snyder *et al.* In addition, the blood, bone-marrow, gonadal, bladder and total absorbed dose will be estimated. The radiation detectors of the organ visualization instrumentation to be compared are: 3 × 2-in. NaI(Tl), 5 × 2-in. NaI(Tl) and 11 × ½-in NaI(Tl) crystals using collimators designed for the photon energy of the radionuclide. Each system will have the same circle of resolution and depth of focus with the exception of the parallel hole in the collimator for the Anger camera. A further constraint on the calculations will be total "scanning" time allowed and the counts per lineal inch, i.e., information density. The various radiopharmaceuticals will be compared with respect to the absorbed dose to the patient in light of the above considerations.

Areas of Reduced Coronary Blood Flow with Developing Collateral Circulation Detected by Serial Scans BY R. O. SMITH, W. D. LOVE, Y. ISHIHARA, M. S. ELLIOTT AND P. H. LEHAN, Univ. of Mississippi Medical Center, Jackson, Miss. (Session XVIII)

A rectilinear scanner, constructed for use with ⁴²K, provides data for computer analysis to locate areas of coronary insufficiency caused by Ameroid constrictors placed on selected coronary arteries of dogs.

Three to five sets of scans were made from each dog. The first set was made just before the constrictor was placed on the artery and the remainder were made at weekly intervals. The serial scans in a set are made by scanning a 6 × 6-in. segment of precordium four times in 20 min while 3-5 mc of ⁴²K are infused intravenously at a continuously decreasing rate to provide a stable blood-isotope concentration. The least-squares rectilinear regression line, representing the rise in radioactivity in each of 960 areas measuring 0.19 × 0.2 in. was calculated by a digital computer. The slope of the regression line is proportional to the local rate of ⁴²K clearance. By comparing adjacent areas, zones of reduced uptake caused by arterial con-

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striction are evident. By the end of the third week after placing the constrictor, collaterals have developed and are returning the areas of low uptake to nearly normal as determined by the first control set of scans. Also, 20 min after cessation of the infusion, a single scan is made as a part of each set and can be used as a control.

Three-dimensional models constructed from histograms printed by the computer are extremely effective for visualizing results. However, automatically produced photographic or dot-tapper displays of computer output in which density is logarithmically related to uptake are being investigated.

Evaluation of a Commercially Available *in vitro* Test to Assay Serum Thyroxine BY WILLIAM M. SMOAK, III, EDWARD M. SMITH, GEORGE W. JAMES, ROBERT K. KATIMS AND ALBERT J. GILSON, Miami Univ. School of Medicine, Miami, Fla. (Session XVII)

A new commercially available kit for measuring serum thyroxine, "Tetrasorb-125" (Abbott Laboratories), has been evaluated. The procedure consists of extracting the serum protein with ethanol and evaporating to dryness. The thyroxine in the sample is quantitated according to its composition with a fixed amount of bound thyroiodine ^{125}I for the binding sites on a fixed amount of serum-thyroxine-binding-globulin. An anionic exchange resin sponge is used to separate the serum-thyroxine-binding-globulin bound thyroxine-125 from the unbound thyroxine-125. Twenty samples using this technique can be processed in $3\frac{1}{2}$ hr. It is felt that this procedure can be adapted to a laboratory currently performing *in vitro* studies.

Over 200 patients have been studied by this technique. In addition to historical data on each patient, a T-4 study in triplicate and a T-3 study in duplicate have been obtained. The majority of the patients also had a radioactive ^{131}I uptake, serum cholesterol and butinol extractable iodine. Our series includes a "normal" control group as well as hyperthyroid, hypothyroid and clinically euthyroid patients. In addition, patients who have received substances interfering with the usual battery of thyroid tests or who have a medical status that normally alters the currently available tests have been studied. The correlation of these studies will be presented.

Cyclotron Generator of High Purity ^{123}I BY VINCENT J. SODD AND JAMES BLUE, National Center for Radiological Health and NASA Lewis Research Center, Rockville, Md. (Session XV)

A cyclotron procedure was developed in which high-purity ^{123}I is simply "milked" from a generator ready for immediate use as a radiopharmaceutical. The generator uses a 95.4% enriched ^{122}Te target which, when

bombarded with alpha particles, ($E \geq 30$ Mev), produces ^{123}Xe according to the $^{122}\text{Te}(\alpha, 3n)^{123}\text{Xe}$ reaction. During bombardment the volatile products are swept out of the target by a recirculating flow of helium gas into a CO_2 trap where ^{124}I produced from the $^{122}\text{Te}(\alpha, pn)^{124}\text{I}$ reaction and other contaminants with freezing points higher than -78°C are frozen out. The helium flow is then directed into a liquid-nitrogen trap where xenon products are frozen out. After bombardment the liquid-nitrogen trap is sealed and set aside for 6–8 hr to allow the 2.1-hr ^{123}Xe to decay to ^{123}I . After decay the remaining ^{123}Xe and other gaseous contaminants, notably ^{125}Xe , are blown out of the trap with inert gas. The ^{123}I is then washed out of the trap with 0.5 *N* NaOH which can then be neutralized to the saline solution with HCl.

A generator charged with 100 mg ^{122}Te produces millicurie amounts of 99.8% pure ^{123}I with a 0.05 coulomb bombardment. The more important advantages of this procedure over the existing $^{122}\text{Te}(p, n)^{123}\text{I}$ and $^{121}\text{Sb}(\alpha, 2n)^{123}\text{I}$ methods are: (1) Dissolution of target and chemical separation of ^{123}I and subsequent chemical recovery of target material are eliminated. (2) The ^{124}I contamination usually associated with ^{123}I is minimal since it is easily separated from the xenon precursor of ^{123}I . (3) The generator is reusable.

It should also be mentioned that while a source of 30–40-Mev alpha particles is necessary for the $^{122}\text{Te}(\alpha, 3n)^{123}\text{Xe}$ reaction to occur with high probability, this same generator could also be used with a lower-energy ^3He source using the $^{122}\text{Te}(^3\text{He}, 2n)^{123}\text{Xe}$ reaction. This suggests the application of this generator with the low-cost isochronous cyclotrons now becoming available as sources of 20 Mev ^3He particles.

^{75}Se -Diselenodibutyric Acid: Parent Compound for a Series of Gamma-Labeled Lipids BY RICHARD P. SPENCER AND KENNETH R. BRODY, Yale Univ. School of Medicine, New Haven, Conn. (Session X)

There are few available gamma-labeled nutrients for quantitating absorption, distribution and excretion during life (by means of external counting). We have therefore begun the synthesis of such compounds, concentrating initially on lipids. The selenofatty acids were selected because we could control the chain length and position of selenium in the chain. There are several synthetic routes to the selenofatty acids. The simplest in terms of presently available starting materials proceeds by formation of a diselenodicarboxylic acid as an intermediate and subsequent cleavage with an alkylbromide. Because the biological handling of diselenides has not been adequately studied, diselenodibutyric acid (an intermediate) was investigated. After synthesis of stable diselenodibutyric acid, it was resynthesized in ^{75}Se -labeled form.

Both stable and radiolabeled forms had the same appearance, melting point and chromatographic behavior. When given orally, there was rapid absorption in the dog and in rodents (peak blood levels are reached at about 60 min). Following intravenous administration in the dog, there was an initial rapid fall of blood radioactivity. Activity localized in the liver, kidneys and urine. About half of the radioactivity had been excreted within 1 day and 90% by the sixth day. The material initially in the bloodstream was protein-bound (TCA precipitable). However, radioactivity was split from the protein by treatment with NaHSO_3 (sulfitolysis), suggesting that Se-S bonds were cleaved. Several days later, remaining protein-bound radioactivity could not be split by NaHSO_3 . Diselenodibutyric acid will be employed to produce monoselenofatty acids. It should be possible to obtain a wide variety of gamma-labeled lipids. (Supported by USPHS CA06519 and AM09429.)

Tumor Blood Flow by the ^{86}Rb Method: Effect of Surface Area BY RICHARD P. SPENCER, Yale Univ. School of Medicine, New Haven, Conn. (Session XVIII)

When rapidly metabolizing or growing regions (tumors, fetus) are considered, it is possible that nutrient extraction becomes a rate-limiting factor. The flow (f) can be described by $f = E/(A - V)$ where E is the amount extracted and A and V represent the arterial and venous concentrations of the substance. At a constant $A - V$ difference, the amount extracted can increase only as the flow increases. Since the vessels enter across the surface of the rapidly growing region, relationships between the flow and the surface area are needed. As a background, it has been shown (Aherne) that the surface area of the chorion is matched to fetal metabolism. To construct a time-dependent function, it can be noted that if nutrients are supplied at a constant rate per unit surface area, the weight (W) gain would depend upon $W^{2/3}$ (Payne & Wheeler). Thus, $dW/W^{2/3} \propto dt$ and $W = a(t - t')^3$. This describes fetal growth in many species. Weight-weight and weight-time relationships may thus have a common basis in surface-limited nutrient availability. Macroscopically, the distribution of nutrients follows blood flow; there may thus be simple relationships between blood flow and tumor-surface area. The radioisotope fractionation technique of Sapirstein, which principally uses ^{86}Rb , had been employed by Cataland and co-workers to measure the fraction of cardiac output (F) going to mouse tumors (expressed as F/gm of tumor tissue). The results can be recast in terms of F as a function of the tumor surface area, $F = aW^{2/3} + b$. The correlation coefficients for this equation in describing the mouse

tumors were 0.81 and 0.88. (Supported by USPHS CA06519 and AM09429 and by the Connecticut Heart Assn.)

