P-6 *"Design and Evaluation of a New Autofluoroscopic Camera."*[1] F. DEAVER THOMAS, WILLIAM H. BEIERWALTES, LAWRENCE W. JONES, AND GORDON M. BROWN, (Department of Internal Medicine [Nuclear Medicine], Department of Physics, University of Michigan Medical School and Bendix Aerospace Systems Division, Ann Arbor, Michigan)

A collaborative effort between the University of Michigan and the Aerospace Systems Division of the Bendix Corporation has produced a prototype autofluoroscope camera designed for the visualization of radionuclide distributions in humans.

This instrument consists of 1) a lead collimator, 2) a 9" × 1" sodium iodide scintillation crystal, 3) a fast lens system, 4) an optical image amplifier tube, 5) an optical transfer lens system, 6) a fast photographic recording system, and 7) mechanical means for positioning the camera adjacent to the patient. Collimation is provided by a choice of various interchangeable pinhole or multihole collimators. The scintillations produced by gamma-ray interactions in the NaI crystal are viewed by a fast f/0.8 lens system which reduces the image size 6:1 and focuses the image on the initial photocathode. The image amplifier is a cascaded, three-stage, magnetically-focused RCA C70021T which contains a 38 mm diameter S-20 input photocathode and a 38 mm diameter P-11 output phosphor. The gain of this tube is such that light created by a single electron from the photocathode can be imaged through a 1:1, f/0.8 transfer lens onto Polaroid Film.

Initial evaluations of this camera system with phantom sources suggest that a resolution of 4-5 mm can be achieved at distances of up to 10 cm. The primary problem has been a high photocathode noise level which limits the sensitivity of the instrument. Cooling of the photocathode to 0° F has resulted in an increase in the signal-to-noise ratio by 100 times. The diagnostic usefulness of the camera in a wide range of route nuclear medicine procedures has been evaluated and looks promising. Further increase in signal-to-noise ratio will be attempted through use of a shutter gate mechanism.

[1]This work was supported by NIH Grants CA-5134-05 and ISO1 FR-053834-04.

P-7 *"A Hybrid Positron Scanner."* CHARLES BURNHAM, AND SAUL ARONOW, (Physics Research Laboratory, Massachusetts General Hospital, Boston, Massachusetts)

This instrument, intended primarily for brain scanning, is a multiple crystal hybrid device. It is a compromise of the advantages of a positron camera and those of a scanner. Horizontal coordinate are obtained by a mechanical motion, vertical coordinates are derived from a columnar array of nine pairs of opposed NaI crystals (each rectangular, ⅜" × 1⅝" by 2" thick). Opposite crystals and first adjacent neighbors provide 25 coincident pairs to give the basic vertical positional information. Up to three vertical steps allow interlace sweeps to fill in the response pattern. The increased crystal area gives a speed advantage of 10 over a single-pair positron scanner, so that a brain scan may be made in five minutes with 1 mc of activity and 1 cm resolution. A two-dimensional thin crystal positron camera would have a further advantage in crystal area, but would sacrifice stopping power in the thinner crystal. By using nine crystal pairs rather than a single large crystal pair, at least nine times more gross target activity may be viewed. The 25 tunnel diode coincidence circuits have a resolving time of 15 ns., to reduce random counts while looking at an integral spectrum above 30 keV.

Integrated circuits are used to encode the vertical positional information of each count as a six-bit number. The horizontal sweep drive is a stepping motor whose pulses are coded as sync signals, as are the interlace steps. The count and sync signals may be decoded and directly displayed on an oscilloscope or recorded on a special very simple tape recorder, for later playback. Since each coincidence is recorded, the playback may be deflected to yield section scans or an unbalance scan. The tape recorder may also be read into a PDP-7 computer through an interface system for more complex processing. Although the instrument was primarily intended to replace an older single pair scanner for routine brain scans, it can operate at much higher count rates, up to 10,000 counts per second and will be used with very short-lived positron emitting isotopes.

