THURSDAY, JUNE 17, 1965

SCANNING: INSTRUMENTATION

Chairman, C. CRAIG HARRIS

Area A

A-1-a *"Quantitative Evaluation of Scintillation Detector Response to Scattered Gamma Rays."* ROBERT N. BECK AND MARK W. SCHUH, (Argonne Cancer Research Hospital[1], The University of Chicago, Chicago, Illinois)

The total response of a scintillation detector to a volume distribution of radioactivity consists of the sum of responses to those gamma rays which enter the collimator "properly", those which enter after penetrating the collimator or shielding material, and those which enter as scattered radiation. While the first two components have been estimated fairly accurately, the scatter component has not been evaluated quantitatively for the source configuration met in radioisotope scanning.

To evaluate this component, it is necessary to know the shape of the scatter spectrum within the photopeak. This can be determined by properly smearing the Klein-Nishina equation for the energy spectrum of scattered photons. The IBM 7094 has been programmed to do this and to compute the scatter fraction as a function of base line setting.

Although pulse height analyzers are ordinarily used to reduce the deleterious effects of scattered radiation, the problem of selecting a base line setting which achieves an "optimum" compromise between the recording of scattered and unscattered radiation has not been adequately discussed. By treating scattered radiation as "noise" or "background", an optimum base line setting can be found which minimizes the statistical error in measuring the number of pulses due to unscattered gammas. This procedure has been carried out for several gamma emitters in a brain phantom for the energy range commonly used in brain scanning, .140 to .510 mev. The practical implications for brain scanning are discussed.

A-1-b *"Section Scanning with a Large, Solid Angle Converging Collimator."* BENEDICT CASSEN, (UCLA Medical School, Los Angeles, California)

The large, solid angle 2,200 hole spherical cap converging collimator, experimentally developed at UCLA, has a high sensitivity enabling fast scanning and a relatively shallow depth of focus. The theory of the depth of focus has been improved and further experimentally verified. The shallow depth of focus enables fast section scans to be made at a succession of levels which are focused on by varying the vertical height of the detecting system. Excellent sections have been obtained with the use of ^{99m}technetium. Experiences will be presented, including the use of ^{99m}technetium section scans for determining approximate stereotaxic coordinates of brain tumors.

A-1-c *"Quantitative Evaluation and Intercomparison of Detectors in Medical Radioisotope Scanning."* P. J. KENNY, (Sloan-Kettering Institute for Cancer Research, New York, New York)

Several methods have been proposed for evaluating and intercomparing the performance of detectors used in medical radioisotope scanning. These include use of a standard scanning phantom and definitions of a "figure of merit".

This report describes a method which has been developed to evaluate and intercompare performance, quantitatively, on the basis of a detector's isoresponse function and sensitivity, for a particular energy gamma-ray.

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[1]Operated by the University of Chicago for the United States Atomic Energy Commission.

A simple technique has been devised, utilizing extended plane sources, which allows accurate experimental determination and integration of a detector's isoresponse function throughout a tissue equivalent volume of arbitrary dimensions.

On the basis of these determinations, graphs have been prepared which give, directly, the absolute change in counting rate for various detector-collimator combinations as a function of the parameters:

(i) Specific activity values in the target and nontarget volumes
(ii) Dimensions of these volumes
(iii) Position of the target volume in the isoresponse function plot.

The absolute change in counting rate between the target and nontarget positions gives the counting time or scan speed necessary to detect differences in tracer concentration to any specified statistical confidence level. Conversely, for specified counting times or scan speeds, the graphs indicate the confidence level associated with any apparent difference between the target and nontarget volumes. The question of which detector-collimator combination is best for any particular scanning application described by the above parameters is thus decided solely from a basic experimental determination.

A-1-d *"Comparison of Isotopes for Scanning."* C. M. E. MATTHEWS, (Hammersmith Hospital, London, W.12, England)

A method for quantitative comparison of the relative merits of different isotopes is presented, considering particularly brain tumour localization. The method is based on a calculation of the minimum tumour size detectable with a given statistical probability, for the same rad dose and time available for the scan for each isotope. The calculation involves two quantities, A and B. A depends on the biological and physical properties of the isotope, and B depends on the physical properties of the isotope and the properties of the counting system. For comparing different positron emitters, for example, B is constant and A may be used as an isotope figure of merit. On the other hand, B may be used as an overall figure of merit for the counting system, and one factor in the expression for B which depends only on the collimator properties may be used for comparing collimators. A depends on relative tumour and normal tissue concentrations of isotope, as well as on other factors. These relative concentrations often do not vary for different isotopes, since many radioactive substances used in scanning, when injected intravenously, rapidly equilibrate with extracellular spaces. A can usually be calculated, and B can easily be measured with a phantom.

Values of A and B for different isotope will be given and the factors involved will be discussed. In this way the relative merits of some of the many new isotopes recently used or proposed for scanning will be assessed. It will be shown that for brain tumours smaller than about 2 cm the number of counts obtained using conventional scanning methods is too small for detection with statistical significance, even if an ideal collimator could be made. Collimator resolution therefore should not be less than this, otherwise count rate will be reduced unnecessarily.

A-1-e *"Contrast-enhancement of Scanning Procedures by High-speed Computer."* W. NEWLON TAUXE AND DONALD W. CHAAPEL, (Mayo Clinic and IBM Corporation, Rochester, Minnesota)

Advances in contrast-enhancement technics have played a crucial role in making isotope-scanning the important, versatile clinical diagnostic procedure it now is. Since the often desirable multiple readouts at various contrast settings frequently involve time-consuming rescanning, or replaying of tapes, we have sought to obtain such information by means of a high-speed computer.

Output from the pulse-height analyzer of a scanner is taped onto one channel of Ampex FM tape, and scan-margin registration points are fed onto another channel. The taped information is then fed into averaging and digitizing circuitry in a 3-digit analogue-to-digital converter, then to an IBM 7090 for analysis, a process which requires aproximately 1 minute. This analysis includes computations of data so that they may be presented in a number of ways in

various formats: at different contrast levels, contour plots, smoothed plots, differentiated plots, and so on. The scans are read out by means of a high-speed printer (600 lines per minute) or by an x-y plotter. Thus, an "on line" operation is capable of producing an enormous number of scans during the time usually required for the development of a single film.

Details of digitizing technics and examples of various scans performed in this and in the usual manner will be presented.

A-1-f *"Recent Developments in Digital Computer Analysis and Display of the Radioisotope Scan."* DONALD W. BROWN, (University of Colorado Medical Center, Denver, Colorado)

In order to bring greater objectivity to the interpretation of the radioisotope scan, methods of processing the data available from the scanner, using a digital computer, are under development. Pulses from the pulse height analyzer are fed into an events-per-unit-time counter and this output is punched onto tape which in turn is processed by a digital computer. After statistical testing and using background erase and contrast enhancement, pictures of the organ under study are automatically printed out by the computer's printer and drawn on an x-y plotter. In some instances this affords strikingly clear demonstration of lesions which could only be suspected by routine methods. In other instances, false-positive results have been eliminated, statistical testing revealing the suspect variation to be insignificant. One of the chief advantages of the computed scan is that it circumvents the frequently occurring technical errors in selecting proper settings for the large number of dials on present commercial scanners, since all of these electronic stages are bypassed. Another advantage is that counts per unit time can be obtained over any desired localized area of the scan, affording information previously not obtainable such as differential kidney concentration of an isotope or percent of dose in a thyroid nodule. It is also possible to enhance strongly the density of certain organs by subtracting one scan from another, for instance the colloid ^{198}Au scan from the ^{75}Se-selenomethionine scan in visualizing the pancreas.

SESSION A-2

Chairman, JOHN G. MCAFEE

Area B

A-2-a *"Information Capacity of Scintiscans."*[1] E. C. GREGG, (Western Reserve University, Cleveland, Ohio)

Application of information theory to scintiscanning has resulted in generalized expressions for the information capacity in bits per unit area for the process of scanning a two dimensional random distribution of S events per unit area plus superposed noise N per unit area with an aperture of area A. Computer solutions show a decided peak in the capacity as a function of aperture area and the position of the peak depends critically on source strength, scan time, noise level, etc.

Calculations show peak capacities of 4 bits per sq inch for straight bores, 7 bits per sq inch for focussing, 22 bits per sq inch for honeycombs, and 43 bits per sq inch for pinhole collimators, all with the same conditions of observation. In all cases, the aperture areas for peak capacities are those which experience has dictated to be optimum. Further, for observations in depth, the straight bore produces the same capacity on the average as when observing a plane, while that for the focussing collimator drops to 1 bit per sq inch. This is due to the large weighting effect of the out-of-focus layers. The above values are to be compared with $10^6/cm^2$ for film, $4000/cm^2$ for a radiograph, $6 \times 10^5/cm^2$ of apparent image for the eye and 0.6×10^6 bits for one television frame.

A-2-b *"Total Body Retention and Localization Scanning with Computer Controlled Output."* J. S. LAUGHLIN, D. A. WEBER, P. J. KENNY AND F. RITTER, (Sloan-Kettering Institute for Cancer Research, New York, New York)

[1]Supported by USPHS Research Grant No. AM-06760.

Search scans for lesions and measurements of total body retention are now done in a single scanning operation. This has been made possible by the construction of a punched paper tape storage and reader system, and its incorporation in the High Energy Gamma Ray Scanning System. The tape drives a digital typewriter and is coded for analysis on a CDC-160A computer. This digital storage and display capacity has allowed the use of two colinearly positioned detectors moving continuously above and below the patient to provide simultaneously the complete search scan as well as the total retention determination. Analog display, film or isometric, may be generated simultaneously with the digital scan. The data are continuously collected and punched onto tape in adjustable preselected intervals. The interval size determines the fineness or coarseness of the plotted scan. A longitudinal profile and any desired numbers of transverse profiles are also provided. These profiles are automatically plotted under computer control with the standard deviation indicated for each data interval. The combination of longitudinal and transverse profiles has facilitated the identification of areas of unusual uptake of the tracer and when taken sequentially, has permitted measurement of redistribution throughout the body. Automatic normalization of the profile plots to the same height simplifies quick inspection. The absolute values associated with each profile are printed by the computer.

This method has been applied in scanning studies with radioactive isotopes of calcium, strontium, selenium, iodine, zinc, etc. Examples of the varied digital and analog displays as well as total activity profiles obtained with this computer-linked scanning system will be presented.

THURSDAY, JUNE 17, 1965
SESSION: THYROID
Chairman, LINDON SEED
Area B

B-1-a *"The Functinal Significance of ^{75}Se Selenomethionine Uptake by the Thyroid Gland."*[1] E. JAMES POTCHEN, HASSAN K. AWWAD, S. JAMES ADELSTEIN AND JAMES B. DEALY, JR. (Harvard Medical School and Peter Bent Brigham Hospital, Boston, Massachusetts)

Chemical suppression by thyroxine of the thyroid uptake of the ^{75}Se selenomethionine has been a useful adjunct to parathyroid scintiscanning, by diminishing regional radioactive interference. It becomes apparent that this unique gamma emitting amino acid analog has as much potential to assess thyroid protein anabolism as it does to evaluate parathyroid metabolism.

The quantitative thyroid uptake of the isotope has been studied in the rat. Experimental observations have demonstrated that the thryoid accreation of ^{75}Se selenomethionine may be taken as an index of the capacity of the thyroid to synthesize protein. The investigation of these mechanisms and their potential application as a clinical measure of thyroid protein anabolism will be discussed.

B-1-b *"Comparison between Uptake of ^{131}I-Triiodothyronine by Erythrocytes and Sephadex Method."* A. CUARON AND M. L. RANGEL, (Comisión Nacional de Energia Nuclear and Hospital General, Mexico)

Thyroid function was estimated by the uptake of ^{131}I-triiodothyronine (T-3) by erythrocytes (RBC) and by gel filtration chromatography in Sephadex of labeled T-3 in serum in 400 subjects (180 normal, 114 thyrotoxic and 106 hypothyroid) chosen at random. Total thyroxine-binding globulin (TBG) capacity and protein-bound iodine (PBI) in serum were also estimated in 89 subjects (31 normal, 35 thyrotoxic and 23 hypothyroid). Gel filtration chromatography was shown to be more accurate (95.8%) than the "in vitro" uptake of T-3 by RBC (89.8%) in the study of thyroid function, and both methods were more reliable in diagnosing hypothyroidism (95.3% and 89.6%, respectively) than thyrotoxicosis (92.1% and 82.4%, respectively).

[1]This project is supported by Atomic Energy Commission Contract NYO-3442-4.

A great correlation was found between both procedures, the uptake of T-3 by RBC being inversely proportional to Sephadex chromatography. The uptake of T-3 by RBC increases and the value for the Sephadex method decreases as the concentration of thyroxine (T-4) in serum is artificially raised, reaching an asymptotic value when saturation of TBG is achieved. A possible relation was found between thyroid function, the asymptotic value obtained when TBG is saturated and the concentration of T-4 at which this value is achieved. Total TBG capacities were not significantly different in normal and thyrotoxic patients, but were significantly higher in hypothyroid subjects. It seems that both methods are dependent on total TBG capacity and on the concentration of thyroid hormones in serum, and consequently on free TBG capacity, and that variations in these are responsible for some negative results obtained by either procedure. It is concluded that both methods could be regarded as a measure of free TBG capacity which depends on total TBG capacity and PBI, and that the binding of T-3 by serum proteins is more accurately studied by the gel filtration chromatography procedure than by the uptake of T-3 by erythrocytes in the diagnosis of thyroid function.

B-1-c *"Use of Radiophosphorus and Radioiodine in the Investigation of Thyroid Nodules."* W. J. K. SIMPSON, (Toronto, Canada)

Clinically solitary thyroid nodules pose a difficult diagnostic problem, for the majority are benign, yet malignancy can be excluded only by histological examination. Various authors have shown that a malignant nodule rarely concentrates radioiodine to any significant degree; however, many nonfunctional nodules are benign. In 1960, Ackerman reported that malignant nodules concentrated radiophosphorus excessively, and therefore a combined ^{131}I -^{32}P study of solitary thyroid nodules was undertaken.

In the past two years, 70 patients have been studied. Twenty-four hours after the intravenous injection of 300 μc ^{32}P, counts over the nodule and over normal thyroid tissue are recorded. The patient is then given 20 - 50 μc ^{131}I orally, and a thyroid uptake and scan are carried out the next day.

Only 22 of the 70 patients have undergone surgery and therefore have a definitive diagnosis. Five of these patients had carcinoma; in only one was the ^{32}P uptake significantly increased (nodule: normal thyroid = 1:1.32). Six had benign adenomas; two of these had an increased ^{32}P uptake. None of the 10 patients with nodular goiter had an increased ^{32}P uptake, nor did the one patient with a thyroglossal duct cyst.

In two other patients, the nodule disappeared completely—and the ^{32}P uptake was increased in one of these patients.

B-1-d *"Autoradiographic Visualization of the Thyroid."* H. R. HAYMOND, P. V. HAIG AND W. R. KIMBALL, Los Angeles County Hospital, University of Southern California and Loma Linda University, Los Angeles, California)

Autoradiographic visualization of a thyroid gland *in vivo* is possible with the use of conventional x-ray grids for collimation of the soft radiation from ^{125}I. The results of this study have application for other nonscanning methods for visualization of radioactive organs, such as a scintillation camera or techniques based on the principle of x-ray intensification.

An autoradiographic image of a thryoid phantom, with excellent resolution of a "cold nodule", 0.5 cm in diameter, can be obtained by using conventional x-ray grids (6:1, 60 lines per inch) crossed perpendicularly to collimate the gamma and x-radiation of ^{125}I. However, a long exposure time is required. With only one grid, the exposure time is greatly decreased, but the image is smeared in the direction parallel to the grid lines if the grid remains stationary during exposure. When a single grid is rotated during the exposure, the edges all around the image are somewhat indefinite, but a good image, in which the 0.5 cm. "cold nodule" is discernible, can be obtained when the distance between the film and the radioactive solution is approximately that obtainable *in vivo*. The exposure time depends on the film and intensifying screens used as well as the grids. The results of our investigation of these factors are similar to those reported by others (Clayton *et al*: J. Nuc. Med., 5:310, April 1964). A satisfactory image of a thyroid phantom has been obtained with the following exposure factors: single

grid, 6:1, 60 lines per inch, rotating during exposure; Kodak Royal Blue film; bakelite front cassette with two Radelin TF intensifying screens; phantom containing 20 μc/ml ^{125}I; 2.1 cm between radioactive solution and film; exposure time 10 mins. The use of Polaroid TLX film with a single DuPont Fluorazure intensifying screen required approximately the same exposure time.

A discernible image of a human thyroid *in vivo* has been obtained with an exposure time of one hour and will be presented. Possible improvements in the technique will be discussed.

B-1-e *"^{131}I and ^{125}I Double-labeled Autoradiographs in Studies of Nodular Goiter."* **J. Martin Miller and Bernice Kawas, (Henry Ford Hospital, Detroit, Michigan)**

The combined use of ^{131}I and ^{125}I has facilitated scintigram studies of the thyroid in various states of activity. Correlation of such scintigrams with the related histology has been possible to a limited degree in small goiters, and virtually not at all in large ones. Therefore, we have attempted the identification of autonomous, suppressed, and inactive thyroid tissue by means of autoradiographs labeled with both ^{131}I and ^{125}I.

The low energy conversion and Auger electrons from ^{125}I make it superior to ^{131}I both in resolution and in efficiency of darkening Kodak Lt. A.R. 10 stripping film. The seven fold differences in half lives makes possible processing duplicate autoradiographs at a short early interval and a long late interval with partial but distinct separation of the activities of the two isotopes, *e.g.* an autoradiograph exposed 72 hours from time 0 would have 4 $\times$ the ^{131}I effect and 1/5 the ^{125}I effect of one exposed for 21 days from time 32 days.

10 patients with autonomous goiter have been studied using this technique. After prior determination of both TSH and suppression uptakes and scintigrams, a labeling dose of ^{125}I was administered 24 hours after TSH and/or 24 hours before suppression. The latter was accomplished by 7 days of liothyronine feeding, and following this, ^{131}I was administered 24 hours prior to surgery. Actual dose calculation depended on the uptake, anticipated volume of distribution, and film blackening efficiency of each isotope. The film reflecting primarily the distribution of ^{131}I was exposed 3-10 days from time 0. That for ^{125}I was exposed 21-50 days from time 32 days. Determination of correct exposure time was aided by duplicate preparations with the much more sensitive Kodak Radiatized Dental Film. The results of such studies in the identification of the TSH responsive tissue in toxic autonomous goiter and the relative function of certain autonomous nodules will be illustrated and discussed.

B-1-f *"The Influence of Antithyroid Drugs upon Immediate Rate Uptake in Thyrotoxicosis."* **S. Taplits, (Jewish Hospital, Cincinnati, Ohio)**

The thyroid trapping mechanism is affected by antithyroid drugs, particularly Tapazole and Propylthiouracil. This established fact is demonstrated quite well by the immediate rate uptake which is not affected by the drugs, as compared to the 24 hour uptake which is affected appreciably. It is therefore evident that the rate uptake measures a parameter, viz: the avidity of the thyroid which differs from its trapping or storage capacity. The method described for the measurement of rate uptake will measure this function quantatively and accurately. It is dependent upon the following principles: (1) any gland or organ that selectively or specifically concentrates or excretes will do so by constant ratio or percentage; (2) the rate of accumulation of counts is proportional to the dose; (3) if the dose is made equal to unity or 100 per cent and the recording ratio is constant, then the slope of the tracing varies with the function of the organ or gland.

SESSION: KIDNEY

Chairman, James C. Coberly

Area B

B-2-a *"Experiences with Gamma-Emitting Inulin and Pah Substitutes in Man."* **Eugene M. Sigman, Monte Blau, Charles Elwood, (Buffalo General Hospital and Roswell Park Memorial Institute, New York)**

Although the renal clearance of inulin as the measure of glomerular filtration and the renal clearance of para-amino hippuric acid (PAH) as the measure of effective renal plasma flow afford the most precise and sensitive tests of renal function, they are used infrequently because of the inherent difficulties encountered in their performance. The chemical determination of inulin in urine and blood, necessary for the clearance calculation, is extremely time-consuming, tedious, and interferred with by the presence of other substances such as high plasma concentrations of glucose. The chemical determinations of PAH, although not as difficult as inulin, may also be interferred with by the presence of other substances such as sulfonamides.