Detection and Location of Abnormalities in Radioisotope Scan Data BY LEE M. SPETNER, The Johns Hopkins University, Silver Spring, Md. (Session IX)

A procedure is developed for detecting and locating abnormalities in radioisotope takeup. The procedure is a Bayesian estimation and uses all the information obtainable from the scan data in the sense that the primary calculation is the conditional probability density of the location of an abnormality given the data that were actually observed. This conditional probability density makes use of whatever *a priori* knowledge is available concerning the size and location of the abnormality. The procedure yields: (1) the probability that an abnormality is present at all, and (2) the location and size of the smallest circle in which the probability of an abnormality center is 1/2.

This procedure was evaluated by calculating what results would obtain on the average. It is concluded that: (1) Satisfactory accuracy is obtainable in locating spherical voids; for example, with a 1/2-in. collimator and count density of about 1,000 counts/in.² the center of a void of radius 0.3 in. can be located with probability 1/2 inside a circle of radius about 0.3 in. (2) Plots of the circular probable error versus count density exhibit a pronounced knee, thereby disclosing an optimum choice for radioisotope dose.

Modified ^{99m}Tc -Iron Complex for Kidney Visualization BY HOWARD S. STERN, LEOPOLD J. ANGHILERI AND RICHARD C. REBA, The Johns Hopkins Medical Institutions, Baltimore, Md. (Session VI)

Reduced ^{99m}Tc -technetium-iron complex, first described by Harper *et al* in 1966, has been shown to bind firmly with diethylenetriaminepentaacetic acid (DTPA) at pH 7.2-8.0. Electrophoretic studies have shown that this new ^{99m}Tc -technetium compound is essentially free from ^{99m}Tc -pertechnetate ion, thereby requiring no purification. Intravenous injection of ^{99m}Tc DTPA chelate into rats showed that from 6 to 17% of the injected dose is localized in the kidneys in 1 hr with approximately 0.1% and 0.2% in the stomach and liver, respectively. Preliminary electrophoretic studies of kidney homogenates and urine indicate that part of this chelate or a metabolite is bound to kidney protein and that the major portion of the injected dose is excreted unchanged in the urine.

In patients with normal renal function, excellent kidney scans were obtained 2-4 hr after intravenous injection with no associated extra-renal radioactivity.

The parameters of the preparation as well as a comparison with other diagnostic renal agents will be discussed. (Supported by USPHS Grant GM 10548.)

Dynamic Studies with ^{75}Se -Cystine in Normal and Irradiated Rats BY JOSEPH STERNBERG AND ARMAND MERCIER (with the technical assistance of Louise Bellavance), Univ. of Montreal, Montreal, Canada. (Session X)

Plasma disappearance rate and organ distribution pattern was studied after intrajugular injection of $10\text{-}\mu\text{C}$ ^{75}Se -cystine in about $20\ \mu\text{g}$ stable amino acid. The plasma disappearance rate differs from the triphasic aspect found in ^{75}Se -selenomethionine as it is multiexponential with the following equation $P(\%)$: $50.4 e^{-0.347t} + 17.1 e^{-0.069t} + 5.3 e^{-0.0041 t}$ (t in min).

The amino acid binds rapidly to plasma proteins which contain about 40–50% of the circulating isotope; a proportion of 4.1% of the labeled amino acid is excreted through the bile, as seleno-cystine or seleno-taurine. There is no lung excretion of ^{75}Se ; the chief excretion route is the kidney (25.6% in 24 hr) and the ratio urine/feces averages 4.1. Although the liver uptake at 2 hr is as high as that of ^{75}Se -selenomethionine, the amino acid remains in the liver for a shorter period of time; the 24-hr content averages only 1/4 of that of ^{75}Se -selenomethionine. Pancreas uptake of ^{75}Se -cystine is considerably lower than that of selenomethionine, about 1/25th of the 2-hr value found for ^{75}Se -selenomethionine; also, heart uptake is significantly lower than with selenomethionine.

These results show that the high uptake of ^{75}Se -selenomethionine by the pancreas is related to the rapid turnover of the Se-adenosylmethionine and its integration into the pancreatic proteins after transmethylation; it does not automatically qualify any other amino acid labeled with ^{75}Se to be used for *in vivo* studies of protein biosynthesis before a thorough knowledge of its metabolic pathway.

The central position occupied by cystine and selenium as peroxide scavengers and possible radioprotective agents warranted the study of the dynamics and organ distribution of ^{75}Se -cystine in irradiated animals. The compound was injected in animals irradiated with a lethal dose of gamma rays (1,100 R) simultaneously or during the radiation sickness (24 or 48 hr after irradiation, the death occurred in 4–5 days with severe gastrointestinal symptoms). In all animals, there was a significant increase of the urinary excretion of seleno-taurine; also, there was a significant increase of labeled amino acid in the adrenals of the animals examined 48 hr after irradiation; work is in progress to determine the nature of the labeled compound in the adrenals and its relationship with the acute radiation disease. Also the metabolic fate of selenocystine in animals irradiated with lower doses is being investigated to gather information on the possible radioprotective effect of this compound.

Turnover of ^3H -L-Methionine and ^{75}Se -Selenomethionine in Isolated Perfused Liver BY JOSEPH STERNBERG AND GERARD LAMBERT, Univ. of Montreal, Montreal, Quebec, Canada. (Session X)

Isolated rat liver was perfused for 2–3 hr with a fluid composed of 35 ml heparinized rat blood and 70 ml Waymouth's solution #MB-754; the fluid was oxygenated and circulated in a closed system with a flow rate of 1–3 ml/gm/min. The labeled amino acids were injected into the portal system, and blood samples were collected every 5–10 min for 2 hr; bile was collected from the cannulated bile duct, and the volatile compounds were trapped in a collecting bottle. Direct recording of the gamma-emitting isotopes was done by placing a loop of the perfusion tubing over a detector-ratemeter system.

^{75}Se -selenomethionine was injected into the perfusion circuit, and the kinetics of plasma-protein biosynthesis was studied for 2 hr; the curve of plasma disappearance was compared with that obtained in intact animals injected intrajugularly with similar amounts of labeled amino acid. L-methionine labeled with tritium uniformly or only in the CH_3 group was also administered to intact animals or into perfusion circuit, and their kinetics were compared to that of ^{75}Se -selenomethionine.

The plasma disappearance curve of ^{75}Se -selenomethionine has a peculiar triphasic aspect: (1) a multi-exponential distribution phase of the free amino acid followed by (2) a plateau with about equal amounts of free amino-acid and protein-bound material and (3) a protein-bound phase with an ascending gradient and very little free amino acid. Both *in vivo* and *in vitro* experiments showed the same triphasic curve, only the *in vivo* curve reaches the plateau more rapidly (20–25 min instead of 60–65 min in perfusion system); also, the slope of the ascending phase is markedly higher in the *in vivo* system. Turnover calculation gave a rate of protein elaboration of 1,400–1,700 $\mu\text{g/hr}$ *in vivo* and 750–858 $\mu\text{g/hr}$ *in vitro*; the turnover time was 5.5 hr *in vivo* compared to 8.6 hr *in vitro*.

About 7.5% of the injected isotope was excreted through the bile both in the *in vivo* experiments as well as in the perfused liver.

The same triphasic curve was obtained after administration of uniformly labeled ^3H -L-methionine; on the other hand, injection of CH_3 -tritiated methionine failed to show the ascending phase, a plateau being reached at 70–80 min after injection. The curve was not peculiar to seleniated amino-acids since injection of ^{75}Se -cystine gave the same multi-exponential curve as for CH_3 -labeled methionine; nor did the curve reflect the release of mineral selenium since perfusions with selenite showed a very rapid binding of the labeled

material to plasma proteins (few seconds after injection) and a slow descending slope for the remaining experimental period ($t/2$: 545 min).

These data suggest that methionine and selenomethionine are recycled into plasma-protein pools after transmethylation, possibly through the pathway of hydrolyzed S-adenosylmethionine. The transferred CH_3 group is not recycled with the same speed as the remaining amino-acid residue, and it entered the other metabolic pathways of transmethylation, chiefly phospholipid synthesis. There must be secondary sites of plasma-protein biosynthesis since the turnover in the perfused system is significantly slower than that in the intact animal.

It is also possible that the metabolic pathway of selenomethionine is quantitatively and qualitatively different from that of natural L-methionine; parallel experiments with ^{35}S -L-methionine seem to support this hypothesis.