Continued from page 316, April 1967 issue of JNM

Friday, June 23, 1967
2:00—3:30 P.M.
Spanish Ballroom

SESSION Q. SCANNING V, EVALUATION OF INSTRUMENT PERFORMANCE

Session Chairman: Hal O. Anger, Berkeley

Q-1 *"Constructional Details and Operating Parameters of the Spark Imaging Camera."* H. N. Horwitz, A. L. Forsaith, and J. E. Lofstrom, (Department of Radiology, William Beaumont Hospital, Royal Oak, Michigan)

The Spintharicon is now used extensively in our laboratory both for clinical applications and experimental work with animals. On the basis of three years' experience in the fabrication and use of the spark imaging camera many techniques have evolved. It is felt that this information should be available in explicit form, so that others may construct this type of instrument in their own laboratories.

The early method of electrode separation by glass spacers has been replaced by a continuous ring turned from a machinable ceramic. This device has eliminated the need for epoxy cements within the chamber. Additionally, this design rids the system of spurious discharges at the periphery of the electrodes. Further benefits from this type of construction will be discussed.

Clean-up of the chamber by pumping to a high vacuum poses many problems and hazards. Elimination of this step may significantly simplify this stage of preparation. Preliminary tests on a purge cycle indicate that it is possible to produce an operable chamber by this method. The cost of the gas and the tendency towards spurious discharge must be weighed in this alternate method.

The modest power requirements permit the use of a battery-operated DC to DC converter for the high voltage power supply. A solid state regulated high-voltage power supply has been developed which effectively provides the energy source. The counting and summing functions are economically and conveniently provided by integrated circuit components. The compactness of the associated electronic components and a modified photographic system now permit complete portability.

Design and construction details of the entire camera system, including photographic components and the collimators will be described. The various physical parameters and their effect on sensitivity, resolution, and useful life will be discussed.

Q-2 *"Body Distribution of Cesium, Iodine, Chlormerodrin as Determined by Sequential Observations Using the Spintharicon—A Comparison of in vivo Findings."*[1] Norman H. Horwitz, Rhoda M. Powsner, and Edward R. Powsner, (William Beaumont Hospital Department of Radiology, Royal Oak, Michigan; Ann Arbor, Michigan; and the Department of Radioisotopes, Veterans Administration Hospital, Dearborn, Michigan)

The spintharicon, spack-imaging camera, permits rapid visualization of tagged compounds. By the method of time-lapse imaging, it is possible to show pooling and clearance of these materials in experimental animals for extended periods after administration. The extremely high resolution of this type of imaging system allows visualization of very small structures, e.g., the organs of animals as small as a mouse. Where sufficiently high doses can be given in the experimental animal, it is possible to obtain distribution patterns as they vary from minute to minute. In addition, the spintharicon can be used to survey the excised organs or intact animal post mortem.

Distribution patterns of chlormerodrin ^{197}Hg, cesium salts ^{131}Cs and iodide ^{125}I have been obtained. As an example, the injection of 1 mC of chlormerodrin ^{197}Hg was followed

[1]Supported by Dearborn Veterans Administration Hospital Research Grant M4-61.

for 22 hours. The radioactivity was detected within the first minute in the heart blood pool and from the fourth minute to 22 hours in kidneys.

In a similar manner, cesium chloride ^{131}Cs was detected in heart and liver and its redistribution through the body was followed for several days. Iodide ^{125}I was detected in the thyroid, kidneys and bladder urine.

Q-3 *"Assessing the Performance of Radioisotope Scanners: Data Handling."* T. D. Cradduck, (Department of Nuclear Medicine, Manitoba Cancer Treatment and Research Foundation, Winnipeg, Manitoba, Canada)

A method has been described (Cradduck, 1966) for assessing the performance of radioisotope scanners. This assessment of performance was strictly limited to the data acquisition system, principally the collimator. The method depends upon the use of a line source to produce the line source spread function from which the modulation transfer function can be calculated.

In order to extend this method of assessing performance to include the data handling system (the ratemeter in most conventional scanners), a procedure has been devised which gives the response to a step function input. The step function is the integral of a delta function input and can be used to give the line source spread function of the ratemeter. This spread function can then be used to determine the modulation transfer function of the data handling system. This latter modulation transfer function can be incorporated with the modulation transfer function for the data acquisition system to give the overall response up to the input of the data display system.