In order to overcome these particular obstacles, a group of substances have been labeled with gamma-emitting isotopes and investigated as substitutes for inulin and PAH. This paper deals with our own experiences with several of these labeled compounds in man. These include:

A. *Gamma-Emitting Inulin Substitutes*
   1. **Contrast media**
      a. Meglumine diatrizoate (Renografin ^{131}I)
      b. Sodium iothalamate (Conray-400 ^{131}I)
   2. **Inulin derivatives**—^{131}I-labeled Allyl inulin

B. *Gamma-Emitting PAH Substitutes*
   1. Iodopyrace (Diodrast) ^{131}I or ^{125}I
   2. Na–ortho-iodohippurate (Hippuran) ^{131}I or ^{125}I

The clearance of the gamma-emitting inulin substitutes were compared to those of simultaneously determined inulin. All the inulin substitutes appear to be freely filtered at the glomerulus. The discrepancy that might occur between the clearances of these labeled compounds and those of simultaneously determined inulin is related to unbound ^{131}I.

The clearances of PAH substitutes and PAH were determined simultaneously. Hippuran ^{131}I was found to be an inadequate PAH substitute while Diodrast ^{131}I, when used at the appropriate specific activity, had the same clearance as simultaneously determined PAH.

B-2-b *"Correct Interpretation of Renograms and Scans in Unilateral Kidney Displacement."*[1] L. A. Swanson, E. K. Dore, D. E. Johnson and G. V. Taplin, (University of California at Los Angeles and the Los Angeles County Harbor General Hospital)

Exact kidney localization is mandatory for accurate renogram analysis and misplacement of the renal detectors is well recognized as a common technical cause for false interpretation of this procedure. However, even with proper positioning of the detectors, anterior displacement of one kidney may lead to erroneous interpretation not only of the renogram but also of the renal scan, particularly if the latter is performed with low energy ^{197}Hg test material. The posterior scan image of an anteriorly displaced *normal* kidney may be absent or only faintly registered and the renogram contour may have a flattened second segment and low amplitude. These findings would ordinarily be interpreted falsely to indicate unilateral impairment of blood flow or function relative to the opposite kidney.

Correct interpretation depends on demonstrating anterior displacement of the apparently abnormal kidney. This is most easily accomplished by measuring the levels of kidney radioactivity (^{197}Hg localizing dose) *anteriorly and posteriorly*. Further proof is readily obtained by scanning the kidney laterally and by repeating the renogram in the anterior position. Illustrative case studies will be presented to demonstrate the effects

[1]These studies were supported by Contract AT(04-1)-GEN-12 between the U.S. Atomic Energy Commission and the University of California at Los Angeles.

A-2-c "A *"Rescanner" With Photographic Color Readout.*" C. C. HARRIS, M. M. SATTERFIELD, HARRY E. KIMBLE AND GUIO UCHIYAMA[3], (Oak Ridge National Laboratory[1] and Oak Ridge Institute of Nuclear Studies[2])

The use of the ORNL "rescanner," a recording densitometer, in the analysis of scan records has been described. In the original device, the output of the light sensor was converted to an output pulse rate related to density of the record being analyzed. These output pulses were then used to produce a "rescan" record from ordinary scanner recording systems.

A new rescanner has been built, with a color photographic output somewhat akin to that of Adams and Jaffe. The output of the solar cell light sensor—inversely proportional to film opacity—appears as angular displacement of a wheel of color filters. A stationary Polacolor camera views a steady light through whatever filter is presented by the wheel.

The color wheel is driven by a dc servomotor; the solid-state servosystem uses a novel optical position-feedback method that reduces servomotor torque requirements.

The entire system is contained in a box about six inches on each side, and together with a small light source behind the record being analyzed, is moved about within a darkened enclosure.

Preliminary results indicate that this inexpensive system is stable and fast. It produces color rescans without the time-lags inherent in the use of a count-rate-meter signal to change colors.

A steady light for the color-recording source was used when a synchronous flashing light failed to produce enough light. With a suitable pulsed light source such as a cathode ray tube, the pulse-rate output of the original version can be used for additional contrast expansion.

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[1]Operated by Union Carbide Corporation for the U. S. Atomic Energy Commission.

[2]Under contract to the U. S. Atomic Energy Commission.

[3]Fellow in Radiological Research of the James Picker Foundation.

A-2-d *"The Three Dimensional Mapping and Display of Radioisotope Distributions."* P. V. HARPER, R. N. BECK, D. E. CHARLESTON, B. BRUNSDEN AND K. A. LATHROP, (Argonne Cancer Research Hospital,[1] Chicago, Illinois)

It appears feasible to consider seriously the full three dimensional mapping of radioisotope distributions in a variety of clinical situations in view of the increased sensitivty of the camera devices and the increased number of countable photons available from short lived emitters such as ^{99m}Tc. While an endless variety of approaches to this problem exist, we have chosen to explore the extension of Kuhl's transverse section scanning mode using the Nuclear-Chicago Anger camera. The photographic records of pictures taken at regular intervals around the subject constitute a most economical information storage. The reconstruction of the three dimensional image is accomplished by projection of parallel light through the photographic scan records so that the lines from each picture converge into an image space at the same angles from which the original gamma rays emerged from the patient. Where a number of these linear image elements intersect they reinforce forming the image exactly as in Kuhl's two dimensional display. To visualize fully the image in three dimensions would probably introduce too much confusing detail. However, a sheet of scattering or fluorescent material introduced into the image space would visualize any plane in any orientation with complete flexibility. The design of the optical systems presents a great variety of possibilities. The present plan is to record the information on 16 mm film, form this into a loop surrounding a .3 mm mercury arc point source, parallelize the transmitted light by using the zone of a deep paraboloid mirror where the slope is 45° and finally to reflect with plane mirrors the parallel rays into the image space at the proper angle. Feasibility studies show clearly that photographic records such as described above can indeed be projected with parallel light without severe degradation of the image from diffraction effects.

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[1]Operated by the University of Chicago for the Atomic Energy Commission

A-2-e *"Transmission Scanning for Improved Orientation of the Emission Scan."* DAVID E. KUHL AND JOHN HALE, (School of Medicine and the Hospital of the University of Pennsylvania and the William H. Donner Center for Radiology, Philadelphia, Penn.)

Accurate interpretation of a radionuclide distribution in the body requires orientation of the spatial relationships of emission scan data and the patient anatomy. Usually, data on the scan record is keyed to the patient's anatomy either by using reference marks or by superimposing a roentgenogram. These methods may introduce inaccuracies due to geometric distortions. Also, if the patient moves during the scan, the counting data and the anatomic reference may no longer correspond.

We have explored transmission scanning as a means of improving this orientation. During a conventional emission scan, a small capsule containing about 100 mc of ^{241}Am under the patient identically follows the motion of the detector. The 59.6 kev photons from this source are collimated and directed through the patient to the detector. The variation of count rate of this beam as the scan progresses is governed by its attenuation by anatomic structures. Pulse-height analysis is used to separate the emission and transmission counting data which are then recorded separately. The transmission scan image is similar to a roentgenogram of the scanned part and can be oriented to the emission scan with no geometric distortion. Any patient movement during the study is apparent in both records.

The method has been successfully applied to pertechnetate ^{99m}Tc emission brain scanning and cholografin ^{131}I emission heart scanning.

A-2-f *"Area Recording and Data Blending in Radioisotope Scanning."* JAMES H. CHRISTIE, WILLIAM J. MACINTYRE, CARL J. FERBER AND RICHARD L. KING, (Cleveland, Ohio)

In most conventional recording systems of photoscanning, the area occupied by each increment of datum display is considerably smaller spatially than the full field of view of the detector itself. In the present system, areas up to one and three-eights inch in diameter are exposed on the film of the photoscan. The intensity of exposure of each area is quasi-Gaussian in character with the highest intensity in the center of the circle graduating down to the lowest intensity at the perimeter.

In addition, the increments of line spacing are small in comparison to the circle diameter so that total exposure may be due to 53 passages of the light beam at increments of 0.19 inches, recorded at speeds up to two hundred inches per minute. The quasi-Gaussian distribution has been obtained primarily by a variable distribution of a large number of small dots, so that one square inch of film exposure may exhibit a total of seventy million dots at a counting rate of six thousand counts per minute. For this reason a wide range relationship in film exposure may be attained, since increased intensity of film exposure is due to both the additive effect of increased dot number as well as the logarithmic effect of dot superimposition.

Clinical examples of liver, thyroid, and brain scans obtained by this method will be shown as well as a discussion of the interrelated factors of count rate, area diameter, distribution of holes, and line increments.

SCANNING: BRAIN

Chairman, PAUL V. HARPER

Area A

A-3-a *"Analysis of 100 Consecutive Abnormal Brain Scans using ^{99m} Tc as Pertechnetate."* JAMES L. QUINN III, WILLIAM HAUSER, AND IVAN CIRIC, (Northwestern University School of Medicine and the Chicago Wesley Memorial Hospital)

^{99m}Tc, used in the chemical form pertechnetate, is a superior radionuclide in brain scanning because of: (1) the higher count rates available and therefore the possibility of faster scan-

ning speeds; (2) a more ideal scanning photon and therefore lighter collimators with thinner septae affording even greater counting rates and yet improving resolution; and (3) reduced patient radiation. The target-nontarget ratios in various intracranial disease states is similar to that obtained from other available brain scanning agents, therefore, the accuracy of ^{99m}Tc brain scans does not appear to be different from the accuracy of ^{197}Hg or ^{203}Hg brain scans.

A short film on preparing ^{99m}Tc for brain scaning ("THE MILKY WAY") will be shown.

One hundred consecutive positive brain scans will be tabulated and discussed. The accuracy of ^{99m}Tc in detecting and depicting intracranial neoplasia and the usefulness of the brain scan in following "stroke" patients will be presented.

A-3-b *"Transverse Section and Rectilinear Brain Scanning Results Using Pertechnetate ^{99m}Tc."* DAVID E. KUHL, (School of Medicine and the Hospital of the University of Pennsylvania and the William H. Donner Center for Radiology, Philadelphia, Pennsylvania)

Over 500 patients were studied using 200 μc/kg doses of pertechnetate ^{99m}Tc for high count rate brain scanning with either of two scanning techniques. The first method produced rectilinear views using a commercial scanner with coarse colimation and unmodified photorecording. Four projections of the brain were obtained in one hour of scanning time. The second method used a research scanner with finer collimation to produce both rectilinear and transverse section projections and included more advanced data processing equipment. Four rectilinear views and a cross-section image of the brain were completed in one hour of scanning time.

With both methods, the brain scan images were excellent. However, false-positives occurred when normal radioactive vasculature was misinterpreted. The transverse section images improved the description of lesion extent and aided in the detection of low lying lesions that were otherwise obscured in the rectilinear views by overlying radioactive muscle.

A-3-c *"Comparison of ^{99m}Tc and ^{203}Hg Neohyrin Brain Scanning."* PHILIP P. RUETZ AND ROBERT C. MEADE, (Wood Veterans Hospital and Marquette University, Milwaukee, Wisconsin)

Two-hundred and fifty ^{99m}Tc brain scans were performed. Fifty of these were also studied with ^{203}Hg Neohydrin for comparative purposes. Seventeen of the fifty were abnormal using both agents. A breakdown of these lesions as well as an inclusive report of all ^{99m}Tc brain scans is presented. One astrocytoma was negative with ^{99m}Tc but positive using ^{203}Hg Neohydrin. A grade IV glioblastoma multiform, originally of equivocal nature with ^{99m}Tc, was definitely positive using ^{203}Hg. A 1 cm pontine-cerebellar-angle meningioma was negative to both agents.

Comparative arterial and air studies in these cases revealed a higher degree of localization using the brain scan. However, the scan was of less value in defining the nature of the lesion. It also is our feeling that ^{203}Hg Neohydrin may offer slightly greater definition of the lesion as representing tumor vs. infarct etc., and therefore aid in prognosticating as well as consideration of surgical approach when indicated, as compared to ^{99m}Tc.

A-3-d *"The Relative Performance of ^{99m}Technetium and ^{203}Mercury Chlormerodrin in Brain Scanning."* R. WILBUR MELBYE, RALPH ADAMS AND HENRY L. JAFFE, (Cedars of Lebanon Hospital, Los Angeles, California)

A series of patients with positive brain scans demonstrated following the use of 700 μc ^{203}mercury chlormerodrin was evaluated after repeat study with 8 mcs ^{99m}technetium pertechnetate. Scans were recorded simultaneously by conventional photoscan and, for quantitative information, in Polaroid color. Most tumors were well demonstrated by both agents. Although ^{99m}technetium brain scans were greatly improved in general counting statistics, the ^{203}mercury scans demonstrated superior selective tumor to normal tissue concentration ratios. Occasional small lesions clearly seen with ^{203}mercury were not clearly demonstrated with

^{99m}technetium. Except for the radiation hazard to the kidneys, the authors believe that ^{203}mercury remains the agent of choice for brain scanning. They urge the necessity for the development of new agents combining the physical properties of ^{99m}technetium with improved uptake in brain lesions.

A-3-e *"The Effect of Stable Mercurial Diuretic on the Renal Retention of ^{203}Hg Chlormerodrin."* JEROLD GREEN, (Strong Memorial Hospital, Rochester, New York)

The postulated ability of previously administered stable mercurial diuretic to reduce renal retention of ^{203}Hg chloromerodrin has been the subject of considerable discussion. A controlled laboratory experiment was performed to test this hypothesis.

Three hundred Sprague-Dawley 300 gm female rats were divided into subgroups and treated in the following ways:

1) ^{203}Hg chlormerodrin IV alone
2) ^{203}Hg chlormerodrin IV + isotonic saline IP
3) ^{203}Hg chlormerodrin IV + meralluride IP 24 hours previously
4) ^{203}Hg chlormerodrin IV + meralluride IP 18 hours previously
5) ^{203}Hg chlormerodrin IV + meralluride IP 8 hours previously
6) ^{203}Hg chlormerodrin IV + meralluride IP 1 hours previously

Commercially available ^{203}Hg chlormerodrin was injected into the saphenous vein, 10 μc in 0.3 ml volume. The meralluride dose was 4 mg Hg/kg body weight (a diuretic dose for the rat) in a volume approximately 0.3 ml. There were no untoward reactions and the animals showed normal weight gain during the period of observation. A preliminary study showed only minimal urine radioactivity six days after injection. It was felt that there was no significant urinary excretion beyond that time and all animals were sacrificed seven days post ^{203}Hg injection. The kidneys were weighed and individually well-counted. Values were expressed in counts per minute per milligram of tissue.

Prior injections of stable meralluride resulted in a three-fold reduction in kidney retention of the ^{203}Hg. There was no essential difference in retention among the rats receiving meralluride at the various times listed above (*e.g.* 24, 18, 8, and 1 hour pre - ^{203}Hg).

There is enough similarity between the biologic fate of mercurial diuretic in rat and man to suggest that these data can be applied clinically. They seem to confirm the previous observation that in humans there is a decrease in ^{203}Hg renal retention by a factor of three after stable meralluride is given the previous day. (Blau, M. and Bender, M., *J. Nucl. Med.* 3:88, 1962). Furthermore, there is evidence that the mercurial diuretic might be given with equal benefit on the same day of ^{203}Hg injection, rather than on the previous day, as generally recommended.

A-3-f *"Evaluation of Conventional Scanning and Anger Camera for Brain Studies."* MERLE K. LOKEN, LUTHER O. WIGDAHL, EDWARD V. STAAB AND J. MICHAEL GILSON, (University of Minnesota Hospitals and Veterans Administration Hospitals, Minneapolis, Minnesota)

More than 1000 brain scans have been performed by us during the past three years. Approximately the first half of these were performed using ^{203}Hg Neohydrin and the latter half with ^{197}Hg Neohydrin. Both agents were used in studies of selected patients. Recently, we have also begun using ^{99m}Tc as pertechnetate and have compared results to those obtained using ^{197}Hg Neohydrin.

Conventional photoscanning (Picker Magnascanner) has been compared to the scintillation camera (Anger) using these agents in both phantom and human studies. Over 100 patients have been studied to date.

A summary of our studies including a consideration of radiation dosage, technical difficulties, equipment settings for optimal results, and a comparison of the scanner and camera will be presented.

B-2-c ***"Sequential Response of T 1/2 of ^{131}I Hippuran Renograms in Renal Homotransplantation."*** ALTON R. SHARPE, JR., E. RICHARD KING, AND DAVID M. HUME.

Sequential determination of the T 1/2 of the ^{131}I Hippuran renogram has been performed on donor and recipient patients selected for renal transplantation. Studies performed on the latter at three, five and seven days and at weekly intervals have established a definite pattern of Hippuran excretion. Excretion measured as the T one-half of the excretory phase has been normal pretransplant. Mean 7.5 minutes with a range of five to fourteen minutes. Posttransplant, excretion times remained elevated during the first week and returned toward normal levels thereafter. Delay in the T one-half occurs early in rejection and correlates well with the appearance of urinary lymphocytes and precedes a rise in serum urea nitrogen and creatinine. Delay in T 1/2 posttransplant has been observed with acute ureteral obstruction and acute tubular necrosis. T 1/2 of the latter two conditions are of a much larger magnitude, however, than that observed in rejection and demonstrates a continued rise in radioactivity. Analysis of 115 studies in fourteen patients reveals that early changes in renal function as a consequence of rejection are first reflected by prolongation of the T 1/2 of the excretory phase of the ^{131}I Hippuran renogram.

B-2-d ***"Effect of Carrier on Simultaneous Hippuran Clearance and Renogram Recording."*** WILLIAM J. MACINTYRE, WALTER H. PRITCHARD, AND DOLORES SCHAPIRO, (Western Reserve University, Cleveland, Ohio)

By means of an external shunt from the left carotid artery to the right jugular vein, a continuous sampling of the concentration of radioactivity in the circulating blood has been accomplished by passing the shunt tubing through a side well scintillation detector. With this method, the clearance of ^{131}I labeled hippuran has been measured at the same time as the appearance and release of the radioactivity over the kidney.

These measurements have been obtained on rabbits with carrier amounts of nonradioactive hippuran varying from 100 μg to 100 mg. The blood clearance curves have been relatively unaffected even with the highest carrier levels. Much greater variations have occurred in the simultaneous renograms, which showed that changes occur not only in the excretory phase of the renogram, but also in the rate of accumulation and the time of peak concentration.

In addition it has been established that accumulation of the hippuran in the kidney is not irreversible but can reappear in large amounts in the circulating blood. Therefore the arteriovenous difference does not necessarily measure the extraction ratio but reflects also a "wash-out" or release of previously cleared material. This study indicates that while the renogram may be empirically analyzed to reflect blood flow, many factors in addition to blood flow may cause variation in all portions of the renogram curve.

B-2-e ***"The Dynamics of Hippuran Dilution and Excretion."*** ROBERT C. MEADE, PHILLIP P. RUETZ AND JAMES D. HORGAN, (Wood Veterans Hospital and Marquette University, Milwaukee, Wisconsin)

The blood clearance of ^{131}I hippuran was studied in both humans and dogs with and without kidney function. Dogs were studied before and immediately following nephrectomy. Pulmonary artery, femoral artery, renal vein and peripheral vein blood samples were compared to external body counting over the kidney, precordium and arm.

Hippuran equilibrates between red cell and plasma water during the first five to ten minutes. A marked A-V difference persists for several minutes and does not appear to be due to diffusion into the lungs. Dilution into total body water spaces is not complete until 60 to 90 minutes after injection. During this time, external body counting over the precordium is a reflection of blood clearance. A large fraction of this clearance is not due to renal extraction but represents dilution into the body water spaces. A one-shot hippuran renal plasma flow determination done from 10 to 30 minutes after injection appears falsely elevated.

Utilizing hippuran dilution data, true renal clearance values can be obtained. The mathematical model of hippuran excretion and the computer simulation of the renogram will be presented.

B-2-f *"Analogue Computer Analysis of Clinical Radioisotope Studies."*[1] RICHARD P. SPENCER, (Yale University School of Medicine, New Haven, Connecticut)

Administration of a radioactive material orally or parenterally is followed by its dilution into several body compartments. Analysis of this distribution, and elucidation of the rate constants, is impractical by hand calculations when more than three compartments are involved. The analogue computer allows the situation to be handled by comparing the observed results with those obtained by means of a realistic model of the biologic situation. The model can be systematically varied until it matches the known data.