Experiences with $^{99\text{m}}\text{Tc}$ -Labeled Antimony Sulfide Colloid as a Diagnostic Scanning Agent BY J. W. STOVER, S. R. LERNER, E. SOPKO, J. PITTMAN AND F. J. PIRCHER, V.A. Hospital, Houston, Tex. (Session XIX)

Liver scans were performed on 150 patients following the intravenous injection of $400\ \mu\text{c}$ of $^{99\text{m}}\text{Tc}$ -labeled antimony sulfide colloid per expected liter of blood volume. No drug reactions were observed in any of the 150 patients. LDH, creatine and BSP were done before and 24 hr and 1 week after the injection on 20 patients. An increase of LDH was observed in three patients, and an increase in BSP in two patients. None of these changes are believed to be related to the drug. The observed blood-disappearance curves were comparable to that of colloidal gold.

The quality of the scans was classified as excellent, good, fair and inadequate. Fifty percent of the scans qualified as excellent, 30% as good and 15% as fair while 5% were inadequate. The retention and distribution of the colloid in the liver was apparently related to the status of the patient's liver function. Extra-hepatic retention in the spleen was noticed in every case, in the kidney seven times out of 10, in the spinal column five times out of 10 and in the cardiac pool six times out of 10. In one case retention in the lungs was noticed. The amount of extra-hepatic retention was apparently related to liver uptake, i.e., decreased liver retention was associated with increased retention in the other organs. In general, the diagnostic accuracy of the compound compared favorably with that reported for other technetium-labeled colloids. On several occasions renal disease could be recognized and consequently verified by kidney scans.

Zinc-Binding Capacity and Zinc Levels of Serum BY WILLIAM H. STRAIN, CHARLES G. ROB, WALTER J. PORIES, JOHN A. HENNESSEN AND JOHN MONTOYA, Univ. of Rochester School of Medicine and Dentistry, Rochester, N.Y. and USAF Hospital, Wright-Patterson AFB, Ohio. (Session XI)

Further investigation of the zinc-binding capacity of serum in various disease states has demonstrated some complexities in the correlation with the zinc levels of serum determined by atomic absorption. Because zinc-binding must measure both exchangeable zinc and zinc-deficiency sites, it is not surprising that some discrepancies have been found. The correlation of zinc-binding capacity and zinc levels of serum will probably become more apparent with greater experience.

The clinical syndromes of zinc deficiency differ greatly, and the response to zinc therapy is not uniform. Zinc sulfate medication is being used in the promotion of healing, the treatment of inoperable vascular disease, oral therapy for certain skin conditions and the alleviation of pain from acute porphyria. Because these various disorders have different etiologies, it is understandable that the zinc-binding capacity and the zinc levels of serum may not always correspond. The differences will be illustrated by data obtained from sera of patients before and during zinc therapy. More consistent values have been obtained in zinc-binding capacity by making the measurements at 0°C rather than at room temperature, just as in the T-3 and iron-binding procedures.

It is probable that element-binding capacity of serum should be investigated for a large group of metals. Cobalt, copper, iron, manganese and molybdenum are known to be definitely interrelated with zinc in plants and domestic animals, and comparable relationships presumably exist in man. The long-lived radioisotopes of cobalt and manganese are especially suitable for study. (This research was supported in part by grants HE-10213 and RH-00042, UPHS; by the Horatio H. Burt Research Fund of the University of Rochester; and by a grant from the Aerospace Medical Division, under approval of the Surgeon General, U.S.A.)

Radioisotopic Estimation of Residual Urine Without Urethral Catheterization BY BERNARD S. STRAUSS AND M. DONALD BLAUFOX, Albert Einstein College of Medicine, New York, N.Y. (Session VII)

Radioisotopic evaluation of residual urine volume and of the dynamics of micturition has valuable clinical potential. This study was designed to investigate the use of radioisotopes in lower urinary tract obstruction; 20 adult male patients, 10 of whom had untreated obstruction of the lower urinary tract were included. The upper urinary tract was tested with an ^{131}I -iodo-

hippurate renogram in each subject. Thirty minutes after completion of the renogram (45 min after injection) each patient was placed in the standing position with a radioisotope detector aimed directly at the bladder. A 2-in. crystal with a 5-in. cylindrical collimator was used and the data were recorded on electromagnetic recording tape. The patient voided into a container which was shielded from the probe, and the initial counts over the bladder, the rate of disappearance of the isotope and the final bladder counts were determined. In each instance the exact time at which micturition began and ended was obtained from the chart recorder. An assumption of no residual urine in the normal patients was based on the negative history of urinary tract disease and the complete disappearance of the isotope from the bladder area. Urethral catheterization was performed on the abnormal subjects in order to measure the actual residual urine volume. The average residual measured was $99\text{ml} \pm 29$ (S.E.) and the calculated residual was $86\text{ml} \pm 22$ (S.E.). There is no significant difference between these values by the paired and standard t tests ($p > 0.5$). The urine flow rate was significantly reduced in the patients with obstructive disease. The average flow rate calculated from the isotope recording was 6.0ml/sec. versus a rate of 20.0ml/sec. in the normal patients. It is concluded from these studies that radioisotope methodology permits the accurate and useful measurement of residual urine and an assessment of urodynamics in patients with lower urinary tract obstruction. Catheterization of the bladder may be completely avoided with no loss of accuracy and with equal ease of performance.

⁵¹Cr Studies in Wilson's Disease BY G. THOMAS STRICKLAND, JR. AND WILLIAM MCC. BECKNER, Naval Medical Research Unit #2, Taipei, Taiwan. (Session XI)

Five patients from two families with Wilson's Disease and a heterozygous sibling had ⁵¹Cr red-blood-cell masses, external-probe counting over the spleen and liver and red-blood-cell survival studies.

The six patients were clinically divided into three groups: (1) The heterozygote without a palpable spleen, (2) two sisters with normal liver function and palpable splenic tips and (3) three patients with abnormal liver-function tests and small livers and large spleens. One of the latter had cirrhosis and portal hypertension documented by liver biopsy and hepatic vein catheterization. The heterozygote had a normal hemogram, ⁵¹Cr RBC mass and calculated blood volume, and RBC survival time. The ratio of external counts over the spleen to the liver was 1.0 to 1.4. The three patients with marked splenomegaly had persistent pancytopenia, normal RBC masses with in-

creased calculated blood volumes, shortened RBC survival times and a ratio of external counts over the spleen and liver of 2.5 to 4.4. The two sisters with normal liver function and palpable splenic tips had borderline findings, not as abnormal as in the three patients with gross splenomegaly.

Interesting correlations were noted in this homogeneous group of patients. Despite low hematocrits, RBC masses were normal and calculated blood volumes were directly correlated with splenic size as noted by palpation. RBC survival time was inversely related to splenic size, being shortest in those with the largest spleens. The ratio of external counts over the spleen and liver was directly related to spleen size. Definite RBC sequestration in the spleen could not be proven since this ratio remained stable and did not increase.

Regional Pulmonary Function Studies in Canine Lung

Allografts BY E. SURPRENANT, G. STEVENS, L. BENNETT, M. WEBBER AND E. FONKALSRUD, UCLA School of Medicine, Los Angeles, Calif. (Session XXI)

Orthotopic left-lung allotransplantation was performed on each of 16 mongrel dogs. To determine the degree of function in the transplanted lungs, the distributions of ventilation and perfusion in both lungs were determined 2-32 weeks following surgery. Twelve of the animals were studied once, three twice and one three times.

At the time of the study, the dogs were prone, lightly anesthetized with thiopental and intubated with an endotracheal tube. The distribution of ventilation was determined by introducing 300 cc ambient air tagged with 1 mc ¹³³Xe gas through the endotracheal tube. A scintiphoto was then obtained of both lungs in the posterior projection with a scintillation camera. The distribution of perfusion was also determined with a similar scintiphoto following the intravenous injection of 1 mc ^{99m}Tc macroalbumin.

The transplanted lungs demonstrated some perfusion in 13 of the 16 dogs while ventilation to this lung was totally impaired in only one dog. Both ventilation and perfusion of the transplanted lung showed some degree of impairment in all of the animals. While both functions were affected to a similar degree in the same animal, the perfusion changes tended to be somewhat more severe than those of ventilation. Post-mortem examination in nine of the dogs demonstrated changes which in each instance closely corroborated the findings seen on the scintiphotos. The dog that was studied three times is currently alive and well 38 weeks following transplantation. This animal initially showed some decrease in function in his transplanted lung, but, subsequently, function to the other lung became more impaired, reflecting a pneumonia in this lung. As the animal improved clinically, both lungs approached normal distribution of function.

Perfusion lung studies are a useful and sensitive indicator of the functional status of a transplanted lung in dogs. The ventilation studies provide complimentary information. (This work was supported by California Institute for Cancer Research (40-820) and by Contract AT (04-1) GEN-12 between the AEC and the Univ. of California at Los Angeles.)

Simplified Procedure for Preparation of ^{131}I -labeled Sulfobromophthalein: Its Applications to Liver Scanning BY ROMSAI SUWANIK AND MANUEL TUBIS, Siriraj Hospital and Medical School, Bangkok, Thailand and V.A. Center, Los Angeles, Calif., and UCLA Center for the Health Sciences, Los Angeles, Calif. (Session XXVI)

A method of preparing ^{131}I -labeled sulfobromophthalein is described. The method is simple and inexpensive. The labeled compound is of particular value where $^{99\text{m}}\text{Tc}$ -labeled preparations for liver scanning are too expensive or not readily available. It has been used as a liver scanning agent with satisfactory results, revealing both morphological as well as functional abnormalities in various liver conditions in the same fashion as ^{131}I -labeled rose bengal. Its use in liver scanning has been extended to the visualization of the liver abscess cavity after intracavitary injection. The method has been used to observe the changes in size and configuration of the abscess cavity during its course of healing under medical treatment. Another extension of the work is the intraductal administration of the labeled compound via a T-tube to demonstrate the dilatation of the biliary tract in cases of advanced opisthorchiasis. The applications of the labeled compound to liver scanning will be illustrated.