Results will be shown which demonstrate the effect of ratemeter time constant and scanning speed on the modulation transfer function of the data handling system.

Q-4 *"Scintiphotography and Scintiscanning: Comparison in Use."* Bertram J. L. Sauerbrunn, Bergene Kawin, and Thomas McNickle, (Veterans Administration Hospital, Washington, D. C.)

In this investigation the clinical use of a 3″ crystal scintiscanner was compared with a scintillation camera of the Anger type.

Following the injection of a single radioisotope, duplicate studies were accomplished with the scanner and with the camera in over 250 patients. The advantages and disadvantages of each method were evaluated.

In general, but with some exceptions, the displays of the radioisotopic image of an organic lesion with camera and scanner were quite comparable in examinations of brain, liver, kidney, lung and thyroid. The count rate, type of organ visualized and operator proficiency each had effects on the time differences required to complete a study on the scintiscanner and the scinticamera. When ^{99m}Tc was utilized, scintiphotos were accomplished in a shorter time. For other commonly used radioisotopes that yield lower counting rates, this time-saving advantage was usually not as apparent. Although the effective size of the scintillation crystal is nine inches, most organs could be viewed in their entirety, but the lungs had to be studied separately in left or right views or in separate quadrants. Occasionally, the kidneys, liver, and spleen could not be viewed satisfactorily as a single field. Operator experience, judgment, and patience in positioning were important factors in determining the total number of camera views that were required to obtain a satisfactory scintiphoto series.

The mobility of the detector head of the scinticamera provided the advantage that patients could be examined in a horizontal, sitting, or standing position.

In critical clinical situations, anatomic landmarks were more easily related to the scan image than to the camera image. This fact was true also when superimposition of a radioisotopic image on roentgenographs was required.

Q-5 *"Dynapix-Design and Performance of a Digital Multi-Channel Scanner."* Robert Hindel, Joseph N. Cecil, and Thomas E. Sloane, Jr., (Intertech, Inc., [Affiliate of Picker Nuclear Corporation], North Haven, Connecticut)

This instrument combines a ten-channel scintillation detector with digital data handling and magnetic tape storage. The design of the information channels and the collimator

performance is discussed. A block diagram illustrates data processing and data display on CRT and a T.V. monitor. The information on magnetic tape and the count accumulation in a six-decade scaler will be discussed.

Several methods of data presentations in clinical use are illustrated with phantoms. The human engineering aspect, which received special attention in the design, is illustrated by two different approaches to operating this instrument. The first is the pragmatic approach, which strives to arrive at the best scan at the shortest time. The other is the theoretical approach, which uses statistical analysis to extract maximum information from the scan data. Typical applications are illustrated. Interfacing for digital computers are also discussed.

Q-6 *"Evaluation of a Multiple Crystal Rectilinear Scanner."* ROLAND C. BRAMLET, GERALD SHAPIRO, LAWRENCE SILVER, AND LESTER LEVY, (Long Island Jewish Hospital, Queens Hospital Center Affiliation, Jamaica, New York)

A multiple crystal rectilinear scanner has been in use at Queens Hospital Center for the last six months and the equipment evaluated for use as a clinical tool in an isotope facility. This scanner was developed by the Intertech Division of Picker Nuclear and consists of ten sodium iodide crystals, 6 inches long, 2 inches thick and ⅝ inches wide. Each crystal has its own focusing collimator unit and spectrometer system with the individual outputs feeding into a buffer storage system which in turn can be read out as BCD pulses for long-term storage on magnetic tape or in analogue form for viewing on T.V. or photorecording of a cathode ray tube.

In this study we will present a comparison of scans of various organs with those obtained from standard three-inch and five-inch color and photo scanners. Data will be shown of the uses of the tape recording system in association with the image readout controls used for modifying the final display image. In addition, dynamic function scans of the liver, kidney and lung will be shown.

Including in these discussions will be various methods of data presentation and recording. Information will also be presented regarding the collimation system including resolution efficiency and isoresponse patterns. The discussing will also cover mechanical and electrical problems encountered to date.