A simple case is provided by the radioisotope renogram. Following injection of o-iodohippuric acid-^{131}I, the compound is extracted from the blood stream by the kidneys. Hence, a compartmental analysis must include the blood and two renal compartments (right and left). In addition, there is concentration within the kidneys, represented by separate compartments. Appropriate rate constants can be introduced for exit of the material from the kidneys to urine. A further refinement includes accounting for radioactivity in the abdominal vessels that is picked up by the renal probes. Solutions of the model were obtained by means of the analogue computer. Excellent agreement can be found between the model and radioisotope renograms done in man. The technique is also useful as a teaching aid, as lesions can be simulated easily by changing the rate constants.

Models have also been built for radioactive iodine uptake by the thyroid gland, and gastrointestinal absorption studies. By means of the analogue computer, better insight can be obtained into the physical processes involved, and clinical results can be expressed in quantitative terms.

[1]Suppored by USPHS Research Grants Nos. CA 6519 and HD 00411.

SESSION: WHOLE BODY COUNTING AND RADIOCONTAMINATION

Chairman, WILLIAM H. BLAHD

Area B

B-3-a *"Preliminary Efficiency and Calibration Studies with A New Whole-Body Counter with An Ultralow Background Shield."* W. D. GIBBS, C. C. LUSHBAUGH AND A. C. MORRIS, JR., (Oak Ridge Institute of Nuclear Studies, Oak Ridge, Tennessee, under contract with the United States Atomic Energy Commission)

Preliminary studies have been made on a recently completed, underground, steel-shielded, whole-body counter that is packed in a cement and olivine "cave." Pulses from all detectors are combined into a single spectrum by an automatic pulse-height analyzing and data-recording system. These studies show that, with eight 5 x 4 inch NaI crystals arranged 55 and 65 cm above and below the patient, this counter has a 1.0 to 1.5 per cent theoretic geometry and an actual efficiency for ^{137}Cs gamma counting of 0.76 per cent. This low efficiency is overcome by a favorable signal-to-background counting ratio achieved by the low radioactivity of the shielded environment and is maintained by efficient air filtration and positive pressures in the cave and assay rooms.

So far, about 200 persons have been assayed for 20 min each in the counter. A 200-min background from the previous evening is divided by 10 and automatically subtracted. These studies show that ^{40}K content can be determined with less than $\pm$ 5 per cent standard deviation. Variations in ^{137}Cs body burden associated with dietary habits are easily demonstrable. Studies of thyroid function in children are feasible with less than 0.5 μc of ^{131}I. Fractions of nanocuries of all clinically used gamma emitting radioisotopes are detectable.

B-3-b *"Rotation Technique for Assessing Quantity and Position of Body Radioactivity."* JESSE I. ANDERSON AND DALE G. OLSON, (Health and Safety Division, U. S. Atomic Energy Commission, Idaho Falls, Idaho)

Quantitative measurements are grossly inaccurate using conventional whole-body counting methods for *in vivo* determinations of radionuclides in human subjects because of the heterogenous distribution of the activity and nonuniform configuration of the body. By employing a technique using body rotation, radionuclides can now be determined *in vivo* by a direct gamma-ray spectrometric measurement with minimum effect from anatomical differences or distribution of the activity. The subject is rotated with simultaneous movement of the detector along the body while being counted. An experimental model was employed to show that the counting rate of a point source at different positions within a sample renders counting rates which are much less variable if the sample is rotated during the period of counting. Point sources displaced from the rotation axis form a helical pattern as they cross the field of view of the detector and produce oscillations in counting rate. If the count rate is plotted as a function of detector position and body orientation the general location of the activity in the body can be determined. This technique is especially applicable to whole-body counting because both the body radioactivity and the approximate distribution can be determined simultaneously. In addition to *in vivo* whole-body counting, application of the method is discussed as it applies to biological samples in which large volumes are required to obtain adequate sensitivity. The procedure is applicable to any solid samples containing an unknown distribution of activity. Many factors affecting absolute counting such as the gamma ray energy, the density of the matrix material in which the activity is contained, and the distribution of the activity in the sample are discussed.

Applicability of the method to *in vivo* whole-body counting has been confirmed by counting ^{131}iodine at various locations inside a human subject. Maximum counting rate variation was 260% for an insoluble radioactive source at different positions in the gastro-intestinal tract using the fifty centimeters arc technique compared to a maximum variation of only 14 per cent when the rotation method was used. The counting sensitivity is comparable for the two methods.

B-3-c *"Enhancement of Radiostrontium Excretion in Man."* HERTA SPENCER, ISAAC LEWIN AND JOSEPH SAMACHSON, (Veterans Administration Hospital Hines, Illinois)

Parenterally administered stable strontium and magnesium have been shown to be effective in decreasing the radiostrontium body burden in animals while calcium was ineffective. In the present study, the effects of stable calcium, strontium and magnesium on urinary ^{85}Sr excretion was investigated in man. A single tracer dose of ^{85}Sr as chloride was given intravenously to each patient on the first day of the control and experimental studies, which were performed during the intake of a constant diet on the metabolic research ward. The ^{85}Sr plasma levels, urinary and fecal excretions were determined. Infusions of stable calcium, strontium and magnesium were given in equivalent amounts on three successive days in separate studies and the ^{85}Sr plasma levels and excretions were determined as in the control study. Each of the agents used increased the urinary excretion of ^{85}Sr in man. Infusions of stable strontium were most effective, while infusions of stable calcium and of magnesium were less effective and resulted in a similar enhancement in urinary ^{85}Sr excretion.

B-3-d *"The Turnover of ^{75}Se in Patients Injected with Labeled Selenomethionine."* K. R. COREY, E. O. ROTHSCHILD, D. A. WEBER AND W. P. MYERS, (Sloan-Kettering Institute for Cancer Research, New York, N.Y.)

It has been shown by others that ^{75}Se labeled selenomethionine may be useful for detection of pancreas and parathyroid disease, but little is known about the distribution and turn-

over of the selenium label in man. Some metabolic data which has been obtained on one patient with parathyroid carcinoma and one with suspected parathyroid adenoma, will be reported here.

Total body retention and contact measurement over liver, sternum, knee and midshaft of the tibia were taken with the previously described techniques utilizing the High Energy Gamma Ray (HEG), Scanner. In addition, the radioactivity in a number of 24 hour collections of urines and stool were assayed. One of the patients was studied by external counting over a period of 118 days. At this time, a parathyroid carcinoma was removed by surgery. Samples of the tumor and of muscle were counted. From the total body retention, measurements of ^{75}Se, a biological half-life of 77 days was determined. Assay of blood and urine samples were done for a period of 226 days. A total of 14 repeated digital scans over the necks of the two patients were performed. Representative results will be illustrated for discussion of scanning techniques.

It is hoped that these results, taken together with the results from other laboratories, will allow improved dosimetric calculations, and in general further the diagnostic uses of ^{75}Se selenomethionine.

B-3-e *"Radiocontamination During Pregnancy. I. Dynamics, Placental Transfer and Fetal Uptake of $^{137}Caesium$."* JOSEPH STERNBERG, AND JEAN-MARC LEGARE, (Faculty of Medicine, University of Montreal, Canada)

^{137}Caesium is the major radiocontaminant in some northern geographic regions, chiefly through the specific dietary patterns of the inhabitants. Its metabolic pathway is supposed to be related to that of potassium, but few data are available concerning its hormonal regulation, especially the high level of steroids encountered during pregnancy.

Carrier-free ^{137}Cs was injected intravenously into control, corticoid-treated and pregnant guinea-pigs; the dynamics of the isotope as well as the placental transfer and fetal uptake were studied in function of time, at intervals ranging from 2 minutes to 10 days after injection.

During the first 45 minutes, ^{137}Cs exhibits an exponential two-steps-curve, with a first phase of short ($t/2=1.3$ minutes) half-life and a second phase ($t/2=6.8$ min) representing probably the mixing and irrigation processes; a third phase follows afterwards, with a long half-life ($t/2=4.5$ days), representing the equilibration with the tissues. There is a rapid passage from plasma to red cells: the ratio RBC/plasma increases from 0.1 at 30 minutes to 1.2 at 4 hours, and reaches 4.0 at 10 days. Both plasma and red cells contain the isotope in an entirely dialysable form.

An average of 6 per cent of the injected isotope is excreted into the digestive tube during the first minutes after injection; total excretion averages 15 per cent per day, equally distributed between urine and faeces; mineralo-corticoids do not change the excretion pattern, even with an increased potassium excretion rate.

In the tissues, a first peak is reached at 2 hours after injection, with the highest levels in kidneys, heart, muscle and liver; an equilibrium is attained in 4-5 days, when the muscle and gonads exhibit slightly higher levels of ^{137}Cs than the rest of the tissues.

Pregnancy does not induce an appreciable change of dynamic or tissular distribution; daily excretion rate averages 15.1 per cent, and fetal uptake ranges between 3.3 and 8.2 per cent per fetus, or an average of 20.1 per cent per litter. Transfer rate is proportional to the size of the litter. The per gram rate remains roughly the same (10.6% per 100 gm litter). The fetal distribution pattern is similar to that of the mother, the critical organs being the muscle, followed by liver, kidney and heart. Placental uptake averages 1.7 per cent per fetus, or 3.8 per cent per litter; the isotope remains in the placenta for at least 10 days after contamination.

If extrapolation to humans is permitted, these data imply that contamination with ^{137}Cs during pregnancy is followed by a significant fetal uptake, and also by some irradiation produced through placental tissue and uterine muscular mass.

B-3-f *"Long Term Distribution and Excretion of ^{95m}Technetium in Humans."* W. B. NELP, T. M. BEASLEY, H. E. PALMER, J. W. BEATTLE AND S. H. TUELL, (University of Washington, Seattle and Battelle-Northwest Laboratory, Richland, Washington)

The increasing use of ^{99m}Tc as a tracer in medicine and the large scale separation of beta-emitting ^{99}Tc (T 1/2 2.2 x 10^5 years) from fission product waste requires adequate knowledge of the metabolic properties of technetium. To study the biological behavior of technetium for a suitable period of time, gamma emitting ^{95m}Tc (T 1/2 60 days) was used. ^{95m}Tc was produced by proton bombardment of enriched ^{96}Mo. ^{99}Tc (T 1/2 4.3 days) was also recovered from the irradiated sample. Both isotopes were administered as the pertechnetate ion to normal volunteers. The rate and route of excretion and the body localization of the technetium was studied for one month by total body counting and linear scanning techniques. These results were correlated with direct measurement of radioactivity of total urine and fecal collections and samples of body fluids and tissues. From these data, mathematical models are being derived for the immediate excretion and long term retention of technetium. Estimates of radiation exposure following internal deposition of ^{99}Tc and ^{99m}Tc are being calculated.

SESSION: BRAIN

Chairman, CHRISTINE M. MATTHEWS

Area A

A-4-a *"^{131}I Colloidal Albumin—A New Brain Tumor Localizing Agent."* ROBERT T. MORRISON AND TITUS C. EVANS, (University of Iowa, Iowa City, Iowa)

Sixty patients suspected of haboring neoplastic intracranial lesions were scanned using ^{131}I colloidal albumin (small particle size) as the localizing agent. Twenty-six of these patients also had scans with ^{203}Hg chlormerodrin. Fourteen of seventeen patients with proven intracranial neoplasms had positive scans with ^{131}I colloidal albumin. Twelve of these patients had scans with ^{203}Hg chlormerodrin and eleven were positive. Cerebral infarcts and arterovenous malformations were shown with about the same efficiency with either agent. The scans were begun 10 minutes after the injection of 10 μc per kilo of ^{131}I colloidal albumin. The radiation dose to the kidneys was estimated to be 2.5 rads.

A-4-b *"Further Brain Scanning Studies with Radioalbumin Aggregates."*[1] J. C. KENNADY AND G. V. TAPLIN, (School of Medicine, University of California at Los Angeles)

Long term cerebrovascular toxicity studies are being continued in primates because brain hemisphere scanning with radioalbumin aggregates has great potential diagnostic value and preliminary investigations last year suggested a 70-fold margin of safety. Sixteen monkeys have received multiple intracarotid injections of 10-100 μ size aggregates of radioalbumin during the past year. Only two animals, who were given more than 2 mgs of carrier albumin had evidence of *transient* CNS injury, the others had no detectable impairment by EEG or by subsequent scanning with ^{197}Hg chlormerodrin. They also had no behavioral changes or evidence of motor weakness. Five animals were sacrificed after multiple injections and microscopic examination of brain sections showed no differences between the control and injected hemispheres. The remaining 11 monkeys are scheduled for further injections and histological study before June 1965.

Four monkeys were given macroaggregates injections 15 minutes following angiographic doses of sodium diatrizoate without reactions. However, the aggregates were released more slowly from the brain, which suggests a vasomotor effect from the diatrizoate. For this reason,

hemisphere scanning in man should be initiated as an independent screening procedure and not in conjunction with angiography.

On the basis of relative brain weights between monkey and man of 1 to 14, and the safety of multiple injections of 2 mg doses in the monkey, normal man should tolerate about 28 mg of 10- 100 μ size aggregates. The safety factor in man should be at least 100-fold because hemisphere scans can be performed with 0.28 mg doses or less.

In recent studies, satisfactory monkey hemisphere scans have been made using high specific activity (1000 μc/mg) albumin ^{131}I aggregates with particles; no larger than 60 μ. With this modification in particle size distribution of the test material, the potential hazard should be further reduced. Clinical trials will be initiated in selected patients provided the histological examinations of the remaining animals also show no evidence of cerebrovascular abnormality in the injected hemispheres.

[1]These studies were supported by Contract AT(04-1)-GEN-12 between the U.S. Atomic Energy Commission and the University of California at Los Angeles.

A-4-c *"An In Vitro Comparison of ^{197}Hg and ^{203}Hg in Brain Tumor Scanning."*

WILLIAM K. OTTE, JR., LUCAS B. BEENTJES AND THOMAS P. HAYNIE, (The University of Texas Medical Branch, Galveston, Texas)

Both ^{203}Hg and ^{197}Hg Neohydrin have been widely used in recent years in the radioisotope localization of brain tumors. ^{197}Hg, because of its short physical half-life of 65 hours, has an advantage of less radiation exposure to the patient; but because of its low energy gamma (.077 mev) presents theoretical difficulties in detection of "deep" lesions. We have evaluated the two isotopes using an Alderson Skull phantom and several commercially available photoscanning devices.

A 2 cm hollow plastic sphere filled with either ^{197}Hg or ^{203}Hg to stimulate a tumor has been placed in the center of the "skull" and scanned with standard techniques using varying concentration differences between "tumor" and background. The table shows that the "tumor" was better visualized by scanning with ^{203}Hg than ^{197}Hg particularly at lower concentrations and at greater distances.

This *in vitro* study confirms that deep lesions are more difficult to visualize with agents having soft gamma rays than with more energetic gamma rays. These studies are currently being extended to include ^{99m}technetium.

TABLE

"TUMOR": Background Concentration

	35:1	15:1	8:1
	^{197}HG		
10 cm	+	+	−
16 cm	+	−	−
	^{203}HG		
10 cm	+	+	+
16 cm	+	+	−

Tumor Visualized = +
Tumor Not Visualized = −

A-4-d *"The Effect of Cerebrovascular Accidents on the Brain Scan."*

JOSEPH L. GLASGOW, ROBERT D. CURRIER, JACK K. GOODRICH AND FORREST T. TUTOR, (University Medical Center, Jackson, Mississippi)

The results of 100 scans of the cranial vault using ^{203}Hg Chlormerodrin in patients with a final clinical diagnosis of cerebral vascular accident, including hemorrhage and thrombosis, are presented. Sixty-five cases were obtained from the routine scanning of every patient with a presumptive diagnosis of cerebral vascular accident admitted to the Neurology Service of the Veterans Administration Hospital since April 1964. Patients were included in the study

after the diagnosis was established. The remaining thirty-five cases were obtained on review of 434 scans from the University Medical Center. Of the 100 scans studied, there were 46 abnormal scans and 54 normal scans. Of the 65 cases from the Veterans Administration Hospital, 55 were scanned within six weeks of the onset of clinical symptoms with 27 (49%) positive. The highest incidence of abnormal scans was found between 14 and 28 days. Of a total of 22 scans during this interval, 17 (77%) were found to be positive. A review of 90 scans of the cranial vault using ^{197}Hg Chlormerodrin revealed 21 cases having final clinical diagnosis of cerebral vascular accident. There were seven positive scans and 14 negative scans.

Although an occasional scan following cerebral vascular accident was highly suggestive of tumor, the majority of the cases could be differentiated by: 1) degree of uptake relative to size of the abnormal area; 2) in distinct border of the lesion, and 3) the configuration and position of the abnormal area.

Neurological evaluation was performed by an independent observer before results of scanning was known. The correlation of the brain scan with the location of the lesion by neurological examination and the subsequent clinical course of the patient will be discussed. Other pertinent examinations and laboratory data will be included.

A-4-e *"Correlation of Point Counting with Brain Scan Image and Pathology."* M. TAKAHASHI AND M. NOFAL, (University of Michigan Medical School, Ann Arbor, Michigan)

One hundred and two ^{203}Hg and ^{197}Hg brain scans with histologically verified brain tumors were studied in an attempt to correlate point counting after brain tumor scanning with pathology of lesions. Although there was a considerable overlap between pathologic groups in differential point counting ratios in individuals, there was a statistically significant difference in differential uptake ratios between meningiomas and glioblastomas, as well as between meningiomas and astrocytomas by "t" test at the 5 per cent confidence level. These data have also been correlated with the location, size and configuration of the positive scan image of the brain tumor.

The following trends were noted;

1. Meningiomas (21) generally showed sharply demarcated round concentrations with moderately high differential uptake ratios (2.7:1). They were frequently large and localized in the parasagittal (7), parasylvian (3), sphenoid ridge and olfactory groove regions (4).
2. Glioblastomas (28) were frequently large, multiform concentrations with high uptake ratios (3.1:1). Site of the tumors was not specific except that most deep-seated tumors seen on brain scans were glioblastomas.
3. Astrocytomas (16) usually presented as small round concentrations with frequent localization in the posterior fossa (10 out of 16 posterior fossa lesions) and have relatively differential uptake ratios (2.3:1). The distribution in the cerebrum was wide.
4. Metastatic carcinomas (27) appeared as small and round densities with low differential uptake ratios (2.4:1). They were frequently found in occipital (10 of 27), parietal, and posterior temporal regions. They were the most common cause of more than one positive image on a brain scan.
5. The most common types of 18 posterior fossa tumors seen on brain scans were cerebellar astrocytoma (10), metastatic carcinoma (3), acoustic neurinoma (2), and ependymoma (2). Accuracy of detecting these tumors was approximately 70 per cent.

A-4-f *"Radioisotope Scanning in Posterior Fossa Lesions."* ROBERT C. FLIPSE AND ALBERT J. GILSON (Emory University Hospital, Atlanta, Ga.)

The authors note that radioisotope scanning of posterior fossa disease is frequently considered to be of little value and that some clinics even report the virtual abandonment of posterior fossa scanning. Twenty-six cases of posterior fossa disease were selected from a group of approximately 2200 scans which were performed for various reasons. While ^{99m}technetium is now being employed, the series reported was based upon the use of a mercurial, either ^{203}Hg or ^{197}Hg neohydrin. Out of 26 cases, 24 were confirmed by means of

surgery, postmortem or other clinical measures. Two were considered to be abnormal but unproven. There was only one false-negative, that being a low grade cystic astrocytoma. Further breakdown of the material will be given at the time of presentation. It is the contention of the authors that posterior fossa scanning should not be undertaken with the pessimism usually associated with this procedure.

FRIDAY, JUNE 18, 1965
SESSION: PHYSICS AND INSTRUMENTATION
Chairman, TITUS EVANS
Area B

A-5-a *"Tuberculosis and the Pulmonary Scan."* G. E. HORTON, R. H. JOHNSTON, JR. AND P. C. JOHNSON, (Caney Valley Memorial Hospital, Wharton, Texas)

Pulmonary scans using ^{131}I Macroalbumin have been performed for 25 tuberculosis patients. These scans were compared to angiograms obtained the same day. The scans were done to show the changes of active and inactive tuberculosis including cavitation and fibrosis. The inactive cavity shows up as an area of decreased concentration. Fibrosis shows in the scan as areas of decreased to absent concentration of macroalbumin. The scan generally shows a greater area of abnormality than is inferred by the routine chest x-ray and angiogram.

B-4-a *"Measurement of ^{197}Hg."*[1] J. S. ELDRIDGE AND W. S. LYON, (Oak Ridge National Laboratory, Oak Ridge, Tennessee)

^{197}Hg ($T_{1/2}$ 65 hr) is receiving increasing interest because of its application to biomedical problems. The primary method of production, ^{196}Hg (n,γ) ^{197}Hg results in the formation of two isomers: ^{197m}Hg (24 hr) and ^{197}Hg (65 hr). An additional interfering radionuclide, ^{203}Hg (47 day) is also formed by the reaction ^{202}Hg (n,γ) ^{203}Hg. The presence of these three radioactive mercury isotopes makes absolute assay of the sample difficult, especially during the first few hours after irradiation.