Tomographic Capacity of a 10-Probe Rectilinear Scanner BY LEONARD A. SWANSON, HIDEO YAMADA, D. E. JOHNSON AND GEORGE V. TAPLIN, Harbor General Hospital Campus, Torrance, Calif. and UCLA School of Medicine, Los Angeles, Calif. (Session IV)

A 10-probe rectilinear scanner with rectangular crystals and unidirectional focused collimators has a definite tomographic capacity. This unique feature has been found most useful in brain scanning for more accurate localization and definition of tumors or vascular lesions and for distinguishing the normal choroid plexus from other causes of excessive radioactivity in the vicinity of the posterior horns of the lateral ventricles. High-resolution section scans made with the 3 1/2-in. focused fine collimator were most informative. Section scanning for negative lesions surrounded by high levels of radioactivity as in the liver, kidney and lung has been less rewarding but deserves further study.

The presentation will include the results of phantom studies, specific clinical applications and a discussion of the limitations as well as the advantages of rapid section scanning with this device.

Application of Catheter-type Semiconductor Radiation Detector Inserted into the Gastro-fiberscope to Diagnose Upper GI-Tract Malignancy BY SEI-ICHI TAKAYANAGI, TETSUJI KOBAYASHI, University of Tokyo, Japan, HIDEO UEDA, HARUO KAMEDA, RYUSHI SASSA, MASAHIRO IIO AND YASUHIITO SASAKI, Central Research Lab., Tokyo Shibaura Electric Co., Ltd., Kawasaki, Japan. (Session XXVI)

At the 13th and 14th Annual Meetings of the Society of Nuclear Medicine the development of a catheter-type semiconductor radiation detector (CASRAD) and its application to clinical medicine including the detection of cancer in the gastrointestinal tract were reported. In this report, the gastro-fiberscope with further miniaturized CASRAD probe inserted in the biopsy needle hole is discussed. This device was developed to detect the malignancy of the stomach using the fiber-scope technique.

A micro G-M counter has been used to detect ^{22}P radioactivity accumulated in the malignant tissue in the upper gastrointestinal tract. Because the CASRAD probe has advantages over the micro G-M counter, such as low operation voltage and durability, the CASRAD probe was used instead of the micro G-M counter for this purpose.

Radioactive phosphorus (125-400 μc) was injected intravenously about 20 hr before examination. Under x-ray fluoroscopy the walls of the organs were scanned by the CASRAD probe (3.2 mm in dia) inserted through the mouth. A more than 50% increase in counting rate above that seen in the adjacent control area was regarded as positive, less than a 20% increase as negative and 20-50% increase as indefinite. Among a total of 15 cases, six out of seven gastric cancers, one gastric sarcoma and six out of seven esophageal cancers were positive. On the other hand three out of four control cases (benign gastric diseases) were negative and one case was indefinite.

Based on the results of this preliminary study the gastro-fiberscope (Machida Co. Ltd., Tokyo, Japan) with the CASRAD probe fixed in the biopsy needle hole was constructed. The probe used for this equipment was further reduced in diameter down to 2.5 mm. With this device the CASRAD probe is easily pointed to the suspected lesion by using fiberoscope manipulation technique under naked-eye guidance. Thus the portion for the biopsy is determined by this method more accurately than before. The results of this study will be reported.

Use of Radionuclides in the Determination of Vascularity of Pedical Skin Grafts BY W. NEWLON TAUXE, PAUL R. LIPSCOMB AND JOHN N. SIMONS, Mayo Clinic and Mayo Foundation, Rochester, Minn. (Session XVIII)

The standard postoperative interval for severing pedical skin grafts is approximately 3 weeks. For some patients severance of the graft at this time results in necrosis. For the majority of patients, however, severance of the graft can be effected much earlier.

Over the past few years, we have developed a test to assist in making the decision in individual cases about the optimum time to sever pedicles. This test has been tried 79 times at various intervals after surgery in 31 patients.

The test consists of preparing the patient for donor end-pedical occlusion by infant sphygmomanometer cuff, injecting 1-5 μc of ^{131}I or $^{99\text{m}}\text{TcO}_4$ subcutaneously near the center of the usually circular implantation site and determining its disappearance rates by placing a scintillation-crystal probe over the injection site.

Falloff of radioactivity is measured over the next 30-60 min. At the end of 10 min, the sphygmomanometer cuff is inflated and occlusion is maintained for another 10 min. The cuff is then released and the curve is continued until a straight line on the activity plot is attained.

From this curve, two disappearance slopes can be discerned: an "occluded" rate (λ_1) and an unoccluded rate (λ_2). Percentage flow is defined as $\lambda_1/\lambda_2 \times 100$.

While precise estimates of minimum flow rates compatible with graft viability are difficult to obtain, we have found the test to be reproducible, reliable and to afford remarkable savings in patient hospitalization time as well as the frequently unpleasant immobilization time necessary for operative procedures. It has permitted cross-leg pedicles to be severed successfully as early as the twelfth postoperative day.

A New Scintillation Camera BY F. DEAVOR THOMAS, WILLIAM H. BEIERWALTES, LAWRENCE JONES, HARRY COLESTOCK AND THEODORE COLVIN, Univ. of Michigan Medical Center and Bendix Aerospace Systems Div., Ann Arbor, Mich. (Session IV)

The first version of a new scintillation camera was presented to the June 1967 meeting of the Society of Nuclear Medicine. The basic device consists of a 9×1 -in. NAI(Tl) crystal, objective lens, three-stage image amplifier, transfer lens and a photographic readout. Various multichannel and pinhole collimators were designed. This system was not clinically useful because of a poor signal-to-noise ratio (i.e., a noisy image tube).

Revisions in the second model include: (1) more efficient multihole collimators designed for a maximum

gamma energy of 200 keV and resolutions of 10 to 28 mm at 10 cm distance; (2) a new objective lens system with 70% transmission efficiency for NaI(Tl) light; (3) a new three-stage image amplifier tube with bi-alkali photocathode surfaces and significant noise reduction; (4) improvements in the photographic readout so that various film types can be used; and (5) parallel development of an orthicon video system that will allow readout of the image directly from the output phosphor. Currently, mechanical redesign and modifications are in progress.

Evaluation of this device with phantoms indicate that it will be clinically useful; concentrations of 10 μc of $^{99\text{m}}\text{Tc}$ in a thyroid phantom can be visualized with 10 min of integration time. This represents a hundred-fold increase in signal-to-noise ratio from the previous device.

Clinical studies will be reported as well as a first assessment of the video readout.

Use of ^{75}Se -Selenocystine for Pancreatic Photoscanning BY JUAN F. TORRES, JR., PHILIP N. BRUNNER AND RICHARD E. PETERSON, Univ. of Iowa College of Medicine, Iowa City, Iowa. (Session XXIV)

With the aim of using the labeled amino-acid analog which can effect a smaller radiation dose for pancreatic scanning, the biologic half-life and tissue turnover of ^{75}Se -selenocystine and ^{75}Se -selenomethionine were studied and compared.

Ten adult mice were each injected with 5 μc in 0.2 ml of ^{75}Se -selenomethionine (sp. act.; 4,166 mc/gm) through the tail vein. Similarly, another group was given ^{75}Se -selenocystine (sp. act.: 355 mc/gm). Each animal had a whole-body count immediately after injection and at various time intervals thereafter. Groups of five each were also injected and then sacrificed at 30 min, 1, 2, 4, 8, 24 hr, 3 and 11 days later. Individual tissue or organ concentration was determined.

Both amino acids showed basically similar disappearance curves with an early fast clearing phase and a subsequent slower portion. The respective half-times were 42 hr and 6.7 days for selenomethionine; 8 hr and 4.5 days for selenocystine. ^{75}Se -selenocystine concentration in the various organs compared well with those observed for ^{75}Se -selenomethionine. In the pancreas significantly high ^{75}Se -selenocystine activity persisted up to 4 hr while observations with ^{75}Se -selenomethionine showed a peak concentration at 1 hr followed by a steady fall thereafter.

The results suggest that the use of ^{75}Se -selenocystine for pancreatic scanning can deliver a lesser radiation dose as well as allow a longer usable time for the procedure.

Patients studied had a pancreatic scan using ^{75}Se -selenomethionine followed by a repeat scan with ^{75}Se -selenocystine after an interval of seven or more days.

Radiohippuran Excretion Test in Asymmetric Renal Parenchymal Disease BY IAN B. TYSON AND LIZABETH SMITTEN, University Hospitals, Madison, Wis. (Session VII)

In renal arterial stenosis, the hypoperfused kidney reduced glomerular-filtration rate (GFR) and effective renal plasma flow (ERPF) produce low urine flows. When 10% mannitol diuresis is superimposed on a water diuresis, the urine flow in the hypoperfused kidney is increased, eliminating differences in excretion rates between the normally and the hypoperfused kidney estimated by the radiohippuran excretion test. Differences between the excretory rates of parenchymally diseased kidneys may occur which are unresponsive to osmotic diuresis.