The short half-life of the ^{197}Hg, however, requires that an accurate assay be obtained at a time as close to the end of irradiation as possible.

The decay schemes of ^{197}Hg – ^{197m}Hg have been studied, half-lives redetermined, gamma branchings obtained, best values for conversion coefficients chosen, and production cross sections for both isomers measured. On the basis of these data two relatively simple methods of assay have been proposed and evaluated: measurement of the total number of K x-rays, and the sum coincidence technique. Corrections necessary because of the presence of ^{197m}Hg and ^{203}Hg have been determined and applied. The resulting procedures enable rapid and accurate assay to be made. In corollary experiments the production of carrier free ^{197}Hg by cyclotron irradiation has been studied, and relative cross sections for production of both ^{197}Hg isomers obtained.

[1]Research sponsored by the U. S. Atomic Energy Commission under contract with the Union Carbide Corporation.

B-4-b *"Absorbed Dose Calculations for Radionuclides that Emit Low Energy Photons."* E. M. SMITH, C. C. HARRIS AND R. H. ROHRER, (Cornell Medical Center, New York City; ORNL and Emory Universities, Atlanta, Georgia)

Classical methods for calculating the gamma component of the absorbed dose resulting from low energy photons underestimate the absorbed dose when compared to Monte Carlo type calculations by 17 per cent for 80 kev photons (photon energy similar to ^{197}Hg) and by 14 per cent for 160 kev photons (photon energy similar to ^{99m}Tc), if the radionuclide is uniformly distributed in a 70 kg standard man (ellipsoid). This is due to the assumptions and constraints in the classical equation:

$$R_\gamma = C\,(t)\,pg\Gamma\ R/sec$$

The values used for the average geometric factor, g, are based on the photon spectrum of radium and an effective tissue absorption coefficient, μ eff. of 0.028cm^{-1} which is assumed to be constant. These conditions are met by radionuclides that emit photons of an energy similar to the energy of the radium photons over a limited range of distances, but are not met by the photons emitted by ^{197}Hg, ^{99m}Tc, etc.

The value for the specific gamma ray constant, Γ, is artificially inflated when low photon energies are included, such as those arising from electron capture and internal conversion. This results from the almost expotential increase in the linear air absorption coefficient below 70 kev. For example, the K_α and K_β x-rays from the ^{99}Tc increase Γ by 29 per cent, while these x-rays make up only 1.2 per cent of the total photon energy released.

These sources of error may be avoided if the Monte Carlo type calculations presented by Ellett *et al* are used. These consist of tabulated values for the fraction of the photon energy emitted that is actually absorbed for a given photon energy with a given radionuclide distribution in a phantom of given mass and shape.

B-4-c *"Sensitivity of Bremsstrahlung Activation Analysis for Iodine Determination."* JOHN A. CARDARELLI, PHILIP F. MULVEY, JR., CHARLES MURPHY, RAYMOND COOPER, AND BELTON A. BURROWS, (Boston Veterans Administration Hospital, U.S. Army Natick Laboratories, and Boston University School of Medicine, Boston, Massachusetts.

Sensitivity of activation analysis using bremsstrahlung irradiation to measure trace quantities of inorganic iodide was studied. Samples of ^{127}I to be analyzed were prepared in distilled H_2O and 0.9% NaCl, then passed through polyethylene syringes containing 0.3 ml of Dowex 50W-X8 cation exchange resin and 0.3 ml of Dowex 1-X8 anionic exchange resin. The anion resin column containing the ^{127}I to be assayed was made radioactive by bremsstrahlung (gamma photon) activation irradiation using a 22 mev linear accelerator. Each sample was placed directly behind a 6 cm thick H_2O cooled aluminum block. Electrons from the "linac" beam were captured in the block and the resultant bremsstrahlung activated the ^{127}I in the resin column. Spectral analysis of the radioactive ^{126}I showed two major gamma rays, 0.386 mev and 0.650 mev with a half-life of 13.0 days. Samples and standards were counted in a completely shielded 2¾ × 2¾" NaI (Tl) well. The results indicated that as little as 1 μg of ^{127}I could easily be measured and it had a gross count 10× the background count. The use of ion exchange resins prior to the gamma photon activation eliminated the need for extensive postirradiation chemistry as no major radioactive contaminants were found during spectrum analysis of ^{126}I, except for a single peak at 0.170 mev. The unknown contaminant has a half-life of only 24 hours. Thus, bremsstrahlung activation analysis was found a reliable and sensitive method for quantitative determination of trace quantities of ^{127}I, useful in studying the dynamics of iodide turnover and utilization in a biological system.

B-4-d *"The Application of Radioactivation Analysis for Selected Trace Elements in Biological Samples."* MILTON H. FELDMAN, RICHARD C. REBA, GINO C. BATTISTONE, KENT T. WOODWARD, (Walter Reed Army Institute, Washington, D.C.)

The 50 kw research reactor at Walter Reed Army Institute of Research has been utilized to study quantitatively selected trace elements in biological samples by activation analysis.

Methods used to assess manganese, fluorine, and gold will be discussed with reference to sample size, limits of sensitivity, reproducibility of results.

Representative results will be presented. The influence of age of animal on manganese content will be discussed. Variations in manganese content of several insect species will be shown as an index of the sensitivity and applicability of radioactivation analysis in biology.

The analysis of trace fluorine in organic matrix is difficult using chemical procedures. Five to 100 mg of fluorine per ml were conveniently analyzed in beef broth media using 10.7 sec F^{20}, an internal standard, and contaminant subtraction by graphical methods.

The distribution and excretion of gold salts were studied in experimental animals prior to clinical use in rheumatoid arthritis. A simple semiautomated method of gold analysis will be presented.

B-4-e *"Surface Counting of ^{32}Phosphorus with a Solid State Detector."* FELIX J. PIRCHER, BANKS ANDERSON, SR., P. J. CAVANAUGH, KATHRYN W. SHARPE AND ROBERT J. REEVES, (Duke Medical Center, Durham, N. Carolina)

In the past, a miniature Geiger-Muller tube was used to measure uptake of ^{32}P in lesions of the skin and eye for the purpose of differentiating malignant from benign changes. The results obtained by this technique suggest that the concentration gradient of ^{32}P from normal to malignant tissue is sometimes less than 1:2. We thought that the differentiation could be more accurate in border line cases if no or little normal tissue is included in the count of the suspicious area. Since the diameter of the detection surface of the popular "Anton" probe is often greater than the diameter of the lesion, we were interested in investigating the usefulness of semiconductor detectors for the ^{32}P technique. They are, in principle, ionization chambers wherein the gas is replaced with a semiconducting solid which is 1800 times as dense as gas. They thus require less volume and can be of considerably smaller dimensions while absorbing the same amount of energy from charged particles as the larger gas ionization chambers. The detector used in our experiments is made of hyper-pure silicon with a window of 0.65cm in diameter and of 0.5mg/cm^2 thickness. It is housed in a gold-plated brass can, 2.24cm long and .8cm in diameter. The detector is connected by a 4 ft long microdot, mininoise, coaxial cable with an ORTEC 207 amplifier, which is equipped with a detector bias, a linear amplifier and a built-in low level discriminator. The detector is operated at a bias of 10 V and a discriminator setting of 75 kev. The efficiency of the detector is 1.09 per cent (1.03% for the Anton probe) but has a background count of only 2 counts per minute. The counts are recorded by a scaler (Nuclear-Chicago 151A). With this arrangement we studied patients with a variety of lesions of the skin and eye. The detector is easy to handle and causes no discomfort to patients with eye lesions. The detector window rarely covered more than the lesion. The results of the experiments indicate that all lesions that proved to be malignant by histological examination had an increase in ^{32}P uptake greater than 100 per cent. The increase in uptake was in fact greater than 200 per cent in the majority of cases, and in some as high as 500 per cent. We have come to the conclusion that the semiconductor detector described here is superior to the conventional miniature GM tube in handling and may be more accurate in differentiating malignant from benign lesions.

B-4-f *"Bone Density Measurement by Means of Radioisotopic Source Photon Attenuation."* ALBERT J. GILSON, MARTIN J. COHEN AND FRANK DAY, (University of Miami School of Medicine, Miami, Florida and Franklin GNO Corporation, West Palm Beach, Florida)

According to its composition, a material will have a specific linear absorption coefficient for a given wave length of electromagnetic radiation. This coefficient of linear absorption is numerically equal to the fractional reduction of the radiation intensity in each centimeter of absorber.

Monochromatic radiation under the above conditions is attenuated according to the well known exponential equation for absorption. If the density of the absorber be known, the linear absorption coefficient may be then converted to a mass absorption coefficient. The magnitude of the mass absorption coefficient for a given energy and a given substance is practically independent of the physical and chemical state of the latter and is therefore only a function of the mass per unit of area.

Gamma ray transmission is therefore related in a known manner to the density of the absorber, in this case the hydroxyapatite content of mineral bone. A transmission factor then obviously becomes useful in detecting changes in skeletal mineralization status.

A device based on these principles would, in fact, be similar to that used for measuring linear x-ray absorption coefficients of elements.

In order to obtain quantitative measurements, however, the following complicating factors must be taken into account:

1. Absorption of beam accountable to surrounding soft tissues.
2. Effect of organic bone matrix.
3. Bone size or thickness.
4. Scatter radiation.
5. Effects of polychromatic radiation.
6. Collimation effects.

Instrumentation capable of measuring bone density *in vivo* to an accuracy of 1 per cent will be described.

SESSION: LOCALIZING AGENTS

Chairman, MONTE BLAU

Area B

B-5-a *"Positive Delineation of Human Tumors with ^{131}I-Human Serum Albumin."* KIN-ICHI HISADA, TATSUNOSUKE HIRAKI AND SATORU OOBA, (School of Medicine, Kanazawa University, Kanazawa, Japan)

We have been searching for substances which have special affinity to tumorous tissue in animal experiments for diagnostic and therapeutic purposes. To our knowledge, this is the first report on the successful delineation of the human tumors other than brain tumor by scinti-scanning technique. 1 mc of ^{131}I-human serum albumin was administered intravenously to each of the volunteers with a cancerous condition.

The crystal size of the scanner was 2 x 2 inches with a 37 hole honey cone collimater and a multi-cut-off-level technique (20, 35, 45, 55%) was adopted. To date we succeeded in obtaining positive scintigrams of the tumor on four individuals with metastatic cancer of the left femur from pulmonary cancer, giant cell tumor (grade II) of the left femur, cancer of the left maxilla and cancer of the larynx.

Furthermore, affinities of the several labeled compounds to the tumorous tissue will be discussed.

A-5-b *"Physiological Changes in Pulmonary Blood Flow Evaluated by Lung Scanning."*[1] N. D. POE AND G. V. TAPLIN, (School of Medicine, University of California at Los Angeles)

Studies of pulmonary blood flow have been limited by the lack of simple laboratory methods which can be repeated at frequent intervals. The recent development of lung scanning by use of radioalbumin aggregates (10-50 μ) has provided a new technique for estimating regional pulmonary blood flow. The level of radioactivity recorded in any region of the scan image of the lung is proportional to the blood flow to that area. Significant changes in radioactivity in areas as small as 2-3 cms in diameter are apparent. This technique has been used in serial fashion in humans to study pulmonary emboli and other diseases which affect pulmonary arterial blood flow. Lung scanning is a unique method for studying alterations in pulmonary blood flow induced physiologically and pharmacologically.

The effects of posture on pulmonary blood flow have been investigated extensively in our laboratory in dogs by scanning and by counting of excised lung tissue and in humans by repeated scanning. Scan results corroborate earlier findings by bronchospirometric and dynamic radioactive gas techniques. Blood flow is greater in the dependent portions of the pulmonary vasculature regardless of posture in normal subjects but in sustained pulmonary hypertension flow to the apices is relatively increased regardless of posture. Effects of pharmacologically induced changes in pulmonary blood flow will also be presented. In many of the serial studies, color dot scanning is used to determine relative changes in blood flow more accurately by inspection.

[1]These studies were supported by Contract AT(04-1)-GEN-12 between the U.S. Atomic Energy Commission and the University of California at Los Angeles.

A-5-c *"Bronchial and Vascular Lung Scans in Pulmonary Disease."* **JAMES L. QUINN III AND LOUIS R. HEAD, (Northwestern University School of Medicine and Chicago Wesley Memorial Hospital)**

The value of the "lung scan," using aggregates of ^{131}I human serum albumin, in the early diagnosis of pulmonary embolism is known. Further applications of this "pulmonary artery bed" (vascular) scan are being investigated.

An outgrowth of the continuing interest in evaluating pulmonary function by photoscan techniques has been the independent introduction, by Taplin and by Pircher, of the "bronchial" lung scan.

The pulmonary bronchial space can be scanned after inhalation of ^{131}I human serum albumin, ^{198}Au colloid, ^{99m}Tc albumin or ^{99m}Tc sulfur colloid as an aerosol.

Using the ^{99m}Tc compounds the bronchial and vascular scan can be obtained one right after the other and gross bronchial/vascular ratios obtained.

The results of using both these pulmonary scan techniques in evaluating 40 patients with proven pulmonary disease, before and after appropriate treatment, will be presented.

A-5-d *"Factors Influencing Regional Pulmonary Blood Flow in Man and Dog."* **HENRY N. WAGNER, JR., VINCENT LOPEZ-MAJANO, DONALD E. TOW, VICTOR CHERNICK AND RALPH TWINING, (The Johns Hopkins & Veterans Administration Hospitals, Baltimore, Md.)**

Radioisotope scanning of the lungs has proved to be a technically simple and safe approach to the study of regional pulmonary arterial blood flow in man and experimental animals. Based on experimental studies, as well as on evaluation of over 40 lung scans in man, the following conclusions could be drawn: (1) regional concentrations of radioactivity in the lungs following intravenous injection of macroaggregated albumin (MAA) were proportional to regional pulmonary arterial blood flow and could therefore be used for its measurement; (2) oxygen uptake by each lung correlated closely with blood flow as measured by the scanning technique; (3) exercise resulted in a generalized diffuse increase in pulmonary arterial blood flow; (4) gravitational effects between O and 4G were readily studied by the scanning method; (5) a variety of pulmonary disorders were associated with a regional decrease in pulmonary arterial blood flow; (6) similar abnormalities in the distribution of blood flow could be produced experimentally by inducing regional hypoxia; (7) vasoactive agents, such as serotonin produced a decrease in regional pulmonary blood flow, while agents, such as acetylcholine produced an increase.

A-5-e *"Diagnosis of Pulmonary Embolism and Infarction by Photoscanning."* **THOMAS P. HAYNIE, CHARLES K. HENDRICK AND MELVYN A. SCHREIBER, (The University of Texas Medical Center—Galveston, Texas)**

The differential diagnosis of pulmonary embolism and infarction presents a formidable problem to both clinician and radiologist. The recent availability of ^{131}I macroaggregated albumin for the performance of lung scans has been evaluated in 20 patients suspected of having this diagnosis. In 12 patients where there was evidence of pulmonary embolism and/or infarction, the lung scan was positive in 10. In five of these patients, angiography was done and was positive in all. The chest x-ray was abnormal in 9 of the 11 patients studied. The two false-negative lung scans were encountered in patients with questionable diagnoses of pulmonary embolism. The remaining 8 patients had a variety of other diagnoses including subdiaphragmatic abscess, pneumonia and pulmonary fibrosis and emphysema. The lung scan was abnormal in five of these. Although a positive lung scan could not be used as absolute evidence of pulmonary infarction, diagnostic features were observed which might lead to suspicion of this disorder. No side effects to the procedure were observed in this series of patients. The lung scan with ^{131}I macroaggregated albumin appears to offer a safe and simple to perform screening test of considerable value in evaluation of patients suspected of having pulmonary embolism or infarction.

A-5-f *"Lung Scanning Following Radioisotope Inhalation (Techniques and Potential Applications)."* G. V. Taplin, N. D. Poe and A. Greenberg, (University of California at Los Angeles and Los Angeles County Olive View Hospital)

Lung scanning after intravenous injection of radioalbumin aggregates (10-50 μ) provides a practical technique for determining pulmonary arterial blood flow distribution and for delineating pulmonary arterial obstruction. Conceivably, equally valuable information on bronchial patency and air flow distribution could be obtained by scanning after radioisotope inhalation, provided the tracer is deposited uniformly throughout the respiratory tract and is retained long enough to scan the chest. Using positive pressure respirator-nebulizer equipment, the entire lung fields have been visualized in animals and man by scanning after inhalation of aerosols of serum albumin ^{131}I, rose bengal ^{131}I, chlormerodrin ^{197}Hg and colloidal ^{198}Au. The exhaled tracer is channeled through a low resistance, high efficiency filter and vented hood to prevent contamination of the test area.

Inhalation scans in normal subjects have a relatively uniform deposition of radioactivity throughout the lung fields. In experimental partial bronchial obstruction in animals and obstructive pulmonary disorders in man, the lung scan images show high concentrations of radioactivity at the sites of obstruction and absent or reduced activity in regions normally ventilated by these airways. The radioaerosol inhalation technique is useful also for determining the rates and pathways of clearance of various inhaled radioactive materials by serial scanning of the chest and abdomen. However, this technique does not reflect true pulmonary ventilation. Therefore, lung scanning is being studied in animals during rebreathing of ^{133}Xe-gas oxygen mixtures. After equilibrium the distribution of radioactivity throughout the lung scan image represents the ventilation pattern. The inhalation and intravenous scanning techniques can be performed in sequence if tracers of different energy are used. In this manner both the pulmonary ventilation and blood flow may be estimated almost simultaneously.

These studies were supported by Contract AT(04-1)-GEN-12 between the U.S. Atomic Energy Commission and the University of California at Los Angeles.

SESSION: NEW IMAGING DEVICES

Chairman, Hal O. Anger

Area B

A-6-a *"The Spintharicon—A New Approach to Radiation Imaging."* N. H. Horwitz, J. E. Lofstrom and A. L. Forsaith, (Wayne State University School of Medicine)

There is now an increasing interest in the development of cameras which can provide distribution patterns of radioisotopes by viewing the entire area of interest. Unlike the mechanical scintillation scanner, these cameras are not restricted to viewing a very small area of the source at any one time. They may accept information in parallel fashion with a significant increase in efficiency. This makes time-lapse imaging feasible.

The authors have developed an instrument which is capable of direct imaging and it is of remarkable simplicity. As it's name suggests, this device produces an image from the pattern of sparks occurring between a metallic cathode and a transparent anode. Gamma-rays emitted by the source eject electrons from the cathode. These electrons trigger a Townsend avalanche in the filling gas resulting in a visible spark. These sparks are localized to the site of the gamma-ray interaction. A Polaroid camera views the sparks and integrates them into the distribution pattern.

Preliminary tests indicate that this instrument when used with low energy gamma-rays is capable of excellent resolution. At the present state of development it is possible to produce high quality images of a thyroid phantom containing 10 μc of ^{125}I in 5 minutes. A clinical instrument has been developed which has the camera integral with the Spintharicon chamber. Under development is a large panel type chamber which will be capable of viewing the liver or both kidneys simultaneously.

A-6-b ***"A Gamma-Camera: Optimum Length of Light Pipe and Evaluation of Mapping Errors."*** **WILLIAM C. MUELLER, JOHN R. CAMERON AND CHARLES R. WILSON, (University of Wisconsin, Madison, Wisconsin)**

A gamma-camera based on Anger's design[1] was constructed. The unit uses an eleven inch in diameter by one half inch thick NaI(Tl) crystal. The lucite light pipe is a disc sixteen inches in diameter by two inches thick. The thickness of the disc for the system used was optimized mathematically using a CDC-1604 high speed digital computer. An equation was developed to calculate the (x,y) position on the "scan" corresponding to each (X,Y) position of a point "source" of light from the crystal for various thicknesses of the light pipe from a quarter inch to five inches in quarter inch intervals. These transformations were analyzed to see how well patterns in the crystal mapped into the same configuration on the "scan". Nine equally spaced points on each of three lines starting from the center of the crystal were used as "sources" for this calculation. The corresponding (x,y) points on the "scan" were examined for distortions in linearity, equal spacing, and angle. It was observed that when the minimum error in the spacing of the mapped points was achieved, linearity and angle errors were also at a minimum. Therefore, a plot of the RMS spacing error was used to find the optimum thickness. These errors ranged from 66 per cent at a quarter inch, diminishing to a minimium of 15 per cent at two and a quarter inches, and again rising to 20 per cent at five inches. It should be noted that the optimum thickness obtained depends on the values of the capacitors used to divide the signal from each tube and the number of tubes, but not upon the crystal or photomultiplier tube diameters.