It has been noted that the induction of osmotic diuresis produced differences in kidney excretory rates which may be minimal. But where time lapses from injection to peak of the curve differed by more than 2.5 min prior to mannitol infusion, marked increases in the differences in excretion rates occurred following mannitol in four hypertensive patients with differences in kidney size greater than 1.5 cm by IVP. All had reduced 24-hr creatinine clearance, none were significantly acidotic, one was uremic (BUN > 30 mg%). Radiohippuran excretion tests showed differences in excretory rates between the kidneys ranging from 0.5 to 14.5% prior to and greater than 25% post-mannitol infusion. Times to peak in the diseased kidney remained unchanged pre- and post-mannitol. In the apparently healthy kidney, this time was markedly reduced. Subsequent split-function tests in which GFR and ERPF were measured showed that in the kidney indicated as diseased by the radiohippuran excretion test, the GFR per nephron was increased with sodium wasting.

It was concluded that in unilateral pyelonephritis with reduced ERPF and increased GFR/nephron, radiohippuran excretion tests showed that the diseased kidney had a reduced response to osmotic diuresis in contrast to the healthy kidney.

Determination of Copper and Manganese in Human Liver by Neutron-Activation Analysis and Introduction of Repeated Pulsed-Neutron Activation Analysis in Nuclear Medicine BY HIDEO UEDA, TOHRU IWASE, HARUO KAMEDA AND MASAHIRO IIO, AKIRA TANI, HIROYUKI NAGAO, YASUHIKO MATSUDA, NAWOYUKI KAWAI, Univ. of Tokyo, Tokyo, and Nippon

Atomic Industry Group Co., Kawasaki, Japan. (Session V)

Copper and Manganese contents in biopsy or autopsy liver samples obtained from 10 cases of Wilson's disease, five cases of hemochromatosis, 12 cases of liver cirrhosis and eight normal cases were measured by conventional activation analysis using the TTR-1 100-kw reactor with a thermal neutron flux of 3×10^{11} n/cm²/sec. Irradiated specimens were analysed both by nondestructive and chemical-separation methods. In the latter method which takes 30-60 min copper was separated with almost 100% yield by the internal electrodeposition technique and manganese with 90% yield by the usual precipitation method.

The amount of hepatic copper was found to be increased significantly in Wilson's disease (88-717 $\mu\text{g/gm}$ dry weight) and also in hemochromatosis (104-2,530 $\mu\text{g/gm}$). (Liver cirrhosis 29-122, normal control about 39 $\mu\text{g/gm}$). On the other hand the amount of hepatic manganese showed no significant difference between hemochromatosis (4-17 $\mu\text{g/gm}$), liver cirrhosis (1.3-13.5 $\mu\text{g/gm}$) and normal control (2-6.3 $\mu\text{g/gm}$).

A simplified chemical-separation method after neutron activation proved to be a useful tool for the evaluation of copper and manganese contents in biopsy liver specimen.

Repeated pulsed-neutron activation analysis for large medical sample is also introduced using a 14-Mev pulsed neutron generator. Advantage of this new method is as follows. Some nuclides with half-lives of a second to microseconds can be analysed with minimum integrated neutron irradiation and without hindrance of other long-lived induced activity.

Results of medical sample analysis and the possibility of whole-body activation analysis will be presented.

Evaluation of Serial $^{99\text{m}}\text{Tc}$ Brain Scans in Cerebrovascular Accidents BY MICHAEL S. USHER AND JAMES L. QUINN III, Northwestern Univ. and the Chicago Wesley Memorial Hospital, Chicago, Ill. (Session I)

Evidence has accumulated that serial brain scanning would accurately delineate tumor from infarct, correlate well with clinical presentation and give an indication of the prognosis. We carried out the following study to critically examine this thesis.

The clinical records and scans were examined in all stroke patients who had at least one of serial brain scans positive between June 1966 and October 1967. $^{99\text{m}}\text{Tc}$ -pertechnetate was used in each case. Twenty-eight cases with 78 scans fulfilled these criteria.

The severity of illness was evaluated and the prognosis ascertained. The density of abnormal uptake was assigned four grades in comparison to the vertex. The areas of uptake were measured by planimetry. Scattergrams were constructed to correlate size, density, pro-

gression of scintigram abnormality, clinical severity and prognosis.

Size and time of appearance of positive scans bore little or no relationship to the severity of onset or course. All patients whose scan became less dense at the same time they clinically improved suffered no significant residual deficit by 2 months after onset. Of those whose clinical improvement corresponded to scan worsening, only 40% recovered completely. Of the three deaths, scan improvement was noted in one.

The site of uptake occurred where expected clinically. The radionuclide concentration was superficial in every case. No other specific characteristics were noted which could differentiate tumor from infarct.

The role of brain scanning in the management of the patient with cerebrovascular accident is discussed.

Pancreatic Concentration of Radioiodinated Phenylalanine BY VIJAY VARMA, WILLIAM H. BEIERWALTES, RAYMOND E. COUNSELL AND LIONEL M. LIEBERMAN, Univ. of Michigan Medical Center, Ann Arbor, Mich. (Session XXIV)

^{14}C , ^{35}S and ^{76}Se -labeled amino acids have been demonstrated to concentrate in pancreas 2 hr after administration with a pancreas:liver concentration ratio of about 8:1. We report here a quantitatively similar specific pancreas localization of ^{14}C and of ^{125}I -labeled phenylalanine.

Thirteen mice with melanomas were given ^{14}C -phenylalanine i.p. and sacrificed at 1, 24, 50, 96 and 168 hr. The radioactivity concentrations routinely were assayed in 13 tissues with a liquid scintillation counter. In three separate experiments using 9 mice each, similar tumored mice were injected with iodo-phenylalanine labeled at the position ortho, meta and para to the alanine side chain. The mice were sacrificed at 2, 4 and 24 hr intervals and 13 to 18 tissues were routinely taken for radioactivity assay in a scintillation well counter.

^{14}C radioactivity was found in highest relative and absolute concentration in the pancreas at 1 hr after i.p. injection, the radioactivity concentration being 5.8 times that in kidney and four times that in liver. There was no significant concentration in melanoma. The mean concentration of ^{125}I in the pancreas was similar after each of the 3-iodinated phenylalanines and similar to the values found after ^{14}C . The mean concentration of ^{125}I in the pancreas was highest at 4 hr, being 6-9 times that in liver and 4-6 times that in kidney. Pancreatic concentration was not remarkable at 24 hr. Thyroid radioactivity concentration was lower than in pancreas during the first 4 hr but two times that in pancreas at 24 hr. Thyroid count were 32-400 times greater at 24 hr after the administration of an equal amount of ^{125}I as Na^{125}I than when given

as the iodinated phenylalanine. No specific concentration of ^{125}I was found in melanoma.

Use of the Brain Scan in Determining Optimum Time for Carotid-Artery Surgery BY THOMAS A. VERDON, JR., ARTHUR COHEN AND FRANK H. ALLEN, Letterman General Hospital, San Francisco, Calif. (Session I)

The brain scan affords the only visual representation of an altered blood-brain barrier. It has been shown that cerebral vascular accidents (CVA) will produce a positive brain scan while the blood-brain barrier is altered. In cases of CVA due to occluded carotid arteries, we believe that surgical corrections of the occluded vessel will aid in repair of the infarcted area and afford more blood flow to the brain. A major problem with carotid artery surgery at the present time is the converting of a bland ischemic infarct into a hemorrhagic infarct with resultant death of the patient. We have found the brain scan to be an indicator to the timing of the carotid-artery surgery. When the scan becomes normal and the blood-brain barrier is restored, we perform surgical correction. This has been successful in 15 patients who have undergone major carotid-artery repair without complications.

Renal Excretory Mechanism of Radioactive Metal Chelates BY HEINZ-GEORGE VILHUBER, Neisler Laboratories, Inc., Tuxedo, N.Y. (Session VII)

The standard substance for estimating glomerular filtration rate (GFR) is inulin. Its chemical determination, however, is inconvenient and alternative methods have been sought. Greater simplicity of measuring GFR is possible using compounds labeled with gamma-emitting isotopes.

Conflicting reports exist in the literature about the excretion of ethylenediaminetetracetic acid (EDTA) and diethylenetriaminepentaacetic acid (DTPA) in mammals. ^{14}C -labeled EDTA and DTPA were reported to be excreted by glomerular filtration and tubular excretion. However, renal clearances of ^{40}La -EDTA and ^{51}Cr -EDTA, respectively, were reported to be similar to that of mannitol and ^{14}C -inulin.

The behavior of radioactive metal chelates was investigated *in vitro* and *in vivo* in an effort to determine the mechanism of renal excretion of these compounds. The plasma binding of the following metal-EDTA and -DTPA complexes was measured by ultrafiltration and equilibrium dialysis: ^{64}Cu , ^{65}Zn , ^{59}Fe , ^{51}Cr , ^{57}Co , ^{114}In and $^{99\text{m}}\text{Tc}$. The ratio of complexing agent to metal ion was 2:1 with a metal ion concentration of 10^{-3} molar. The DTPA chelates generally showed less interaction with plasma constituents than the EDTA complexes in the *in vitro* tests, with ^{57}Co -DTPA being the least bound.