[1]The Review of Scientific Instruments, Vol. 29, No. 1, 27-33 January, 1958.

A-6-c ***"High Sensitivity Radioisotope Imaging System for Dynamic Function Study."*** **Y. WANG, E. L. KELLER AND E. J. STERNGLASS, (Pittsburgh, Pennsylvania)**

A new type of gamma ray camera system capable of imaging dynamic processes in organ compartments on a time-scale of a few seconds will be described. Spatial resolutions as small as 2 mm have been observed in thyroid phantoms using ^{125}I radiation. The system employs an x-ray image intensifier coupled optically to a new type of image storage tube possessing a very large dynamic range exceeding that of a photographic film. The image of the isotope distribution is stored as an electrical charge pattern in the camera-tube and can be presented on a standard television monitor for interpretation. The high sensitivity permits a lowering of the radiation dose to the body and to use isotopes of short half-life and low energy.

A-6-d ***"Minimizing the Motion Artifact with ^{99m}Tc Colloid and the Gamma—Camera."*** **A. GOTTSCHALK, P. V. HARPER, F. JIMINEZ AND J. P. PETASNICK, (University of Chicago, Chicago, Illinois)**

Utilizing moving phantoms, the effect of respiratory motion upon image resolution has been assessed for conventional speed scanning, high-speed scanning (up to 400 cm/minute), and the gamma scintillation camera.

In general, during quiet respiration (diaphragmatic excursion of 1.5 cm-rate 12/min), the motion artifact is prominent at slow-speed scanning, less evident with high-speed scanning, and almost negligible with the scintillation camera.

In patients using 1-2 mc of ^{99m}Tc sulfur colloid, excellent quality scintiphotographs of liver and spleen can be obtained with the gamma-camera in 1-5 minutes. 200,000-500,000 dots are collected in this interval. The dose to the liver and spleen is less than 1 rad. In cooperative individuals, excellent quality photos are possible while the patient holds his breath, thus eliminating motion entirely.

Examples of both phantom studies and clinical material will be shown.

A-6-e *"Intestinal Iron Absorption Studies Using ^{52}Fe and Anger Positron Camera."* **R. A. FAWWAZ, H. S. WINCHELL, M. POLLYCOVE AND J. H. LAWRENCE, (University of California, Berkeley)**

With the availability of the positron camera it has become possible to follow the passage of orally administered tracer doses of positron emitting isotopes through the gastrointestinal tract. The rate of systemic absorption of iron can thus be related to the anatomical location of iron in the intestinal tract at any given time, by correlating positron camera pictures with plasma isotope levels using orally administered ^{52}Fe in the intact human.

Intravenous administration of ^{55}Fe is used to measure the plasma iron turnover rate. ^{59}Fe administered orally in conjunction with the ^{52}Fe, is used to quantitate the total amount of iron absorbed by the use of total body counting measurements performed 2 weeks after the oral dose. Following the oral administration of 40-80 μc of ^{52}Fe and 1 μc of ^{59}Fe in 4 mg of carrier $FeSO_4$, serial plasma analysis for ^{52}Fe and concurrent positron camera pictures are made.

The preliminary results obtained indicate that although the maximum rate of iron absorbed occurs when the ^{52}Fe is in the duodenum and proximal jejunum, significant amounts of iron are being absorbed at a slower rate when virtually all of the administered iron is found to be in the distal ilium and colon. Although the results are preliminary they suggest that in man some delayed absorption of iron may occur in the distal bowel, contrary to presently accepted theories.

The results obtained using these techniques suggest the general usefulness of orally administered positron emitting isotopes in studies intended to localize intestinal sites of absorption of labeled materials.

A-6-f *"The Hybrid Radioisotope Scanner."*[1] **THOMAS P. DAVIS AND RONALD J. MARTONE, (The University of Rochester School of Medicine and Dentistry, Rochester, New York)**

A radioisotope mapping system intermediate in speed and complexity between a mechanical rectilinear scanner and a stationary camera-type device has been developed in this laboratory. In this instrument, electronic scanning is used for the determination of the activity distribution in one direction, while the complete area map is developed by a mechanical traverse at right angles to the scan direction. Because of the combination of an electronic scan with a mechanical traverse, the instrument has been termed the "hybrid scanner."

The operating principle of the electronic scanning system is based on the experimental observation that for a scintillation event within a long rod of fluor, the logarithm of the ratio of fluorescent fluxes issuing from opposite ends is directly proportional to the position of the scintillation event in the direction parallel to the long axis of the rod. The detector in the present instrument is a two inch diameter by eight inch long NaI(Tl) crystal rod with a multiplier phototube coupled to each end. A linear collimator between the detector and the subject translates the distribution of activity across the subject into a corresponding distribution of scintillation events along the crystal axis. For each such event, a position-dependent signal proportional to the logarithm of the ratio of pulses from the endviewing phototubes is applied to the vertical input of a read-out cathode ray oscilloscope, while the subject is traversed across the collimator-crystal array with this movement coupled to the horizontal input of the oscilloscope. A position-independent sum signal is presented to a wide window pulse height analyzer which generates beam brightening pulses for total absorption events. A camera integrates the oscilloscope presentation and delivers the finished map as a transparency which may be further processed by a TV flying spot scannermonitor system.

At present, clinical experience with the hybrid scanner is limited; however, the instrument has yielded satisfactory scans in one-half to one-fifth the time required by a commercial rectilinear scanner. The device is inherently quite simple, and has proved to be extraordinarily

[1]This paper is based on work performed under contract with the United States Atomic Energy Commission at the University of Rochester Atomic Energy Project, Rochester, New York.

easy to align. Because of its speed and simplicity, the hybrid scanner can fill a gap between the slower rectilinear scanners and the faster but more complex stationary devices. Experience gained with this instrument during development leads to considerable optimism that it will become a useful addition to the array of mapping systems now available.

B-5-b "*^{75}Se Selenite for Brain Scanning.*" RALPH R. CAVALIERI AND KENNETH G. SCOTT, (V.A. Hospital and University of California Medical Center, San Francisco)

Studies in rats with transplantable sarcoma have shown that ^{75}Se sodium selenite given *in vivo* is selectively concentrated by tumor and relatively excluded by brain, skeletal muscle, and bone. This led us to investigate the possible usefulness of this agent for tumor localization in man. To date, 23 patients have been studied. The usual intravenous dose for scanning is 4.0 μc/kg body weight. Scans are done at intervals from 4 to 96 hours. The results are compared with arteriograms, ^{197}Hg chlormerodrin scans, and operative findings. Follow-up is complete in ten cases. Six had brain tumors correctly localized by ^{75}Se. Four other patients with negative ^{75}Se scans proved to have cerebrovascular disease mimicking tumor. (Three of these had positive ^{197}Hg scans.) With ^{75}Se best results are obtained by scanning at 24 or 48 hours, when target to nontarget ratios are maximal. Using a 3 inch sodium iodide (Tl) crystal and 19 hole focusing collimator, count rates over tumor range from 1100 to 1600 cpm, which is 3 to 5 times the count rate over normal brain areas or temporal muscle. We have also localized neoplasms in other areas, such as chest wall, lung, and large bowel.

From distribution and excretion data we have estimated the radiation exposure from a single dose of ^{75}Se selenite (4 μc/kg) to be 1.0 rad total body, 4.5 rads to the liver, and 2.1 rads to kidneys. Advantages of this agent for brain scanning include: (1) Long shelf-life (120 days); (2) Radiochemical stability; (3) Convenient gamma energy (269 kev); (4) Ability to do repeat scans with a single dose; (5) Low background over neck and facial muscles, and; (6) Apparent accuracy in distinguishing cerebrovascular disease from tumor.

B-5-c "*The Uptake of Radioiodinated Atabrine by Experimental Tumors.*" NORMAN B. ACKERMAN,[1] (University of Minnesota Hospitals, Minneapolis, Minnesota)

The localization of aminoacridine compounds in experimental tumors was studied in this laboratory using Sprague-Dawley rats. After administration of some of these compounds, a bright yellow-green fluorescence was seen in implanted lung tumors (Novikoff hepatoma and Walker carcinosarcoma), but no fluorescence was noted in implanted liver and gastric tumors. Nearly 100 different aminoacridines were screened for ability to cause lung tumor fluorescence, and the required chemical configuration for this has been determined.

Among the compounds giving positive tests was the antimalarial drug, atabrine. Further localization studies were performed with radioiodine (^{131}I and ^{125}I) labeled atabrine. Doses of 4 to 60 mg of the compound containing 16 to 126 μc of radioiodine were given to rats with tumors in the lungs, liver or stomach. The animals were sacrificed at 1 hour to 5 days, and after examination under a fluorescent light source, radioautographs were made with the tissues containing tumors.

Lung tumors in animals sacrificed at 1 to 5 days fluoresced brilliantly, and on the radioautographs of these specimens, the tumors were clearly identifiable by the areas of increased radioactivity. Hepatic and gastric tumors did not fluoresce under ultraviolet light stimulation. However, on the radioautographs, areas of increased radioactivity coincided with the location of the tumor implants. Fluorescent microscopic studies have indicated that the atabrine appears to be located primarily in the nucleus and nucleolus. Since it is believed that aminoacridines form complexes with nucleic acids, it could be expected that all actively growing tumors would concentrate atabrine. This compound may ultimately prove to be of value clinically in the diagnosis of tumors.

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[1]Present address: Biophysics Division, Chemical Research and Development Laboratories, Edgewood Arsenal, Maryland.

B-5-d *"Preparation, Properties and Uses of ^{131}I Labeled Diethylstilbestrol Diphosphate."* MANUEL TUBIS, WILLIAM H. BLAHD, JOHN S. ENDOW AND MATT M. MIMS, (Veterans Administration Center, Los Angeles, California and UCLA Center for the Health Sciences, Los Angeles, California)

An ^{131}I labeled diethylstilbestrol diphosphate was prepared as a compound for use in the external scanning of the prostate gland for tumorous lesions and metastases and for malignancies as an ancillary therapeutic agent.

The material, of suitably high specific activity, has been prepared and used for scintillation scanning of human prostate glands and for distribution studies in animals and man. Scanning has indicated the deposition of the labeled compound in the prostate and other organs in man and dogs.

The labeled compound has facilitated studies of its distribution in mice, dogs and man and the patterns of distribution are similar to those of ^{14}C, ^{3}H and ^{32}P labeled materials. The toxicity of the ^{131}I labeled material is similar to that of the parent compound, stilbestrol.

The advantages of the ^{131}I label which is incorporated into the stilbestrol moiety are: (1) The ^{131}I appears to be firmly bound; (2) the label is not removed by dephosphorylating enzymes which are ubiquitous; (3) the ^{131}I is a gamma emitter of sufficient energy to permit external scanning; (4) the beta and gamma emissions may enhance any direct cytotoxic effect of the labeled compound on malignant cells; (5) the hormonal (estrogenic) properties are only slightly altered by labeling, and (6) the compound may be doubly labeled with ^{131}I and ^{32}P.

Further studies are in progress on improving the scanning technique in normal and carcinomatous prostate glands and metastases. The material will be used in therapeutic trials.

B-5-e *"The Tissue Distribution and Diagnostic Applications of ^{99m}Tc Compounds."* McAFEE, J. G., FUEGER, G. F., STERN, H. S. AND SUBRAMANIAN, G. (E. R. SQUIBB & SONS, New Brunswick, New Jersey)

The tissue distribution of ^{99m}Tc labeled albumin was compared with ^{131}I albumin in experimental animals. This substance was then used for visualization of the placenta in the third trimester of pregnancy, for the detection of placenta praevia and other abnormalities of late pregnancy.

Various preparations of ^{99m}Tc–sulphur colloid were studied in animals, and their reticuloendothelial localization compared with colloidal ^{198}Au and heat-aggregated albumin ^{131}I. This colloid was then employed for scanning of the liver, spleen, and bone marrow. The advantages of these compounds in preference to older agents will be discussed.

B-5-f *"Detection of Venous Thrombi by Scintillation Scanning."* IRVING L. SPAR, RUTH L. GOODLAND AND SEYMOUR I. SCHWARTZ, (University of Rochester School of Medicine and Dentistry, Rochester, New York)

The ability to localize intravascular thrombi by a simple technique has obvious clinical application. The present study represents an evaluation of the use of radioactive antibodies which concentrate preferentially in peripheral thrombi and thus enable its detection by scintillation scanning.

In earlier studies, thrombi were induced in adult mongrel dogs by ligation of the femoral vein and injection of thrombin into the blood vessel. At intervals of 1, 2 and 3 days after this procedure, the animals were injected with ^{131}I-labeled rabbit antibody to dog fibrinogen. One day later they were scanned and blood samples and thrombosed blood vessels were removed, weighed and counted in a well-type NaI scintillation counter. The ^{131}I accumulation in the clot-containing vessels was 2.5–10 times greater than a comparable amount of blood.

In an intitial series of patients with deep venous thrombosis, intravenous injections of 400-650 μc of ^{131}I rabbit antibody to human fibrinogen were administered. Scanning was performed 12-24 hours later over both legs. In all cases, scintillation scanning defined unusual

concentrations of radioactivity which coincided with phlebographically demonstrated thrombi. In several instances, surgical removal of the clots were performed and the ^{131}I content determined. These values were several fold higher than an equal weight of blood.

SESSION: LIVER AND SPLEEN

Chairman, ROBERT GREENLAW

Area B

B-6-a *"Diagnosis of Porto-Pulmonary Shunt in Liver Cirrhosis."* HIDEO UEDA, MASAHIRO IIO, KENICHI KITANI, HIDEO YAMADA AND HARUO KAMEDA, (University of Tokyo, Tokyo)

Presence of porto-pulmonary shunt in cases with liver cirrhosis was studied by pulmonary scanning after splenic injection of ^{131}I labeled macroaggregated albumin (MAA). This technique was compared with the splenic injection of radioactive rare gas solution with expiratory air monitoring and x-ray examination of esophageal varices.

Simultaneously with intrasplenic injection of radioactive rare gas solution, hepatic clearance was measured by the detector placed over the liver and liver blood flows were estimated by this procedure.

Three cases with hemolytic anemia showed no appearance of MAA in the lung after splenic injection, showing only liver and spleen by scanning. Radioactive rare gases appeared in the expiratory air later than 20 sec after splenic injection. These findings indicate the absence of functioning shunt through splenoportal circulation to the lung. Average hepatic blood flow was calculated 185 ml/100 gr/min. Seven cases with liver cirrhosis showed accumulation of MAA in the lung in various degrees. A case showed almost no accumulation of MAA in the liver with significant visualization of the lung. This case also showed instantaneous appearance of radioactivity in the expiratory air after splenic injection of rare gas solution. However there were several cases who were considered to have functioning porto-pulmonary shunt by the moderate to slight accumulation of MAA in the lung accompanied with either no early appearance of radioactive rare gases into the expiratory air or no sign of esophageal varices by x-ray examination. Liver blood flows in these cases decreased ranging from 67 to 98 ml/100 gm/min.

It was suggested that splenic injection of ^{131}I MAA followed by scanning of the lung can reveal sometimes the presence of splenopulmonary shunt in liver cirrhosis with more sensitiveness than radioactive rare gas method or x-ray examination of esophagoscopy.

B-6-b *"Photoscanning for Assessment of Liver Damage from Therapeutic External Irradiation."* JAMES A. USSELMAN, (U. S. Naval Hospital, San Diego, California)

The long held concept of the liver as a relatively radio-resistant organ can be effectively challenged by radioisotope photoscanning of patients whose liver has been included in radiation therapy portals. This has been demonstrated in a series of patients subjected to external irradiation for testicular tumors. In such cases, the left lobe of the liver is included in the midline portals used to treat lymph node drainage areas.

^{198}Au and Rose Bengal ^{131}I photoscans made subsequent to the course of radiation treatment have shown sharp vertical cut-off of activity in the left lobe of the liver, demarcating the border of the radiation beam. Pretherapy liver scans available in some of these same cases showed normal activity in these areas. Case histories and photo scans of five patients (followed from 9 to 14 months) are presented. Although recent reports (Ingold *et al Am. Journ. Roent.* Vol 93 Number 1 Jan 1965) suggest administered whole liver doses of 3500 rads in fours weeks would appear safe as our patients showed a lack of activity in irradiated areas with as little as 2400 rads. The transition zone from normal function to lack of it was sharp, particularly with television enhancement. Follow-up and further studies are underway to evaluate doses required to produce dysfunction and to assess the degree of permanence of liver impairment.

B-6-c ***"Increased Absorption of ^{59}Iron Citrate in Patients with Hepatic Cirrhosis."*** **BEN I. FRIEDMAN, JOHN W. SCHAEFER AND LEON SCHIFF, (University of Cincinnati College of Medicine, Cincinnati, Ohio)**

Portocaval anastomosis has been thought to be associated with increased absorption of iron from the gastroenteric tract in patients with hepatic cirrhosis. In an attempt to evaluate the role of liver disease, decompensation, and portocaval shunt, the absorption of ^{59}iron was studied in eight patients without liver disease and twenty-two patients with hepatic cirrhosis. Two of the cirrhotics were studied before and after portocaval shunt. At the time of study, two of the cirrhotics had neither decompensation nor shunt; seventeen were decompensated without shunt; two had shunt without decompensation; and three were both decompensated and postoperative.

One microcurie of ^{59}iron (ferrous citrate), 100 mg of carrier iron (700 mgm of ferrous ammonium sulfate) and 300 mg of ascorbic acid were given orally. All stools were collected for seven days after the oral dose of ^{59}iron, dried, and aliquots counted in a well type scintillation counter.

The mean of ^{59}iron absorption in the control group was 50.37 ± 18.57 per cent and of the cirrhotic group was 73.97 ± 17.42 per cent. The "t" test was performed comparing absorption of ^{59}iron between controls and cirrhotics, compensated and decompensated hepatic cirrhotics, and shunted and nonshunted cirrhotics. Significance to less than .005 level was found between the controls and patients with hepatic cirrhosis. The presence or absence of a portocaval shunt or decompensated liver disease did not result in a significant "t" value.

The data indicate that there is increased absorption of radioactive iron from the gastroenteric tract in patients with hepatic cirrhosis. The significant feature is the presence of cirrhosis rather than the state of compensation or presence of a portocaval shunt.

B-6-d ***Continuous Flow Monitored Dialysis Determination of Sodium-Serum Protein Binding."*** **ERVIN KAPLAN, J. GRECO, P. J. TALSO AND H. H. LO, (Veterans Administration Hospital, Hines, Illinois, and the Department of Medicine, Stritch School of Medicine, Loyola University)**

A dialysis bag in a rapidly flowing stream of dialysate permits the escape of permiable particles at a constant rate while allowing no significant re-entry to the bag. This is assumed in a steady state system in the absence of active interaction with the membrane. The escape rate may be observed if the particles in question are gamma emitters and the bag is contained in a scintillation well crystal.

In the system reported, a reusable dialysis bag functions as its own control for repeated determination of elution rates. The NaI(Tl) detector operates in a constant temperature environment. The dialysis flow is precise and adjustable, utilizing a Milton Roy "Mini Pump." The output of the EMI photomultiplier operates a modular "RIDL" digital count-rate system with numerical and analog printout.

The kinetics of the system have been derived allowing the determination of a rate constant of elution for specific gamma emitter in solution. The rate constant may also be determined as the emitter interacts or binds with a nonpermiable, nonradioactive substance within the dialysis bag. The difference in the two rate constants is interpretable as an interaction or dissociation constant.

Specific examples of biomedical application using this device will be discussed. Currently the most notable is the interaction of ^{22}sodium with human serum protein which may be interpreted as minimal but detectable binding. This interaction is expressable in quantitative terms, for the sodium, serum protein combination, indicating approximately 30 percent increase in elution rate of ^{22}sodium when interacting with pooled human serum protein.

B-6-e ***"Studies of Selective Splenic Sequestration with Radioactive Mercuri-Hydroxypropane (MHP-^{197}Hg)."*** **DONALD R. KORST, JOHN C. NIXON, DELBERT E. BOBLITT AND JANET QUIRK, (St. Joseph Mercy Hospital, Ann Arbor, Michigan)**

Erythrocytes that have been damaged or altered by a mercurial compound are selectively sequestered or trapped by the normal spleen. This appears to be a reproducable phenomenon which is altered by various pathologic changes in the spleen.

A new radioisotope procedure utilizing radioactive ^{197}mercury, mercuri-hydroxypropane (MHP-Merprane-Squibb) is useful in measuring the selective sequestration function of the spleen. The test requires careful adjustment of chemical concentration of the number of cells in order to damage cell membrane but not hemolyze the cells. External counts are made of the sequestering ability of the spleen as compared to precordium and liver in a period of an hour followed by scintiscan of the spleen.

Studies would indicate that the dose is relatively safe to use in all age groups and that the posterior aspect of the spleen is preferred for counting and scanning. Four patterns of spleen and liver uptake are recognized: 1. Patients with splenic involvement and infiltration due to leukemia and lymphoma have a decreased function of spleen sequestration. 2. Patients without spleen function because of fibrosis or irradiation have increased hepatic sequestration of the cells. 3. Patients with hypersplenism have increased splenic sequestration of cells. 4. Patients with cirrhosis have decreased liver uptake of cells with a normal splenic uptake.

The information obtained by MHP spleen uptake curves and scans may be helpful in diagnosis of lymphoma and in the degree of hypersplenism prior to surgery. There appears to be a correlation between the selective sequestering function of the spleen and the underlying disease processes.

B-6-f "*^{197}Hg MHP Spleen Function Study.*" Y. WANG, (University of Pittsburgh, Presbyterian-University Hospital, Pittsburgh, Pa.)

Wagner's group has recently introduced ^{197}Hg MHP for spleen scanning. It offers advantages over the previous technique using heated ^{51}Cr-tagged erythrocytes. Furthermore, the function state of spleen could be evaluated with this new agent. ^{197}Hg MHP tagged RBC showed a rapid clearance pattern from the spleen after reaching a peak in a period of one to two hours and flattening out thereafter. Using this method, we have observed the four different classes of RBC sequestration: (1) excessive sequestration in the spleen; (2) nonexcessive sequestration in either spleen or liver; (3) excessive sequestration in the liver; and (4) excessive sequestration in both liver and spleen. A marked reduction of splenic sequestration of ^{197}Hg MHP was observed in cases of anemia due to hepatic cirrhosis, lupus involving spleen, thrombocytopenia and lymphoma, and the spleen scanning was not successful. ^{197}Hg MHP method for studying splenic sequestration or function will take three to four hours by external counting every thirty minutes for the first ninety minutes and every sixty minutes for two additional hours. The results were compared by a comparative study using ^{51}Cr-tagged RBC in the patients examined with ^{197}Hg MHP method. The results of two different techniques are very similar; however, the ^{197}Hg MHP method takes only three to four hours instead of two to six days with the ^{51}Cr method. Our preliminary experience has indicated that using ^{197}Hg MHP for the study of RBC sequestration is adequate and simpler.

SESSION: SCANNING WITH ^{75}SE SELENMETHIONINE

Chairman, E. JAMES POTCHEN

Area A

A-7-a "*^{75}Se Methionine as a Diagnostic Agent in Malignant Lymphoma: A Preliminary Communication.*" N. E. HERRERA, RAFAEL GONZALEZ, RAPHAEL SCHWARTZ, A. MONROE DIGGS AND JOSEPH BELSKY, (Danbury Hospital, Danbury Connecticut)

In the course of evaluation of a case of obstructive jaundice a pancreatic photo scan demonstrated a large abdominal tumor mass with high uptake of ^{75}Se Methionine. The tumor proved at biopsy and at autopsy to be a recurrent lymphosarcoma of gastric origin. Two further cases (recurrent lymphosarcoma of abdominal lymph nodes, Hodgkin's disease) had enough uptake in the lesions to be demonstrable on repeated photo scans.

The report of our continuing studies will attempt to determine:

1) Whether this is an exclusive property of the initial cases versus a larger series of lymphomas.

2) The specificity of this uptake in terms of the histologic nature of a variety of abdominal tumors.

3) Residency time of radioactivity in tumor tissue (preliminary data from the first case suggests a long residency time in excess of 14 days)

4) Comparison with uptake of lymph nodes in subjects who do not have lymphomas and who undergo pancreatic scan and in patients with lymphosarcoma following therapy.

5) Studies of uptake, tissue content and biological half life of the agent in tumor tissue.

A-7-b *"Uptake of Amino Acid Analogues by the Parathyroid Gland."* WALTER DIGIULIO

To date we have performed over 30 photoscans on ten patients with hyperparathyroidism. Neck explorations have been performed on 8 of these patients. In 5 of these 8 patients scans were negative and the maximum weight of parathyroid adenomas removed was 1.15 gms. In three patients with positive scans the weight of the adenomas was greater than 3.35 gms.

Parathyroid, thyroid, muscle and blood were collected during surgery in four of these patients and were assayed for radioactivity. The activity in the parathyroid varied from 8.5 $\mu\mu$c/mg to 43$\mu\mu$ c/mg and was twice that in thyroid or blood and 3 to 4 times that in muscle.

The administration of (a) thyroid hormone in an attempt to suppress protein synthesis in the thyroid gland, (b) a high protein diet to suppress amino acid uptake in large pools of protein synthesis, and (c) a low calcium diet to stimulate an increased rate of parathormone synthesis, was not detectably effective in experiments in half of these patients and in 10 dogs.

The fecal and urinary excretion studied in six patients indicate a biological half life of 140-150 days for ^{75}Se methionine.

Because of obvious limitations of the present technique, studies in dogs are continuing in an effort to develop a method for parathyroid scanning that will enable detection of small adenomas and adenomas located in the mediastinum. ^{14}C labeled L-parafluorophenylalanine was found to concentrate in parathyroids, muscles, and blood of dogs comparable to concentration of ^{75}Se methionine.

To date we have been unsuccessful in obtaining high specific activity ^{18}F labeled parafluorophenylalanine.

The possible enhancement of parathyroid scanning with labeled amino acids by use of an 8 inch crystal scanner and/or by carotid artery injection is currently under exploration.

A-7-c *"Progress in Medical Radioisotope Scanning Pancreatography."* D. BRUCE SODEE, (Doctors Hospital)

Photoscanning of the pancreas utilizing selenomethionine-^{75}Se has recently been shown to be a practical technique. In a series of 185 patients who underwent 555 such photoscans, the pancreas was visualized in over 90 per cent of the cases. The physiological stimulation of the pancreas was found to be the most important factor in pancreatic selenomethionine-^{75}Se concentration. Utilizing a 30 g protein meal, physiological stimulation of the pancreas was begun one hour prior to the intravenous administration of 250 μc selenomethionine-^{75}Se. Fifteen minutes later continued stimulation of the pancreas was insured by the oral administration of 90 μg of glutamic acid hydrochloride. Prior to scanning the pancreas, a ⅜-inch curved lead shield was placed over the liver bed previously outlined by an ^{198}Au liver scan. This lead shield blocks the radiation from the concentration of selenomethionine-^{75}Se in the liver that in the past impaired accurate delineation of the pancreas.

Recently, a 5-inch × 3-inch crystal and a 121-hole lead collimator with a 5-inch focal distance has been utilized. Our technique has been finalized, and we can now visualize pancreatic carcinoma ½cm in size when located in the head.

The results show that pancreatic carcinoma does not concentrate selenomethionine-^{75}Se as well as normal tissue. Eight of nine patients with pancreatic carcinoma had their disease correctly interpreted by this procedure. The smallest carcinoma not visualized was obscured

by an enlarged liver. Acute and chronic pancreatitis are also confirmed by the pancreatic scan as the impaired cells of the pancreas do not concentrate selenomethionine-^{75}Se. Twelve of twelve patients with pancreatitis were correctly interpreted. We have had three cases of perforating ulcer and scan interpretation was correct.

In addition, selective uptake of selenomethionine-^{75}Se by parathyroid tissue was ascertained. Utilizing the same scanning technique, parathyroid adenomas in a small group of hyperparathyroid patients have been visualized.

Photoscanning of the pancreas is already a practical technique and an investigation of photoscanning of the parathyroid is now being undertaken. With the renewed interest in organs that previously could not be visualized by standard radiographic techniques, selective organ scanning, by means of labeled compounds chosen for their biochemical properties, becomes an important technique of the future.

We will present our animal data on a new radiopharmaceutical for pancreatic scanning.

A-7-d *"Pancreatic Scanning Utilizing ^{75}Selenium-Methionine and Morphine."* ANTONIO RODRIGUEZ-ANTUNEZ, (Cleveland Clinic, Cleveland, Ohio)

At the Cleveland Clinic Foundation the following protocol for pancreatic scanning has been on trial since a few months ago. Preceding the scanning, food and fluids by mouth are withheld from the patient from six o'clock in the evening until the following morning, when a fat-free breakfast is given. The patient is served fruit juice, chicken broth, jello, eggnog made with skim milk, tea, and three or four packets of sugar. When the patient finishes his breakfast, ¼ grain of morphine is injected intramuscularly. Fifteen minutes later 2½ or 3 μc of ^{75}Se-methionine are injected intravenously. The scan is started about ten minutes after the injection of ^{75}Se. With this protocol we find we have been able to get a fairly good visualization of the pancreas in a high percentage of cases.

We feel that the addition of morphine with its known effect of contracting the sphincter of Oddi helps in holding the pancreatic enzymes within the canaliculi for a period of time suitable for scanning.

Discussion of about fifteen pancreatic scans will be presented.

SATURDAY, JUNE 19, 1965

SESSION: BONE AND RETICULOENDOTHELIAL SYSTEM

Chairman, RICHARD E. PETERSON

Area A

A-8-a *"The Pathologic Basis of Positive Strontium Bone Scans."* DAVID M. SKLAROFF, IRVING M. YOUNG AND N. DAVID CHARKES, (Albert Einstein Medical Center, Northern Division, Philadelphia, Penna.)

Since 1961 we have performed more than 350 ^{85}strontium bone scans in cancer patients with proven or suspected metastatic disease. In 26 of these cases, specimens of bone were obtained from scanned areas by needle biopsy, open biopsy, or autopsy, and were examined histopathologically. In 10 patients the ^{85}Sr concentration per gram of bone was determined by means of well-scintillation counting and was correlated with the microscopic findings. Positive strontium bone scans were associated with histologic evidence of active new bone formation incited by the presence of malignant tissue. The ^{85}Sr concentration in the biopsy specimens in these cases was increased over normal levels. Heavily calcified reactive bone (roentgenographically "osteoblastic") did not pick up as much radiostrantium as did younger osteoid, and apparently represents a later phase in the reactive process. In some biopsy specimens the magnitude of the osteogenic activity simulated Paget's disease. In four patients biopsies were obtained from bone lesions which were demonstrable roentgenographically as osteolytic areas but which did not accumulate abnormal amounts of ^{85}Sr on scan. New bone formation was not found in these cases. Malignant tissue was seen in the bone biopsy of 18 of 22 scan-positive lesions.

A-8-b "*^{68}Gallium as A Bone Scanning Agent.*" R. L. HAYES, J. E. CARLTON AND B. L. BYRD, (Oak Ridge Institute of Nuclear Studies)[1]

^{72}Gallium and ^{67}Ga have in the past been studied as possible therapeutic agents for sarcoma of the bone. They were ineffective therapeutically but were shown to localize selectively in certain bone tumors, primary and metastatic. Because of the vast improvements in scanning instrumentation since these studies were made, we believe that radioisotopes of gallium may now be of diagnostic use in bone scanning. Of the available radioisotopes of gallium, ^{68}Ga seems best suited for this purpose. Its half-life is 68 min and its gamma-ray emission is almost entirely 0.51 mev annihilation radiation. Further, it is readily milked from a long-lived ^{68}Ga ($T_{½}$ = 280 d) cow. If ^{68}Ga is administered to rats intravenously as the EDTA chelate (form in which ^{68}Ga is milked from the cow), it does not localize in bone. When, however, ^{68}Ga is administered as gallium citrate, localization does occur. The effect of gallium carrier level and the molar ratio of citrate to gallium on the distribution of ^{68}Ga have been studied in the rat. At carrier levels of gallium in excess of 1 mg/kg and with a citrate to gallium ratio of 5, the bone/liver and bone/blood ratios are approximately 15 at 2 hr post-IV administration. With a high-resolution focusing collimator, excellent bone scans of the rat can be obtained after a laps of as little as 30 min after IV administration of ^{68}Ga. Clinical trials of ^{68}Ga are planned.

[1]Under contract with the U. S. Atomic Energy Commission.

SESSION: THERAPY

Chairman, WILLIAM S. MAXFIELD

Area B

B-7-a "*Radiobiological Effects of ^{90}Yttrium Containing Ceramic Pellets in Brain.*" M. J. BRENNAN, L. E. PREUSS, J. H. BURROWS, D. M. LEAHY, M. W. NICHOLSON, K. D. MCGINNIS AND J. BEBIN

The distribution of radiobiological damage in tissue following the intra-arterial injection of 55 micron ceramic pellets containing ^{90}yttrium has been studied in the brain. Three rhesus monkeys and three rabbits were given direct intracarotid injections of pellets suspended in carbapol. Control injections with nonradioactive pellets did not produce acute or late signs of central nervous deficit nor any detectable histological alterations. However, radioactive samples at a specific activity of 2.5 mc/ml caused multiple lesions 0.5 to 2.0 mm in diameter. Within 96 hours, intense damage was produced in these foci. Fiber tracts, glial elements, and neuron bodies were destroyed and there was absence of glial reaction in these zones. Hemorrhage was not produced.

The topography, geometry, statistics of distribution, and histological characters of the effects will be described and illustrated on the basis of whole organ and thick-slice scans, radioautographs, and microphotographs. It is concluded that ^{90}Yttrium pellets cause acute multifocal necrosis in central nervous tissue.

B-7-b "*The Use of Low Energy Photon Emitters for Interstitial Therapy.*" K. A. LATHROP AND P. V. HARPER, (Argonne Cancer Research Hospital, Chicago, Illinois)[1]

Low energy photon emitters may produce gamma radiations, or fluorescent x-rays following internal conversion or electron capture. To be useful, they should have suitable penetration in tissue and a reasonably long half-life to preclude the handling of large millicurie quantities to produce therapeutic radiation fields; and production methods and costs must be within reach. The chemical form of the isotope poses some limitations 10 day ^{131}cesium, which emits 30 kev fluorescent x-rays, must be used in sealed applicators, as must 60 day ^{125}iodine which emits principally 27.3 kev x-rays, as does 58 day ^{125M}tellurium (daughter of 2.7 year ^{125}antimony). The great advantages of the low energy emitters are the ease of handling and shielding, and the localization of the radiation field. The penetration of the low

energy photons through tissue, even when the half value layer is as low as one cm, is sufficient to give a relatively uniform radiation field in the region of the implant. Our clinical experience has been limited to this energy using ^{103}palladium as the radiation source. The material is produced either by proton activation of ^{103}rhodium or neutron activation of ^{102}palladium. Twenty-five patients with a variety of inoperable lesions have been treated with various forms of implants during the past five years, and significant palliation has been achieved in many cases.

[1]Operated by the University of Chicago for the United States Atomic Energy Commission.

B-7-c *"The Destruction of Small Volumes of Tissue with β Sources."* P. V. HARPER AND K. A. LATHROP, (Argonne Cancer Research Hospital, Chicago, Illinois)[1]

What started out over ten years ago as an effort to achieve hypophysectomy without major surgery has blossomed into a number of experimental and clinical projects. Destruction of the hypophysis with implanted ^{90}yttrium sources has become a rather widely used procedure. Recently the technique was modified by the use of a strong ^{90}strontium-^{90}yttrium source applied for a short time. This was attended by considerably fewer complications and produced equally good results. The same source has been used extensively by the neurosurgeons for interruption of the pain tracts in the spinal cord (at C-2) without open operation.

Yttrium sources have been used most successfully by the neurologists to produce experimental lesions of the thalamus in monkeys. The cardiovascular group has used them in attempts to produce experimental coronary damage, and to produce myocardial infarcts and conduction defects. Smaller lesions have been produced with ^{106}palladium sources in the globus pallidus for the control of Parkinsonism, and the auditory physiologists have produced medullary lesions in cats with similar sources. The opthalmologists have studied the effect of intense β radiation dosage to the sclera using ^{90}yttrium sources.

The characteristic which makes these sources so favorable for the above studies is the very sharp localization of a very intense radiation field, producing destructive radiation a millimeter or less away from trivial radiation, so that the lesions are very discrete, well controlled, and circumscribed. The original photographic dosimetry using the method of Tochilin and Golden appears to be satisfactory.

[1]Operated by the University of Chicago for the United States Atomic Energy Commission.

B-7-d *"Polyploidization of Human Chromosomes Induced In Vivo and In Vitro with Ionizing Radiations."* CARLOS E. NASJLETI, (Veterans Administration Hospital and University of Michigan School of Dentistry, Ann Arbor, Michigan)

Chromosomal aberrations were demonstrated in cultured leukocytes from patients treated with x-rays and ^{131}I. A survey of chromosome damage in patients having therapy for malignancies is in progress. Seventy-two hour leukocyte cultures using Moorhead *et al* method were established, before, during, and after therapy in 12 patients: 3 treated with x-rays, 4 with gamma rays, and 5 received radioactive iodine orally. For the *in vitro* studies, one-hundred hour leukocyte cultures were made using blood from 5 normal individuals. Duplicated aliquots were made, planted and incubated at 37°C in an atmosphere of 5% CO_2 and 95% air. Five aliquots, one from each blood (controls) were undisturbed, the other 5 were irradiated at 48 hours and reincubated. X-radiation was administered with a conventional Westinghouse therapy machine, and each culture vessel received 200r total dose. Chromosome karyotypes from baseline and controls were normal. Aberrations were present in the irradiated series, consisting of: breaks, translocations, polyploidy, and endoreduplication of chromosomes. Chromosomal analysis shows, that polyploidy and endoreduplication were present, up to 11 per cent in *in vivo*, and up to 10 per cent in *in vitro* preparations from treated cultures. Short-term cultures of human leukocytes provide a satisfactory system in which to examine irradiation effects. Since, euploidy was constantly high in unirradiated cells from both sources, the appearance of ploidy and endoreduplication could be a valuable criterion for measuring radiation effects, this not only in humans, but also in experimental animals.

SESSION: CIRCULATORY DYNAMICS

Chairman, RAYMOND L. LIBBY

Area B

B-8-a *"Serial Determination of Cardiac Output From Precordial Isotope Dilution Curves."* HORST ZEKERT, FRANCIS K. HERBIG AND THEODORE COOPER, (St. Louis University, St. Louis, Missouri)

In 73 subjects 118 dilution curves were recorded simultaneously by precordial sensing of emitted radioactivity with a collimated radiation detector and by densitometric measurement of dye concentration in brachial arterial blood following rapid injection of a bolus of an indocyanine green–RIHSA ^{131}I mixture into the antecubital vein. Optimal detector probe placement, guided by fluoroscopic localization of the proximal ascending aorta, and utilization of a large crystal resulted in satisfactory dilution curves with an activity as little as four microcuries. The coefficient of correlation for the two methods is 0.84. In order to test the isotope method under conditions of altered cardiac output, determinations were carried out before and after 1 mg of atropine intravenously. The activity required for satisfactory precordial dilution curves during the second and third determination was 8 and 12 μc, respectively. An increase in cardiac output induced by the administration of atropine was demonstrated by both methods, although the quantitative changes were not necessarily identical.

B-8-b *"Radiotracer Dilution Studies in Single Tube Systems:*[1] *Significance to Radiocardiography."* M. M. AKCAY, D. E. JOHNSON AND G. V. TAPLIN, (University of California at Los Angeles and the Los Angeles County Harbor General Hospital)

Recent studies with radioalbumin macroaggregates (RAMA) suggested that this agent might be used in quantitative radiocardiography, if the variables affecting an externally recorded dilution curve were more clearly defined. Therefore, a systematic series of experiments was conducted with single tube model systems.

The parameters of an externally registered indicator dilution curve are affected by three main variables: flow, dilution volume, and detected volume. The area under the dilution curve is not only inversely proportional to flow but is *also directly proportional to detected volume.* Mean transit time, (MTT) peak to peak time, (PPT) and transit time (TT) are not affected by detected volume, but configuration time is affected by both dilution and detected volumes. Dilution volume calculated from FXT = V does not include the detected volume. MTT values are 18 per cent longer when calculated from dilution curves registered at 500 msec time intervals than those registered at 50 msec. PPT may replace MTT for volume measurements by applying an 8 per cent correction. The height of the dilution curve is not affected by flow. It is inversely proportional to dilution volume and directly proportional to detected volume.