The EDTA and DTPA chelates were also studied in dogs and rats. In dogs the blood disappearance curve was measured by taking blood samples at time intervals and calculating the renal clearance from these values. Experiments in rats followed the single-injection technique with external measurement of the plasma disappearance curve. In both cases, organ-distribution studies revealed only minor uptake of the complexes by the liver. The method used was then correlated with the glomerular filtration rate as measured by ^{125}I -iothalamate.

The metal chelates are a potentially practical and inexpensive group of radiopharmaceuticals for use in nuclear medicine. Their major excretory pathway appears to be by way of the kidney.

Studies on the Retention of ^{137}Cs Following Accidental Internal Deposition, BY JOHN M. VOGEL, USPHS Hospital, San Francisco, Calif., AND JOHN A. ECKERT, Southwestern Radiological Health Laboratory, Las Vegas, Nev. (Session XI)

Six men involved in an industrial accident received internal burdens of ^{137}Cs in connection with the rupture of a sealed source. Four men were whole-body-counted five times over a period of 4 months. Significant contamination of the hands occurred, necessitating counting with the hands shielded and unshielded to arrive at valid estimates of the body burdens. These burdens ranged from 1 to $5\ \mu\text{c}$ ^{137}Cs , and the average half-time in the individuals was 110 days after an initial more rapid exchange. Blood and urine specimens were also collected. Blood-clearance values remained constant, ranging from 1.07 to 2.73 ml/min with maximum coefficient of variation of 40% for any individual. Data was also obtained on the retention of the ^{137}Cs in the hands of the individuals. One hand scan taken 3 weeks after the contamination incident still revealed very localized activity on the distal segment of the right thumb.

Complex of $^{99\text{m}}\text{Tc}$ and L-Cysteine for Renal Scanning BY A. G. WALKER AND J. McRAE, Univ. of Sydney, Sydney, Australia. (Session VI)

The high radiation dose to the kidneys from the mercury compounds makes the production of compounds of short-lived radioisotopes desirable for renal scanning. $^{99\text{m}}\text{Tc}$ -iron complex has been described by Harper *et al* and used in several centers. A new complex of $^{99\text{m}}\text{Tc}$ and L-cysteine with potential usefulness as a renal-scanning agent has been produced. On descending paper chromatography it appears as a peak with R_f 0.45, and evidence from gel filtration and paper chromatography suggests that it is of low molecular weight. The method of preparation will be presented. There is a consistent yield of 75%, and free TCO_4^- is separated either with a very short column

of Amberlite IR-4B or by gel filtration with Sephadex G-25.

In mice, renal excretion after 1 hr is 65–70%, and 10–12% remains in the kidneys. When compared to $^{99\text{m}}\text{Tc}$ -iron complex, uptake by the kidneys is significantly higher and uptake by the liver and gut significantly lower. A renal scan of good quality has been performed 1 hr after intravenous administration to a sheep. A 1/1,000 dilution with magnetic stirring, simulating dilution on intravenous injection into man, demonstrates that this complex is stable, while $^{99\text{m}}\text{Tc}$ -iron complex dissociates to a considerable extent. Complete separation of free $^{99\text{m}}\text{TcO}_4^-$ from the complex may be achieved, while on separation of free $^{99\text{m}}\text{TcO}_4^-$ from Tc-iron complex further dissociation occurs.

A suggested dose for man is 1–5 mc with the scan to be performed at 1 hr or more after administration. This agent should compare most favorably with other $^{99\text{m}}\text{Tc}$ compounds which have been used for renal scanning.

Endothelial Lesions—Demonstration by Scintiscanning BY MILO M. WEBBER and ROSCOE C. WEBB, JR. Univ. of California, Los Angeles, Calif. (Session XVI)

Collections of tracer accumulations have been noted by the authors as well as by others in the axillary regions on certain patients who have undergone pulmonary scanning. Reviewing these cases it was noted that a common denominator existed. The patients had been, almost without exception, subjected to venous catheterization with the purpose of administering intravenous fluids. A catheter had been inserted and remained in place for a variable length of time. In some cases accumulation of tracer was seen in the axillary region for on repeat lung scans several weeks after the removal of the catheter. An experimental method was developed in which focal vascular lesions were created within the vascular system. The method consisted of the use of an electrocautery electrode at the end of an intravascular catheter. Electrocautery was applied to the wall of the vessel under fluoroscopic control. After creation of the lesions, tracer doses of various substances including radiotechnetium-labeled albumin macroaggregates were introduced intravascularly. Scintiscanning techniques were used to visualize the distribution of tracer. This paper will discuss the distribution of tracer following the production of intravenous and intra-arterial lesions. It is expected that this technique may be applied to many situations in which the vascular endothelium is damaged. Possible applications include demonstration of vascular disease, such as thrombophlebitis, localized vasculitis and arteriosclerotic ulceration (as may be

associated with cerebral emboli). (This work was supported in part by Contract AT (04-1) GEN-12 between the AEC and UCLA.)

Gastrointestinal Absorption of Copper Studies with ^{64}Cu , ^{95}Zr , Whole-Body Counter and Scintillation Camera BY P. M. WEBER, S. O'REILLY AND M. POLLYCOVE, Univ. of California School of Medicine and San Francisco General Hospital, San Francisco, Calif. (Session V)

Interest in Wilson's disease has stimulated inquiry into studies of gastrointestinal (GI) absorption of copper. While metabolic balance studies are difficult to perform, the use of a whole-body counter capable of detecting small amounts of gamma-emitting radionuclides *in vivo* greatly simplifies measurements.

Since a variable fraction of the absorbed copper is promptly excreted into the GI tract, ^{64}Cu was administered orally to measure net copper retention and later intravenously to quantitate fecal excretion. ^{95}Zr was administered orally as a nonabsorbed stool marker. GI absorption of copper was calculated as the ratio of net ^{64}Cu retention after oral administration to net ^{64}Cu retention after intravenous administration both corrected for completeness of GI excretion. Corrections were also made for loss in urine. Scintiphotos were taken to localize site of maximal absorption. Blood sampling was performed in some subjects and related to scintiphotos and whole-body-counter data.

Data are presented in 16 studies performed in nine subjects. Though normal subjects absorbed an average of 60% of the oral ^{64}Cu tracer dose, the range of absorption from 15% to 97% was very broad. GI excretion after intravenous dose averaged 11 1/2% with a range up to 23%. Carrier copper when varied over a thousand-fold range did not influence GI absorption. Penicillamine in addition to increasing urinary loss of copper tended to decrease GI loss after intravenous administration without significantly effecting net absorption. Net absorption was high in two patients with Wilson's disease. Scintiphotos and blood-sampling data reveal maximal absorption during the first hour when copper is in the stomach and duodenum.

Technetium Kinetics in Humans — the Effect of Heavy-Ion Pretreatment on Optimal Time for Brain Scanning BY M. WELCH, M. ADATEPE AND E. J. POTCHEN, Washington University, St. Louis, Mo. (Session I)

Perchlorate or iodide pretreatment has been advocated for technetium brain scanning in an effort to reduce the radioactivity emanating from the choroid plexus. By blocking the technetium tissue accretion this pretreatment may well alter the blood background significantly and thereby influence the quality of

brain scans. In an effort to further evaluate this, serial blood samples were drawn on 21 patients undergoing technetium brain scans. Patients were divided into three groups: (1) a control, (2) pretreated with perchlorate and (3) pretreated with iodide.

The activity of the blood was plotted against time, and trends were found to fit a model:

$$\text{Tc in tissue} \xrightleftharpoons[K_2]{K_3} \text{Tc in blood} \xrightarrow{K_1} \text{Tc in urine}$$

The tissue compartment is found to be almost completely blocked by the heavy ion, the rate constants were found to be $K_1 = 0.19 \text{ hr}^{-1}$, $K_2 = 1.47 \text{ hr}^{-1}$ and $K_3 = 1.7 \text{ hr}^{-1}$.

From these observations it was concluded that heavy-ion pretreatment markedly influences blood-background kinetics, and it is suggested that the optimal time for scanning if one used heavy-ion pretreatment is approximately 3 hr after the intravenous injection of the technetium.

Study of Preliminary Experience with the Use of ^{123}I for Thyroid Function and Scanning Compared to ^{131}I BY H. N. WELLMAN AND J. F. MACK, National Center for Radiological Health AND B. I. FRIEDMAN, AND E. L. SAENGER, Cincinnati General Hospital, Cincinnati, Ohio. (Session XV)

The advantages of ^{123}I for thyroidal studies has only recently been recognized. Newly developed techniques for production of this radionuclide promise to make its use more practical in the near future. ^{123}I produced by the $^{122}\text{Te} (\alpha, 3n) ^{123}\text{Xe} \rightarrow ^{123}\text{I}$ reaction has been used to do routine thyroid-function studies. Thyroid uptakes and scans are obtained in patients at both 6 and 24 hr after oral administration of 50-100 μc of ^{123}I . Uptakes are performed both with a standard uptake system at 25 cm and with the low-energy dual-crystal detector previously described by our laboratories. Thyroid scans using both the 28-keV x-ray and the 159-keV gamma ray of this radionuclide are obtained with a high-resolution Brookhaven collimator. In addition, thyroid scintiphotos are obtained at both times using the single pinhole collimator and the gamma scintillation camera. These studies are compared to a 24-hr scan and uptake done with ^{131}I .