The results of these studies are being applied to the calculation of cardiac output and right heart blood volume from undistorted RAMA radiocardiograms.

[1]These studies were supported by Contract AT(04-1)-GEN-12 between the U.S. Atomic Energy Commission and the University of California at Los Angeles.

A-8-c *"Primary and Metastatic Bone Tumor Scanning with ^{18}F."* H. J. DWORKIN, N. F. MOON, P. D. LAFLEUR AND R. J. LESSARD, (University of Michigan Medical Center, Ann Arbor, Michigan)

The principal disadvantages of ^{85}Sr for bone scanning are excessive absorbed radiation dose, low count rates, excretion in feces, postdose delay for a day or two before scanning. ^{87m}Sr circumvents most of these problems but availability may be erratic and target to nontarget differences also are small.

Since the report of Blau and Bender, we have developed an improved, low ^{3}H, rapid

method of ^{18}F production and explored the use of ^{18}F in 25 dogs and 30 patients. Less than 15 per cent of the dose remains in the blood at 1 hour and less than 5 per cent at 4 hours. Fifty per cent or more is excreted in the urine (flow dependent) within 6 hours. External point counting and bone sample counting *in vitro* demonstrated that the average concentration of ^{18}F in tumors and healing fractures is 3 times that of nearly normal bone. Uptake of ^{18}F was seen in fractures before callus formation was visualized by roentgenogram and persisted in dogs at least 180 days after fracture and for at least 120 days after apparent complete healing.

^{18}F concentrated in adolescent epiphyses (but not in adult epiphyses) and in areas of active rheumatoid arthritis. The apparent concentration is not due to ^{18}F in the blood pool as blood activity and bone activity rise similarly but blood activity falls much more rapidly. Concentration in primary bone tumors is not limited to reactive bone but also occurs in the tumor proper.

There have been no cases of a negative scan in the face of positive x-rays and/or biopsies. Scans in three patients were positive before roentgen diagnosis of tumors in bone could be made. Chondrosarcoma, osteochondroma, Ewing's sarocma and giant cell tumor, all proved by biopsy, were positive on bone scan. Metastatic tumors to bone visualized by scan included: breast, renal cell, malignant melanoma, prostate, lung and reticulum cell sarcoma.

A-8-d *"Whole-Body Scanning of the Bone Marrow Organ."* R. M. Knisely, G. A. Andrews, R. Tanida, C. L. Edwards and G. C. Kyker, (Oak Ridge Institute of Nuclear Studies, Oak Ridge, Tennessee)[1]

Radioisotopic scanning has been successfully applied to the evaluation of the hematopoietic organ. The objective is to delineate with radioisotopic compounds the size and location of functioning marrow and to quantitate if possible the extent of abnormalities produced by marrow disorders or responses to various stresses. We have delineated the marrow by intravenous radioactive colloids, particularly ^{198}Au; others have used ^{52}Fe. Improved isotopic labels and improved colloidal properties promise lower exposures and more favorable marrow localizations, for example ^{159}Gd. Instrumentation has included the gold-tungsten collimator-detector for area views; the linear scanner for profiles and semi-quantitations; and a new whole-body scanner, which provides a 5:1 reduction ratio view of the patient's body. Patterns of marrow alteration have been collected and analyzed in patients with acute leukemia, chronic leukemia, multiple myeloma, lymphoma, hemolytic anemia, polycythemia vera, and in patients with local marrow lesions. Some unexpected and unexplained findings include marrow expansion where none was expected, lack of expansion in situations where it was expected, and some asymmetry especially of expansion of marrow into lower extremities.

[1]Under contract with the U. S. Atomic Energy Commission.

A-8-e *"Scanning of Bone Marrow in Animals."* Granvil C. Kyker and John J. Rafter, (Oak Ridge Institute of Nuclear Studies)[1]

Selection of radioisotopic preparations suitable for scanning functional bone marrow includes two possible approaches: metabolic incorporation of a natural elemental tracer (iron) or selective localization of unnatural elemental tracers in a manner that parallels hemapoietic activity. The lack of a convenient natural tracer usable with most present scanners has prompted a comparative study of various new colloidal preparations of unnatural elemental tracers with colloidal gold in animals. These include a technetium-sulfur sol, metal complexes, and citrated hydrous oxides of selected elements of the lanthanide series. Most of the tracer metal studies used ^{144}Ce (282 d) for convenience. The results with this element predicted very closely those obtained with two other lanthanide isotopes that have properties suitable for medical use: ^{159}Gd, 18 hr, and ^{165}Dy, 2.32 hr. These new isotopes were reactor-produced in high yield and purity from enriched ^{158}Gd and ^{164}Dy (28 and 60 mc/mg delivered, respectively). When radiocolloidal gold and citrated hydrous oxides of Ce, Gd, and Dy were compared in the rat, rabbit, guinea pig, dog, and nutria, the rabbit proved the best experimental animal for localization studies of the marrow. The ratio of radioactive isotope in bone

[1]Under contract with the U. S. Atomic Energy Commission.

marrow (femur) to liver averaged 0.9, 1.3, 1.5, and 1.2, respectively, for Au, Ce, Gd, and Dy. The lanthanon hydrous oxides delineated marrow in rabbits better 4 or 5 hr after intravenous administration and the pattern seen with long-lived cerium remained the same for several days. ^{165}Dysprosium, therefore, decays too fast for best results. On the other hand, ^{159}Gd appears worthy of clinical evaluation.

A-8-f *"Spleen Scanning with ^{99m}Technetium Sulfur Colloid and the Scintillation Camera."* J. P. PETASNICK AND A. GOTTSCHALK, (Chicago, Illinois)

^{99m}Technetium sulfur colloid has proved to be a good agent for imaging the spleen. Excellent quality scintiphotos can be obtained using the scintillation camera with multiaperture collimator. Exposure times of only 1 to 5 minutes are needed when an intravenous dose of 1 to 3 mc of this agent is used. This gives a dose of less than one rad to the liver, spleen and bone marrow.

Because of the short time needed for each scintiphoto, anterior, posterior and lateral views are routinely obtained. Occasionally it is necessary to use an oblique angle on the lateral projection to separate the liver and spleen. The resultant examination provides three dimensional information about splenic size, shape and location.

SESSION: MISCELLANEOUS

***Chairman*, W. J. SIMPSON**

Area A

A-9-a *"Pattern and Rates of Removal of Particulate Material from the Respiratory Tract in Man."* DONALD E. TOW, HENRY N. WAGNER, JR., VINCENT LOPEZ-MAJANO AND DONALD F. PROCTOR, (The Johns Hopkins Medical Institutions and the Veterans Administration Hospital, Baltimore, Maryland)

Increasing air pollution in addition to the continuing problem of respiratory infections has focused attention on the function of respiratory mucous membranes. Objective techniques for its *in vivo* measurement in man have not been completely satisfactory. One of the functions of the respiratory mucous membrane is the maintenance of a blanket of mucus, on which inhaled particulate matter is continuously propelled by ciliary activity. We have used ^{131}I labeled aggregates of human albumin in studies of mucociliary activity of both the nasal passage and the tracheobronchial tree. Serial scintillation scanning delineated the pattern of movement of the particles; two external detectors determined the transit time required for the labeled particles to pass between two fixed points. In the study of the nasal passage 10-20 μc of labeled macroaggregates of human serum albumin (^{131}I MAA) were placed at various positions in the nasopharynx. Scintillation scanning was performed at two to five minute intervals to determine the pattern of flow as the material moved into the pharynx. Results from 38 studies in 19 normal subjects indicated an average transit time of 6 mm per minute (range 3-9 mm). No movement was detected in the unciliated anterior portion of the nasal passage. In the study of the tracheobronchial tree, a polyethylene catheter was inserted through an 18-gauge needle in the crico-thyroid membrane. Fifty to 100 μc of labeled aggregates of human serum albumin (^{131}I AA) were injected with minimal physiological disturbance. Scanning was performed at 15 to 45 minute intervals. Results from studies in normal subjects indicated an average transit time of one cm per minute as the particles moved toward the pharynx. In patients with pulmonary tuberculosis islands of relative immobility were demonstrated, presumably due to local abnormality of ciliary activity. The techniques provided simple and objective means of studying respiratory mucociliary function in different environmental conditions and pathological states.

A-9-b *"Tumor Scanning with Radioactive ^{131}Cesium."* N. DAVID CHARKES, DAVID M. SKLAROFF AND ROBERT E. CANOTR, (Albert Einstein Medical Center, Northern Division, Philadelphia, Penna.)

While performing a myocardial scan with ^{131}cesium on a patient with widely disseminated malignant lymphoma, the isotope was seen to localize within the pulmonary lesions. We have subsequently studied 16 patients with histologically verified cancer with ^{131}cesium and have obtained satisfactory scans in 7 out of 12 cases. In all of the positive scans the tumors were within a few inches of the skin surface. Scans of three intraabdominal lesions were unsuccessful. The greatest tumor-to-background ratio occurred within a few hours of injection, presumbaly related to tumor blood flow. In selected cases external measurements made over tumors showed greater ^{131}Cs uptake than over heart and liver. Biopsies of tumor in four cases revealed greater isotope concentration than in normal tissues, but in one patient with renal carcinoma the concentration of radiocesium 1½ hours postinjection was less than in normal kidney. The chief drawback to scanning with ^{131}Cs is the marked attenuation of its soft x-ray (29.4 kev) by overlying soft tissues.

A-9-c *"The Basis for Detection of Myocardial Infarcts by Photoscanning."* R. J. Gorten, B. H. McGraw, G. D. Lumb, L. B. Hardy and J. R. Stokes, (VA Hospital, Durham, N. C. and James Walker Memorial Hospital, Wilmington, N. C.)

Diagnosis of myocardial infarcts by photoscanning has been reported recently by Carr *et al* and by Evans *et al.* The following studies were undertaken to correlate diagnostic scans with direct tissue examinations and to more fully appreciate the reasons for abnormal uptake of radioactive chemicals.

Sixty-eight pigs surviving myocardial infarcts produced by application of an ameroid constrictor to the left circumflex artery were given ^{203}Hg chlormerodrin intravenously 3-5 days (Group I), 6-8 days (Group II), and 9-12 days (Group III) after arterial occlusion by the constrictors.

By photoscanning, "hot" areas could be identified in the distribution of the circumflex artery on 75 per cent of excised intact hearts and more accurately delineated in "unrolled" specimens. There was excellent agreement as to site and extent with gross and histologic evidence of myocardial damage. Observations indicate that selective uptake of ^{203}Hg chlormerodrin occurs in areas of extensive as well as patchy necrosis.

The scans were graded by the degree of contrast between the "hot" area and the rest of the myocardium. This was generally greatest in Group I. In scans of Group II there was a less marked and also less varied pattern of selective uptake of ^{203}Hg chlormerodrin. Whereas in the first group infarcts could be identified on all scans, only ⅔ were positive in the second group. While about ⅔ were also detected in Group III scans, these were all of lesser contrast. One would guess that selective uptake ceases to occur when fibroblastic activity becomes pronounced.

On the basis of additional studies, vessel congestion and inflammation are not thought significant in the demonstration of infarcts. It is more likely that localization of mercury occurs in damaged and degenerating myocardial fibers but not in fibrous replacement or in normal myocardium. This would explain the high contrast in early infarcts and less obvious detection in the older ones and the absence of areas of increased uptake in sham-operated animals.

A-9-d *"I.H.S.A. Joint Scans."* William S. Maxfield, Thomas E. Weiss, Paul J. Murison, Roger H. Tutton and John U. Hidalgo, (Ochsner Clinic, Ochsner Foundation Hospital, New Orleans, Louisiana)

Iodinated Human Serum Albumin ^{131}I (I.H.S.A.) has been used as a tracer for scintillation scanning of the joints of the extremities in a series of patients with normal joints and patients with arthritis. The types of arthritis studied include rheumatoid arthritis, osteoarthritis and gout. Prior to administration of the I.H.S.A. the thyroid gland has been blocked with Lugol's solution. The I.H.S.A. has been administered intravenously in a dose of 25 μc per 10 pounds of body weight or by direct injection of 15 μc into a joint space. Joint scanning will be compared to routine methods of evaluating arthritic involvement of a joint. Preliminary data sug-

gests that joint scanning is a sensitive, objective method for evaluation of the degree of arthritic involvement of the synovial membrane of a joint.

A-9-e *"Diagnosis of Placenta Previa by Photoscanning Using ^{99m}Tc Labeled Albumin."* STEVE M. LARSON AND WIL B. NELP, (University of Washington, Seattle)

To date, 18 patients in the third trimester of pregnancy (11 selected normals and 7 patients with vaginal bleeding) have been scanned following intravenous injection of 200 to 500 μc of ^{99m}Tc–labeled albumin. ^{99m}Tc was labeled to human albumin, according to the method of Stern. Extensive sterility and pyrogen testing of the effluents of BNL ^{99m}Tc generators, commercial resins and the labeled product have been performed in conjunction with these studies. In each patient the size and position of the placenta was readily appreciated. Placental position was confirmed at the time of delivery by manual exploration of the uterus or by indirect inspection. Three of the patients had placenta previa and were delivered by cesarean section. In these patients, the photoscan showed the correct location of the placenta and provided a valuable adjunct in their preoperative management. The placental transfer of ^{99m}Tc was 3 per cent or less (based on the concentration of radioactivity in fetal plasma) when studied up to 23 hours following injection of ^{99m}Tc albumin into the mother. In contrast the free pertechenite ion rapidly entered the fetal circulation (70% equilibration in 30 minutes). Radiation exposure to the fetus from the procedure is estimated at 5 millrads or less. Photoscanning of the placenta promises to be very useful for the diagnosis of placenta previa and the management of third trimester bleeding.

A-9-f *"Anteroposterior and Lateral Placental Localization by Polaroid Color Scanning."* HENRY L. JAFFE, RALPH ADAMS AND LEON KROHN, (Cedars of Lebanon, Los Angeles, Calif.)

Until recently, placental localization was limited to establishing the diagnosis of placenta previa. Now the knowledge of the location of the placenta has taken on greater significance because of the development of the technique of amniocentesis. This requires the precise knowledge of the placental site in order to minimize the risk of placental puncture when performing amniocentesis.

The authors have designed and built a seven port straight bore collimator for use with conventional scanners in order to obtain satisfactory localization of the placenta in both the anteroposterior and lateral positions. After 10 μc of ^{131}I labeled human serum albumin is injected intravenously into the maternal circulation, our seven port collimator used with a three inch detector records about 1,000 cpm over the placental site. The seven port collimator with a five inch detector focused at eight inches records about 2,000 cpm over the placenta. The coarse spatial resolution required for adequate counting statistics is not a serious hindrance to placental localization.

Placenta scans in a series of 31 patients will be presented. Simultaneous black and white and color scans were recorded in both anteroposterior and later positions. The lateral scan shows the anterior or posterior position of the placenta very clearly.

B-8-c *"A Method for the Study of the Peripheral Circulation in Man."* HENRY N. WAGNER, JR., ELLIS JONES, DONALD E. TOW AND JAMES K. LANGAN, (The Johns Hopkins & Veterans Administration Hospitals, Baltimore, Md.)

Evaluation of the peripheral circulation in man is usually based upon observations of skin color and texture, temperature and sweating activity, or upon measurements of the clearance of radioactive tracers from depot injection sites, venous occlusion plethysmography, indicator dilution techniques or thermal conductivity. The method described in this report is based upon delineation and quantification of the distribution of radioactivity throughout the leg following intra-arterial injection of macroaggregates of human serum albumin labeled with ^{131}I (MAA ^{131}I). Because of the exceedingly small quantities injected and their rapid metabolism, the particles cause neither hemodynamic nor toxic effects. By comparing the concentration of radioactivity from one region to another, one obtains the relative distribution of blood flow through

vessels whose diameter is less than that of the injected aggregates.

Quantification of the radioactivity in the areas delineated by scanning was based upon densitometric evaluation of photoscans and upon external counting with a specially constructed stationary detector.

The distribution of radioactivity and therefore the blood flow corresponded to the distribution of the muscle masses. In normal persons the regions of the knee and ankle were relatively avascular. In patients with peripheral vascular disease, regional circulatory abnormalities could be delineated.

Advantages of the technique are technical simplicity, safety, ready availability and provision of information that has been unavailable with previous techniques, namely regional muscle blood flow. Effects of a variety of physiological and pathological conditions upon peripheral blood flow could be demonstrated.

B-8-d *"External Monitoring of Cerebral Blood Flow Using ^{133}Xenon Inhalation."* **ALBERT E. JOHNSON AND FRANK GOLLAN, (VA Hospital, Coral Gables, Florida)**

Cerebral blood flow measurements in man using radioactive xenon inhalation and extracranial recording are open to criticism since the results obtained may not only reflect extra and intracranial blood flow but also the volume of radioactive gas distributed in the oral, nasal, sinus and middle ear cavities. These serious objections against the inhalation of ^{133}xenon as compared to its injection into the internal carotid artery have deterred most investigators from using this approach. We have found that careful shielding and the strict constancy of geometry of the sitting subject and the collimated detector give reproducible results in the same subject and that the variability is due to physiological rather than technical factors.

Carbon dioxide tesion of inhaled, exhaled and alveolar air was manitored with an infrared analyzer and it was found that at a normal alveolar carbon dioxide tension the average cerebral blood flow amounted to 42 ml/100 g/min. When the alveolar carbon dioxide tension was gradually raised by rebreathing oxygen in a closed circuit, a linear increase in cerebral blood flow was recorded. The coefficient of correlation of cerebral blood flow and carbon dioxide tension amounted to 0.88.

Since these values agree with those reported in the literature using other inert gases and methods of administration and counting, this atraumatic and harmless method may lend itself for widespread clinical investigations.

B-8-e *"Measurement of Brain Blood Pool Hematocrit."* **W. H. OLDENDORF, MASAMI KITANO AND SHIRO SHIMUZU, (VA Center, Los Angeles, Cal.)**

Because the hematocrit of capillary blood is lower than found in large vessels, the mean hematocrit of organs is usually lower than in large vessels. To determine the hematocrit of the human brain blood pool, separately labeled red cells and plasma were injected intravenously and allowed to distribute uniformly. Uniform efficiency cranial detectors measured the amount of each label in the cranial portion of the head.

^{51}Cr red cells were injected and four minutes allowed for distribution. A four minute scaler count of the cranium was made. This count represents cranial red cell volume. ^{51}Cr albumin sufficient to triple the first scaler count was administered and four minutes allowed for distribution. A four minute scaler count was then made. This count, after subtracting the red cell count, represents cranial plasma volume.

In the middle of each scaler counting period, a venous blood sample was drawn. By comparing the ratio of red cell to plasma volumes in the cranium and a similar ratio in the drawn blood samples, a mean brain blood hematocrit was derived.

An alternate technique was evaluated utilizing RISA as the plasma label because of its availability and greater stability. By introducing a correction factor to make the efficiency of cranial and blood counting equipment comparable, a similar brain blood pool hematocrit was obtained.

A total of 32 cases have been studied, 16 by each method. The brain hematocrit was found to be approximately 85 per cent of the vein hematocrit.

B-8-f *"Regional Pulmonary Blood Flow—Clinical and Physiological Studies with ^{133}Xenon."* GERALD L. DENARDO, MAJOR, M. C., JON B. GLAZIER, CAPTAIN, M. C., PAUL J. LEACH, LIEUTENANT, M. S. C., (Fitzsimmons General Hospital, Denver, Colorado)

A whole body profile scanner, magnetic tape and read out system, was specifically designed and constructed for use in the study of pulmonary ventilation-perfusion relationships utilizing ^{133}xenon. The instrumentation and technique have been previously described. Clinical and physiological studies have been performed during the past 18 months. Results are formulated in terms of ventilation-perfusion relationships, as well as the proportion of total ventilation or perfusion distributed to a specific lung area. Physiological studies of normal and emphysematous patients in the horizontal, upright, 30° head-up, and 30° head-down positions indicate that both ventilation and perfusion are greater in the dependent portions of the lung, although the changes in perfusion are more marked than those in ventilation. These changes are believed to be at least in part hydrostatic in origin.