Results suggest that 6-hr scans can be achieved which are as satisfactory as 24-hr scans. Furthermore, better resolution can be achieved because of the low-energy gamma emission. The 28-keV x-ray is useful in describing superficial nodules. Considerable dose reduction to the patient, better scanning resolution, plus the demonstrated practical usefulness would encourage wider use of ^{123}I for routine thyroid studies.

Processing and Display of Radioisotope Data BY S. WILENSKY, A. B. ASHARE, S. M. PIZER, C. A. BURNHAM, S. ARONOW AND G. L. BROWNELL, Massachusetts General Hospital, Boston, Mass. (Session IX)

The increased use of multichannel systems for collecting radioisotope scan data has made it necessary to use some type of data-processing system for data analysis and presentation. Presently at the Massachusetts General Hospital there are several multichannel detecting systems which have been equipped with seven-channel 1/4-in. digital magnetic-tape recorders. The tape recorders have been interfaced to a PDP-7 Data Processor which is used to process and display the data.

The interface has been designed to read data from the magnetic tape either as a 7-bit parallel-coded word or as seven independent channels of counting-rate information.

The output of the hybrid positron brain scanner is a series of 7-bit words which contain x-y positional information and the address of the detectors which recorded a coincidence. Computer software has been written which reads the 7-bit words from the magnetic tape, decodes the words and writes the information on computer tape for permanent storage and rapid retrieval.

After preliminary processing which includes the transformation into a 128×128 matrix and focusing, the scan can be subjected to a number of statistical techniques which are designed to improve the quality of the picture. The software for these operations include an executive routine which permit personnel unskilled in computer programming to routinely process scan data.

The output device used to display the brain scans is a television-type display which is capable of displaying a matrix as large as $1,024 \times 1,024$ with up to 16 levels of intensity. For display of the brain scans the output is limited to a 128×128 matrix with eight levels of intensity which achieves a flicker-free display of 40 frames/sec. A routine has also been written to obtain a volumetric-type display. Although the system is presently used only with the hybrid positron scanner, the processing system is applicable to any imaging device whose output can be digitized.

The data-processing system has also been applied to the analysis and display of pulmonary and cerebral-blood-flow dynamic-function studies. These studies are performed by recording the pulses from six scintillation detectors on magnetic tape. The magnetic tape is then read into the computer via the interface, and the computer constructs the counting rate versus time curve for each of the six detectors. The effective "time constant" of the counting rate curve can be varied by

changing the time interval over which the computer averages the pulses. The dynamic-function data can then be plotted on a Calcomp plotter or displayed on the scope using either a linear or a logarithmic scale. Provisions have been included to subtract background, normalize all channels to a zero time, calculate appearance time, transient times and dispersion time.

A wide range of experience has been gained with the processing system and results will be presented which illustrate the techniques described above. The advantages and limitation of the system will be discussed.

Radionuclide Studies in Evaluation of Renal Response to E.S.T. in Normal and Renal Transplanted Animals BY ROBERT H. WILKINSON, JR., M. J. SHORT, AND JACK K. GOODRICH, Duke Univ. Medical Center, Durham, N.C. (Session VII)

The laboratory and clinical evaluation of renal response to various drugs and clinical procedures is frequently difficult and requires the implementation of methods which introduce a nonphysiologic state. The purpose of this presentation is to demonstrate by example the possible contribution of renal radionuclide studies using the Anger scintillation camera in renal investigative studies.

The present study was stimulated as a result of the necessity for electric-shock therapy in a severely depressed and suicidal renal transplant patient. While no detrimental effect on renal function was anticipated nor encountered, further investigation into the renal response to electric shock therapy was deemed worthwhile. Normal dogs and renal transplanted animals were employed. An unexpected although transient renogram curve variation was encountered in normal animals.

Renograms and renal scintiphoto studies were used because they offered a means of demonstrating transitory changes during a prolonged dynamic study in as normal a physiologic state as could be attained. Renal arteriograms, ureteral catheters and electromagnetic flow meters introduce abnormal physiological states. It was felt that changes in renal blood flow and glomerular filtration rate might be reflected by renogram-renal scintiphoto studies while maintaining the "normal" physiological state. Two radiopharmaceuticals, sodium iodohippurate and sodium iothalamate, were used. The studies revealed that following a single electric shock treatment, the previously normal canine renogram curves demonstrated statistically significant prolongation of the "second" or "renal blood flow" phase. The explanation for this phenomenon has been pursued employing various drugs including those affecting the autonomic nervous system. The findings derived from these studies will be discussed. The results in renal transplanted animals will be presented. (This

study supported by a Duke Endowment Grant and by USPHS Grant No. HE-11309.)

Observations on the return of Blood Flow Following Pulmonary Embolism BY J. W. WINEBRIGHT, A. J.

GERDES AND W. B. NELP, Univ. of Washington School of Medicine, Seattle, Wash. (Session XXI)

Serial lung scanning was used to evaluate the pattern of recovery of lung perfusion following pulmonary embolism. Seventy patients were studied who had one or more perfusion abnormalities characteristic of pulmonary emboli on their lung scans. All of the patients were treated for emboli. Over 60 of these patients have been followed for periods up to 15 months after their last embolus. A total of more than 190 separate scans was analyzed.

The size of the perfusion defects was estimated on each scan using a template method. The perfusion defects on the patients' initial scans were divided into three groups: those equivalent to less than 15% of the total pulmonary blood flow, those over 30% and those intermediate in extent.

In all, one-fifth of the patients resolved their perfusion defects completely. This was documented by a normal lung scan on the average 11 days after the onset of clinical symptoms. One-half of the patients were considered to have significant improvement—that is, they restored at least 50% of the pulmonary perfusion originally affected. The remainder of the patients showed little or no improvement over an average period of 6 weeks.

Most of the patients who resolved their perfusion defects completely had smaller initial defects. Pre-existing, overt cardiovascular diseases of various types seemed to be a major factor in retarding and reducing resolution of embolic defects. Similarly, the patients' age had a significant effect on resolution. No one over 60 years old reverted to a normal scan pattern, and two-thirds of those who failed to show any significant improvement were also over 60.

The resolution patterns in several conditions predisposing patients to embolization (e.g. thrombophlebitis) have also been examined, as has the frequency of occurrence of certain signs and symptoms associated with embolization.

Localization of Hyperfunctioning Parathyroid Adenomata Using Radioisotope Methods BY JOSEPH B. WORKMAN AND THOMAS B. CONNOR, Univ. of Maryland School of Medicine, Baltimore, Md. (Session XXIV)

The localization of hyperfunctioning parathyroid adenomata by external scintillation-scanning techniques, when successful, may be of immeasurable aid to the clinician. However, when a tumor weighs less

than 3.0 gm, detection percentage by external scanning has been reported as quite low. A more precise and efficient method for localization of hyperfunctioning parathyroid adenomata at the time of surgery would be welcomed by most operating surgeons.

The Division of Nuclear Medicine at the University of Maryland School of Medicine has been working with a method for detecting hyperfunctioning parathyroid adenomata at the time of surgery using ⁵⁷Co labeled vitamin B₁₂ and a small surgical probe. Since 1960, 25 patients with proven hyperfunctioning parathyroid adenomata have been studied using this technique and successful localization reported in 19 for a positive detection percentage of 75%. Details of the procedure as well as the special problems inherent in the method will be discussed.

Sequential Liver and Upper Abdominal Scanning in Hepatobiliary Disease BY H. YAMADA, L. A. SWANSON, D. E. JOHNSON AND G. V. TAPLIN, UCLA School of Medicine, Torrance, Calif. (Session XIII)

With the advent of rapid organ-imaging devices such as the scintillation camera and the 10-probe rectilinear scanner, sequential imaging of the liver and upper abdomen at 5–10-min intervals is now both possible and practical. One can visualize the rates of radio-rosebengal liver uptake and its normal rapid entry into the upper intestine. In severe *intrahepatic* jaundice, tracer accumulates more slowly in the liver, and little or no activity appears in the intestine, gallbladder or in the intra- or extrahepatic bile ducts for several days during which time the heart, spleen and kidney blood pools remain visible. By contrast, in complete *extrahepatic* biliary obstruction from cancer of the head of the pancreas, useful distinguishing features are the gradual accumulation of activity in the major bile-duct regions together with increasing levels of radioactivity in the gallbladder and kidneys during the first 24 hr. Partial biliary obstruction (stone) is characterized by excessive accumulation of radioactivity in regions of the common-bile duct and large intrahepatic branches during the first few hours followed by delayed removal of tracer from the extra and/or intrahepatic biliary passages.

Preliminary findings with this procedure in 15 jaundiced patients have demonstrated its capacity to disclose evidence favoring either intra- or extrahepatic causes of biliary tract obstruction in several instances. Although sequential scanning shows considerable promise as an aid in the differential diagnosis of jaundice, much further investigation is needed to establish its clinical usefulness, particularly in cases of long-standing jaundice associated with severe liver-function impairment.