Clinical studies of patients with pulmonary emboli, cysts and effusion, and mitral valvular disease have been performed. All patients with proven pulmonary emboli had abnormalities of regional perfusion, but not all of these patients had abnormalities of regional ventilation. Patients with pulmonary cysts had abnormalities of regional ventilation and perfusion, as did patients with pleural effusion. In mitral valvular disease, there is a redistribution of ventilation and perfusion with a decrease in the basal portions of the lung, similar to the changes occuring in the head-down position or with exercise. Examples of normal and abnormal studies in these situations will be demonstrated, and compared with studies of regional pulmonary blood flow using radioiodinated macroaggregated albumin. The advantages of the technique over other methods of determining regional perfusion are speed, simplicity and sensitivity. These factors are important in clinical studies, for example, in the diagnosis of pulmonary embolism. Experience has verified the clinical as well as physiological usefulness of the method.

SESSION: MISCELLANEOUS

Chairman, RICHARD P. SPENCER

Area B

B-9-a *"Transfer Rates of Gamma Globulin Between Cerebrospinal Fluid and Blood Plasma in Multiple Sclerosis."*[1] STUART W. LIPPINCOTT, SAMUEL KORMAN AND LOUIS C. LAX, (Winston-Salem, N.C. and New York)

The origin of the excess gamma globulin present in the cerebrospinal fluid of patients with multiple sclerosis is at present unknown. If all of it comes from and returns to the blood plasma, transfer rates between plasma and cerebrospinal fluid should be the same in both directions, provided the gamma globulin within the cerebrospinal fluid is in a dynamic steady state. It has been suggested, however, that part or all of the excess gamma globulin may originate in the central nervous system and be associated with an autoimmune process capable of initiating or augmenting demyelinization in the brain. If this is so, the transfer rate from cerebrospinal fluid to blood plasma should be greater than in the opposite direction.

To investigate these rates in patients with multiple sclerosis, ^{131}I labeled gamma globulin was first injected intrathecally, and specific activities were determined in serial cerebrospinal fluid and blood plasma samples. Subsequently, the experiment was repeated in each subject with the same sampling procedure, except that the ^{131}I labeled gamma globulin was injected intravenously.

The rate of appearance of gamma globulin in the cerebrospinal fluid, as determined by intrathecal injection of ^{131}I labeled gamma globulin, was 1.3 ± 0.91 (S.D.) mg/hour. The rate of appearance of gamma globulin in the blood plasma, as determined by intravenous injection of the tracer, was 312 ± 103 (S.D.) mg/hour. In addition, the average transfer rate of gamma globulin from the cerebrospinal fluid to the blood plasma was 0.43 mg/hour, as determined by intrathecal injection of ^{131}I labeled gamma globulin. This is more than ten times as great

as the average transfer rate from blood plasma to cerebrospinal fluid, which was determined by intravenous injection of the tracer to be 0.037 mg/hour.

These results indicate that gamma globulin does not appear in the cerebrospinal fluid solely as a result of exchange from the blood plasma, and suggest that in multiple sclerosis the gamma globulin in the cerebrospinal fluid may come from the central nervous system as well as from the blood plasma.

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*(Bowman Gray School of Medicine, Winston-Salem, North Carolina, Jewish Chronic Disease Hospital, Brooklyn, New York and the Medical Research Center, Brookhaven National Laboratory, Upton, Long Island, New York).

[1]This work was supported by National Multiple Sclerosis Society Grant 339.

B-9-b *"Direct Venous Absorption of Albumin (^{131}RIHSA) from Subcutaneous Space."* DR. HAROLD H. SAGE, (New York University, School of Medicine)

It is now generally accepted that plasma protein normally leaks out of blood capillaries into the interstitial space. Certain proteins leak out in larger amounts than others depending on the relative size of molecules. Investigators have generally concluded that all or almost all proteins in the interstitial space, particularly those above 20,000 mol wt, enter lymphatics from which they do not escape until they are returned to the blood through anatomotic connections from the lymph vessels.

Experiments were designed to determine the amount of albumin absorbed directly into the venous blood following subcutaneous injection of ^{131}RIHSA in humans. The great saphenous vein was cannulated at the ankle within four inches of the site of subcutaneous injection of ^{131}RIHSA in the foot and quantitative isotope measurements were made of blood samples at 1, 3, 5, 15, 30, 45, 60, 90, 120 minutes after injection. Blood samples were also obtained simultaneously from an upper extremity vein. All samples were analyzed for albumin bound ^{131}I as well as free ^{131}I. Prior to injection, samples of ^{131}RIHSA were assayed for per cent of free I^{131} and ^{131}I albumin.

Radioactivity in blood samples was calculated in microcuries. Total radioactivity was calculated by multiplying radioactivity per cc by the rate and time of flow. Measurements were also made of disappearance amount of ^{131}I and ^{131}RIHSA, thyroid gland ^{131}I uptake and urinary ^{131}I.

Samples of saphenous blood taken one minute after injection did not show any radioactivity, thus excluding vein penetration. At 5, 15, 30, 60 and 120 minutes all saphenous blood samples in all volunteers contained significant radioactivity in both ^{131}I albumin bound and free ^{131}I form. Diffusion of ^{131}I albumin into the saphenous vein follows an exponential curve similar to leakage of albumin out of capillaries. Free ^{131}I is absorbed into the venous circulation much more rapidly than albumin bound ^{131}I. ^{131}I albumin percentage of total ^{131}I radioactivity in saphenous blood increases from a range of 56-72 per cent at five minutes to 98-99 per cent at two hours. At five minutes free ^{131}I in the saphenous blood constitutes 1.2 to 3.5 of the total disappearance amount whereas at one hour it is less than 0.1 per cent.

Although the greater part of the amount of ^{131}I albumin which disappears from the injected site is transported through lymphatics, direct absorption of ^{131}I albumin into the great saphenous vein represents a significant part of the disappearance of ^{131}I albumin (^{131}RIHSA) from the injection site. As measured, direct blood absorption of ^{131}I bound to albumin constitutes 2.8 to 8.5 per cent of the total radioactivity which has disappeared from the injection site for the first five minutes, 3.9 to 6.9 per cent for one hour and 1.95 to 6.85 per cent for two hours.

B-9-c *"Sodium Selenate (^{75}Se) A Substitute for Sodium Sulfate (^{35}S) for Measuring Extra Cellular Fluid Space."* S. N. ALBERT, E. F. HIRSCH AND C. A. ALBERT, (Washington Hospital Center, Washington D.C.)

Almost 20 per cent of the body weight is extra cellular fluid which is in rapid equilibrium with the intravascular fluid compartment. The importance and the role this large fluid space plays in regulating blood volume, maintaining a buffer zone between the cellular fluid space and the intravacular compartment, and the relationship between this volume and disease has been explored to a very limited extent. In the last decade or so the E.C.F. space

was explored by applying the dilution principle and utilizing molecules which would cross the capillary membrane, diffuse in the E.C.P. and not penetrate the intracellular fluid space. Sulfate labled with ^{35}S has been utilized with success to measure a sulfate space closely associated to the E.C.F.

35 S is a weak beta emitting nuclide. The method for measuring this isotope is tedious and requires special gas flow counters. There is ample evidence in the literature that selenium behaves and is metabolized in the body in the same manner as sulfur. ^{75}Se has a wide range of strong gama emissions and can be easily detected with available scintillation counters. Studies in animals will be presented to demonstrate that the space measured with sodium selenate (^{76}Se) labeled approximates the values obtained with sodium sulfate. A triple tracer technique whereby ^{51}Cr labeled red cells ^{125}iodinated albumin and ^{75}selenate sodium are administered together and blood samples are analyzed for each isotope with a scintillation counter and a pulseheight analyzer will be described. The procedure is simple and will enhance further studies on this little explored fluid space. This will permit determining its value as a diagnostic tool in clinical medicine.

B-9-d *"The Interrelationships Between Distribution of ^{86}Rubidium and Myocardial Blood Flow."* SHELDON H. STEINER AND ROBERT D. KING, (Indianapolis, Indiana)

The early uptake phase following a bolus intravenous injection of tracers of potassium has been suggested as a measure of the nutrient myocardial blood flow fraction of the cardiac output. In 32 dogs, both coronary arteries were perfused with left atrial blood at flows calibrated from 45-230 ml/min. Three hundred μc of ^{86}RbCl, and 2.5 mg of indocyanine green were injected simultaneously into the vena cava. Cardiac output was determined by indicator dilution using a photodensitometer. Since myocardial tracer uptake shows negligible change from the maximum value obtained during initial delivery to at least two minutes postinjection, the heart was excised after one minute, and the ^{86}Rb uptake fraction was determined. This fraction, multipled by cardiac output, was defined as nutrient myocardial blood flow. At pump flows of 227±0.9, 147±2.7, 96±11.8, 51±7.0 and 0±0 ml/min calculated flows were respectively 230±17.8, 125±8.0, 86±10.3, 60±21.3, and 21±7.0 ml/min. The correlation coefficient is + .96, and the regression equation is $y = 1.10x - 11.1$; where y = pumped flow, and x = calculated nutrient myocardial flow. Pulmonary tracer loss has been demonstrated previously to be negligible. However, the noncoronary endomyocardial contribution may be significant, and was assessed by comparing flows calculated both immediately after bilateral coronary occlusion, and after perfusion at 144-312 ml/min from a delay reservoir containing tracer free blood. Under these conditions calculated flows were respectively 17±4.5 and 19.5±10 ml/min which agree reasonably with that obtained from the y intercept of the equation. These data suggest that under certain circumstances the uptake of ^{86}Rb immediately following an intravenous injection may reflect the nutrient myocardial blood flow fraction of cardiac output. Control measurements from indicator injections into 16 trained, awake dogs averaged 134±35 ml/min, where myocardial tracer content was determined in the extirpated heart subsequent to sacrifice by electronarcosis and ventricular fibrillation.

B-9-e *"Pulmonary Clearance of Large Labeled Particles."* ANGELO TOIGO AND ERVIN KAPLAN, (Veterans Administration Hospital, Hines, Illinois)

Large carbon particles measuring between 40 and 70 microns are mixed with a gold chloride solution and allowed to stand. Gold chloride adsorbs to the carbon particles. The gold chloride is reduced to metallic gold. Four hundred milligram portions of the resulting gold-carbon compound are placed in a neutron flux and gold ^{197}Au is converted to ^{198}Au.

The labeled carbon mixture is placed in a delivery system and is deposited in the tracheobronchial tree of the subject by forced voluntary ventilation over a five-minute period.

After deposition is complete, the subject is placed between two highly collimated 2x2 sodium iodide scintillation crystals. One crystal is collimated to monitor the trachea and main stem bronchi; the other is collimated to monitor both lungs. The crystals are connected to count

rate meters through pulse height analyzers which drive a two-channel recorder. Each subject is monitored in this system for a period of two hours.

Pulmonary clearance has been studied in a group of 29 normal young males. Tracheal clearance is 90 per cent complete within two hours; lung clearance is 70 per cent complete within two hours.

Patients with chronic lung disease have been studied. In emphysema and alveolar proteinosis, tracheobronchial clearance is markedly impaired. In acute viral infections, tracheobronchial clearance is also impaired. In one instance, bracheobronchial clearance was determined serially over a five-month period following a viral respiratory infection. An initial impairment was observed followed by gradual return of clearance to normal.

B-9-f "^{75}Se *methionine Incorporation into Fibrinogen.*"[1] **HASSAN K. AWWAD AND E. JAMES POTCHEN, (Harvard Medical School Peter Bent Brigham Hospital.)**

The disappearance of intravenously injected ^{75}Se -methionine is soon followed by the appearance of the label in several plasma protein components, including fibrinogen. The specific activity of these fractions build up over a few hours to be followed by a steady drop. This provides a means of assessing both the anabolic and catabolic rates of fibrinogen metabolism.

The adavntages of this technic, using a γ-emiting label, over other methods of fibrinogen labeling will be discussed.

[1]This project is supported by Aromic Energy Commission Contract NYO-3442-7.

Teaching Sessions—Abstracts

(T-1-a) *Thyroid Diagnosis I*—A. STONE FREEDBERG, M.D. Associate Professor of Medicine, Harvard Medical School; Director of the Cardiology Unit, Beth Israel Hospital, Boston, Massachusetts.

A presentation of the current methods of evaluating thyroid function in man with radioactive isotopes.

(T-1-b) *Hematology I*—DONALD R. KORST, M.D., Head, Department of Hematology, St. Joseph Mercy Hospital, Ann Arbor, Michigan.

The use of ^{59}Fe for the study of ferrokinetics; erythropoietin assay and ^{32}P therapy.

(T-1-c) *Medical Internal Radiation Dose Calculations* EDWARD M. SMITH, D.Sc., Hospital for Special Surgery, New York, New York.

The problem of calculating the radiation dose to the patient from diagnostically administered radionuclides will be approached by asking and answering the following questions:

1. Why calculate the dose?
2. What factors go into this calculation?
3. How does one evaluate these factors?
4. How does one calculate the dose?
5. For what organs does one calculate the dose?
6. What do these calculations mean?

(T-1-d) *Scanning I—Brain & Liver* JOHN G. MCAFEE, M.D. Head, Division of Nuclear Medicine, Johns Hopkins Hospital, Baltimore, Maryland.

The various radiopharmaceuticals for cerebral and hepatic scanning will be reviewed and their biological distribution excretion and radiation dosimetry compared.

Problems in interpretation of cerebral scans will be discussed in detail including normal landmarks, normal variations, detection of neoplasms, and positive scans in nonneoplastic and extracerebral lesions. A survey of hepatic scans will be given to include normal variations and anomalies, the differential diagnosis of hepatomegaly, hepatic atrophy, single and multiple filling defects and displacements.

Representative cases from a series of over 1,200 cerebral scans and 1,000 hepatic scans will be used for illustration.

(T-2-a) *Thyroid Diagnosis II*—A. STONE FREEDBERG, M.D., Associate Professor of Medicine, Harvard Medical School; Director of the Cardiology Unit, Beth Israel Hospital, Boston, Massachusetts.

A continuation of the current methods of evaluating thyroid function in man with radioactive isotopes.

(T-2-b) *Hematology II*—DONALD R. KORST, M.D., Head, Department of Hematology, St. Joseph Mercy Hospital, Ann Arbor, Michigan.

The use of ^{51}Cr for the measurement of erythrocyte surgical and sequestration; vitamin B-12 absorption studies.

(T-2-c) *Instrumentation I—Counting Instruments* MONTE BLAU, PH.D. Principal, Cancer Research Scientist, Department of Nuclear Medicine, Roswell Park Memoral Institute, Buffalo, New York.

This brief survey of counting equipment will include detectors, scalers, pulse height analyzers and ratemeters. Particular emphasis will be placed on stable operation of scintillation counters.

(T-2-d) *Scanning II—Lung & Spleen* HENRY N. WAGNER, JR., M.D. Associate Professor of Medicine and Radiology, Johns Hopkins Medical Institutions, Baltimore, Maryland.

The measurement of blood flow to different regions of the lungs by radioisotope scanning after intravenous injection of ^{131}I labeled macroaggregated albumin is a clinically useful adjunct to pulmonary arteriography and the use of radioactive gases. Its particular advantages are safety, ease of performance and repeatability. In studies of nearly 500 patients with a variety of pulmonary diseases, lesions greater than 2-3 cm could be readily identified. Characteristics of massive pulmonary embolism are: (1) crescent-shaped areas of decreased radioactivity of the lateral borders of the scans; (2) frequent involvement of the lower lobes; and (3) decreased vascularity in areas that appeared normal on chest roentgenography. Parenchymal diseases of all types that appeared as increased opacification on x-ray examination are found to be avascular from the standpoint of the pulmonary arterial circulation.

If a mass in the left side of the abdomen is spleen, it can be identified by scanning. The technique makes possible the identification of functioning splenic tissue and reveals nonfunctioning areas due to tumor, infarct, or abscess. First real success was achieved by using heated red cells, labeled with ^{51}Cr and during development of this method, much was learned about sequestration of damaged red cells. Recent advance utilizes 1-mercuri-2-hydroxypropane, la-

beled with ^{197}Hg or^{203} Hg, a method yielding satisfactory scans with considerably simpler technique.

(T-3-a) *The Radioisotope Renogram—Current Techniques and Interpretation*

GEORGE V. TAPLIN, M.D. From the Nuclear Medicine Divisions of the Laboratory of Nuclear Medicine, University of California at Los Angeles; and the Los Angeles County Harbor General Hospital, Torrance, California.[1]

When performed after exact kidney localization, the hippuran (OIH) radiorenogram provides reliable information on differential renal blood flow, urine flow and the patency of the upper urinary passages. Its main value is in the detection and evaluation of renal vascular, parenchymal and obstructive disease affecting one kidney or ureter more than the other. Experimental and clinical evidence will be presented to demonstrate that the renogram's second segments are indicators of individual renal blood flow, the time to peak activity or to first entry of tracer into the bladder is an index of urine flow and that the renogram is closely related to the clearance of hippuran or PAH as a test of renal blood flow and to T_{mPAH} when performed after PAH loading.

Various technical aspects of radiorenography will be discussed. These include proper methods of exact kidney localization, upright vs supine or prone position of the patient during testing, the effects of hydration and fluid restriction on tracer transit time and on urine drainage, and an evaluation of different types of radiation detection and recording instrumentation. A method by which numerical values of individual renal blood flow may be obtained from the renogram and a separate determination of total renal blood flow will be presented. Pitfalls in radiorenography and means for their avoidance will be described and illustrated from selected case reports.

[1]These studies were supported by Contract AT(04-1)-GEN-12 between the U.S. Atomic Energy Commission and the University of California at Los Angeles.

(T-3-b) *Blood Volume*

SOLOMON N. ALBERT, M.D. Director, Anesthesiology Research Laboratory, Department of Anesthesiology, Washington Hospital Center, Washington, D. C.

Blood volume is measured indirectly by the dilution principle. A known quantity of tracer material is administered into the blood stream, allowed to mix, and a blood sample is removed for analysis to determine the concentration of the tracers in circulating blood.

Since blood is the sum total of the plasma volume, a solution, and red cell mass, a suspension in plasma, the extent of dilution of a single tracer in circulating blood does not actually denote blood volume. The hematocrit of the blood sample analyzed only serves as a convenience for measuring the concentration of the tracer on a whole blood sample and should be adjusted to denote body hematocrit for calculating the two components of blood. The significance of the F_{cell} ratio in the calculations will be demonstrated by showing the different dilutions obtained with two different tracers, each distributed in a specific compartment of blood.

A technique for measuring blood volume with two tracers, ^{51}Cr label red cells and ^{125}Iodinated albumin will be discussed. Both tracers can be injected simultaneously and the concentration of each tracer can be determined on whole blood samples.

The basic equations utilized to calculate blood volume with single tracers will be discussed. The validity of a blood volume determination with a single tracer and in particular radioactive iodinated human serum albumin will be presented.

(T-3-c) *Instrumentation II—Scanners*

JAMES L. QUINN, III, M.D. Director of Nuclear Medicine, Chicago Wesley Memorial Hospital, 250 East Superior Street, Chicago, Illinois.

The basic fundamentals of scintillation scanning, as we know it today, will be outlined and discussed. Emphasis will be placed on scanning systems currently available.

Optimization of scan interpretation through the intelligent understanding of the limitations of the scanning machine, the patient, the radiochemical and the interpreter will be stressed.

Specific topics include:

I. The Scanning
   - A. Patient
   - B. His Disease
   - C. The Radiochemical

II. The Scanning Machine and its Operator
   - A. Detector
     1. Collimator Design
     2. Crystal
     3. Photomultiplier
   - B. Spectometer
   - C. Data Manipulation
   - D. Data Presentation

III. The Interpreter

Physical and physiologic capability as a system integrater.

(T-3-d) *Scanning III—Pancreas and Kidney Scanning* THOMAS P. HAYNIE, M.D.

Assistant Professor of Medicine; Director, Nuclear Medicine Service, University of Texas Medical Branch, Galveston, Texas.

The kidney scan with ^{203}Hg or ^{197}Hg Neohydrin has proven a useful procedure in clinical practice in the diagnosis of a variety of renal diseases. The technique of performance and interpretation is relatively easy, though pitfalls in diagnosis exist. Kidney scans with ^{131}I Hippuran and routine scanning equipment were disappointing but scintillation cameras offer the exciting possibility of "dynamic" scans using this agent.

The pancreas scan with ^{75}Se selenomethionine though in use for several years, is still in the development stage. Many different methods of patient preparation and performance have been tried, but variability in concentration and interference of liver uptake continue to cause problems. Scanners with larger crystals and deeper focusing collimators have recently improved results and clinical experience has been promising, if not inspiring. Parathyroid adenomas have also been visualized with the use of Selenomethionine ^{75}Se, but here again results have not been uniform. Newer instrumentation may also improve these studies.