Combined Circulation-Scan Technique for Differential Diagnosis of Cerebral Infarct and Tumor BY Y. L. YAMAMOTO AND W. FEINDEL, Montreal Neurological Institute, Montreal, Quebec, Canada. (Session II)

The differential clinical diagnosis of brain tumor, cerebral infarct and intracerebral haemorrhage often presents a formidable problem. Although positive brain scans of cerebral infarcts occasionally present some characteristic features, in most instances these have not been proven to be specifically diagnostic.

As an addition to scanning, we have developed a technique of monitoring cerebral blood flow using a rapid intravenous injection of the radioactive tracer dose given to the patient for the purpose of brain scanning. This cerebral-circulation transit-time study and quantitative contour brain scan together demonstrate not only alteration of hemodynamics over the cerebral hemispheres but also the location of the cerebral lesion.

The technique uses twin detectors placed on the forehead and designed to record gamma counts separately from each cerebral hemisphere. In addition, two detectors are also placed on selected areas over either side of the head. The direct comparison of curves from the bilateral symmetrical detectors minimizes the variables due to geometrical factors or to changes in systemic circulation. The flow curves are analysed in regard to six main features.

Because of its simplicity, this combined circulation-scan method has been of value as a rapid screening test in helping to differentiate cerebral infarct from neoplasm. On the basis of examination of 350 patients, a characteristic change in cerebral infarct was found to be prolongation of certain parts of the circulation transit-time curves recorded over the side of the lesion. From the quantitative brain scans also some distinction can be made between the quantitative uptake in intracerebral hemorrhage as compared to cerebral infarct.

The comparison of intravenous cerebral circulation-time studies and quantitative cerebral-perfusion studies using ^{133}Xe in the same monitoring system will also be discussed briefly.

Visualization of Blood Vessels and Organs with Ultra Short-Lived Radioisotopes and the Scintillation Camera BY YUKIO YANO AND HAL O. ANGER, Donner Laboratory, Univ. of California, Berkeley, Calif. (Session XVIII)

Ultra-short-lived radioisotopes with half-lives ranging from a few seconds to a few minutes can offer advantages in imaging major blood vessels, heart and other organs.

Because venograms and angiograms are usually completed within 1 min after injection of the activity, isotopes with very short half-lives are feasible for these

studies. Since there is no buildup of radioactivity in surrounding tissue, repeat studies may be done rapidly and different views may be obtained.

Radiation exposure is reduced to a minimum because the activity decays away within a few minutes after the infusion is completed.

Very-short-lived isotopes are most easily obtained from a long-lived parent isotope retained on an ion-exchange column from which the short-lived daughter can be rapidly eluted and infused. A mechanical elution apparatus has been developed to obtain controlled flow rates of sterile eluant solution through a closed system for infusion into the subject.

Ultra-short-lived isotopes which have been investigated include; 4.9-sec $^{191\text{m}}\text{Ir}$ which decays by emission of 0.129 Mev gamma rays and is the daughter of 16-day ^{191}Os , 80-sec ^{82}Rb which decays by positron emission and is the daughter of 25-day ^{82}Sr , and 3.8-min ^{128}Cs which decays by positron emission and is the daughter of 2.5-day ^{128}Ba .

Nuclear reactions for producing the long-lived parent isotopes have been developed and ion-exchange separations of the daughter isotopes with physiologically compatible eluant solutions have been successfully tried in both animal and human subjects.

Scintillation camera pictures have been obtained of blood vessels, heart and lungs with $^{191\text{m}}\text{Ir}$. Positron camera pictures have been obtained with ^{82}Rb showing selective uptake in the myocardium of dogs. Preliminary work has also been done with ^{128}Cs which demonstrates clearance by the myocardium in dogs as shown with positron pictures.

Distribution and Scintiphotography Studies of New Liver Scanning Agent: $^{99\text{m}}\text{Tc}$ -Toluidine Blue 0 Colloid BY S. YEH, JOAN E. DELAHAY AND JOSEPH P. KRISS, Stanford Univ. School of Medicine, Palo Alto, Calif. (Session XXVI)

A $^{99\text{m}}\text{Tc}$ -toluidine blue 0 colloid has been synthesized as follows: (1) reduction of $^{99\text{m}}\text{Tc(VII)}$ with ascorbic acid in the presence of thiocyanate to $^{99\text{m}}\text{Tc(V)}$ -thiocyanate complex; (2) molecular aggregation of toluidine blue 0 (TBO) bound to $^{99\text{m}}\text{Tc(V)}$ -thiocyanate complex at $\text{pH} > 3.8$; and (3) thermal degradation of the aggregates in the presence of gelatin or methyl cellulose. The formation of the colloid is rapid and complete. The product can be identified by paper radiochromatography in 85% methanol, and its colloidal character verified by microscopy and filtration through Millipore filters.

The tissue distribution of the $^{99\text{m}}\text{Tc}$ -TBO colloid was performed in the rat. When the colloid was injected intravenously, most of it was rapidly cleared from the blood with a half-time less than 5 min. On sacrifice at 15 min after injection, the recovery of

radioactivity was 70–80% in the liver and less than 5% in the spleen. No significant radioactivity was noted in the stomach, salivary gland and intestine.

Scintiphotographic studies using an Anger-type scintillation camera fitted with a multichannel collimator were performed in rats. The scintiphotographic findings confirmed those of the distribution studies. After intravenous injection of approximately 200 μC /kg of the $^{99\text{m}}\text{Tc}$ -TBO colloid, the liver was clearly visualized. There were no toxic effects observed. The simplicity of preparing the colloid, the physiologic behavior of the compound and the favorable physical characteristics of $^{99\text{m}}\text{Tc}$ indicate potential clinical usefulness of this agent for hepatic visualization by scintillography.

Prospective Study of the Clinical Evaluation of Solitary Thyroid Nodules BY ROBERT L. YOUNG AND EDWIN M. BRADLEY, Wilford Hall USAF Hospital, Lackland Air Force Base, Texas. (Session XII)

The malignant thyroid nodule can not be consistently identified by any single laboratory or clinical parameter. For the past three years we have carried out a prospective evaluation of all out patients with solitary thyroid nodules seen by the radioisotope, endocrine and general surgery services. Clinical impression and scans were obtained in all patients. All patients whose nodule did not disappear with thyroid therapy were operated.

Twelve percent of the patients who received thyroid responded with disappearance of the nodule. The incidence of malignancy in the 97 patients in whom operations were performed was 12%. In an additional 6% of patients whose nodule was benign, there was an "incidental" finding of a microscopic focus of carcinoma in otherwise normal thyroid tissue. Seventy-four percent of the scans were "cold" in the area of the nodule. The incidence of cold nodules in patients with pathologically malignant nodules was the same as in those with benign disease. Twenty-two patients had normal scans and only one of these had a carcinoma.

Eighteen patients were operated without considering thyroid suppression because of the clinical impression that the nodule was malignant; seven had malignant nodules. The incidence of malignancy in males was 27%; in females 7%.

Several points from our prospective study deserve emphasis. There was a 6% incidence of "incidental"

carcinoma. We do not feel these microscopic abnormalities can be assumed to have the same prognostic significance as a malignant nodule. The reasons for this will be discussed. A normal scan indicated benignity rather than cold areas indicating malignancy. We have formulated an approach to solitary thyroid nodules using response to thyroid, appearance of scan, sex and clinical impression. If we had used this approach in our series, approximately 50% of the patients would have been operated upon with one false-negative diagnosis. The justification for use of such a formulation in larger series will be discussed.

Properties and Uses of Radioactive Albumin Microspheres, BY ILSE ZOLLE, BUCK A. RHODES, JULIA W. BUCHANAN AND HENRY N. WAGNER, JR., The Johns Hopkins Medical Institutions, Baltimore, Md. (Session XXIII)

Radioactive particles have been widely used for lung scanning. Their use in the quantification of right-to-left circulation shunts and in studies of the systemic circulation in man have been limited because previous preparations have been either nonuniform in size and shape or nonmetabolizable. We have prepared radioactive microspheres with a narrow range of particle diameters (20–44 microns) that are metabolized within several hours of injection. The microspheres are made from inorganic precipitates encapsulated in human serum albumin. These microspheres can be labeled with almost any radionuclide. We have prepared and studied microspheres labeled with the short-lived radionuclides $^{113\text{m}}\text{In}$ and ^{125}I . Of particular importance is our ability to label the particles with $^{113\text{m}}\text{In}$ after they have been prepared. Depending on the conditions of preparation, the mean particle diameter can be varied from 5 up to 50 microns and the rate of degradation from 0.7 to 55 days. Toxicity studies in animals have indicated that the microspheres are nontoxic in the doses employed and are not antigenic. Studies are in progress to determine the safety and efficacy of these particles for the quantitative measurement of the distribution of cardiac output and the degree of systemic shunting in man. These measurements depend on external counting systems which can be calibrated for quantitative organ uptake. The calibration can be achieved by using other $^{113\text{m}}\text{In}$ compounds which are known to localize completely in specific regions such as the liver, lung and kidneys.