Q-7 *"Preliminary Experience with a Ten Probe Rapid Scanner."* LEONARD A. SWANSON, MICHAEL HAYES, AND GEORGE V. TAPLIN, (The Nuclear Medicine Divisions of the Department of Radiology, Los Angeles County Harbor General Hospital and the UCLA Laboratory of Nuclear Medicine and Radiation Biology)

Prior to clinical application of this new instrument, thorough studies were performed with various types of phantoms to determine its reliability, efficiency and resolving power. Phantoms were scanned with a conventional single probe instrument for comparative purposes. The 10 probe device has a more distinct sectioning capacity than the three-inch single detector scanner. This capacity is limited to the plane perpendicular to the direction of scanning, as one would expect from the rectangular crystals and focusing collimator arrangement. It may be minimized when desired by simply shielding the outside appertures of the collimator and accentuated by covering the center holes.

Direct comparisons between multiprobe and single probe scanners were then made in patients. Good correlation exists for all large organs studied. The major advantage of the ten probe device is best demonstrated in lung scanning, where four projections of the chest are obtainable in less time than for one with a conventional three-inch detector scanner and seven-hole collimator. Another feature is its capacity to produce repeated images of *both* kidneys simultaneously at two-minute intervals or less, following 400-500 μC doses of ^{131}I hippuran. The scans picture the changing intrarenal distribution patterns of *tracer* during its passage through each kidney. Differences between kidneys are readily recognized and abnormalities of intrarenal transport kinetics can help distinguish reneal artery occlusive disease from partial ureteral obstruction. Similar dynamic studies with ^{131}I rose bengal depict abnormalities of biliary excretion with equal clarity. In our opinion, the ten probe

scanner fulfills the current need for a rapid imaging device for most routine service functions and several research purposes. Its sectioning capacity further increases its value by permitting more accurate localization of both surface and deep seated lesions, particularly in brain scanning.

Friday, June 23, 1967
4:00—5:30 P.M.
Spanish Ballroom

SESSION R. SCANNING VI, INSTRUMENTATION AND COLOR REPRESENTATION

Session Chairman: **Benedict Cassen, Los Angeles**

R-1 *"Optimization of Spectrum Analysis for Pancreas and Parathyroid Scanning with Selenium-75."* ALEXANDER GOTTSCHALK, TOBY COHEN, AND ROBERT N. BECK, (Argonne Cancer Research Hospital, [Operated by the University of Chicago for the United States Atomic Energy Commission], Chicago, Illinois)

In those instances when a nuclide has more than one potentially useful gamma ray for scanning, it may be difficult to assess the optimum photopeak to use for each scanning situation. Selenium-75 with a major peak at both 126-131 keV and 265-280 keV is such an isotope. Although commonly used at the higher energy, the photon flux at the lower energy is comparable and collimation is easier. Also, for devices such as the Anger camera, crystal efficiency is higher at the low energy. On the other hand, although sensitivity is increased at 126-131 keV, resolution is degraded by scattered radiation.

Analysis of the complex interplay of sensitivity and resolution was accomplished by using the expression $Q = G_R \times (MTF)^2$ where Q = figure of merit, G_R = relative sensitivity, and MTF = the modulation transfer function. The MTF describes the spatial resolution over a continuum of frequencies and can be obtained by the Fourier transform of the line spread function.

In the first study, pancreas scanning was simulated by obtaining line spread functions with four inches of unit density scattering material between the selenium-75 line source and the collimator face for both gamma camera and three-inch scanner. The MTF was calculated for each spectrometer setting and the figure of merit computed.

The computation indicates that with the Anger camera, superior results are obtained with the 265-280 keV peak at all relevant spatial frequencies corresponding to structures four inches or less in size. With the rectilinear scanner, on the other hand, vastly superior results are obtained when both the 126-131 keV and 265-280 keV peaks are included in the pulse height analyzer window. If only one peak is used, however, the high energy peak gives results that are better than the low energy peak.

Comparison of the relative figure of merit for the 265-280 keV peak on the gamma camera with the combined peaks on the scanner shows that the camera gives markedly superior results.

A second study comparable to parathyroid scanning was also undertaken with the rectilinear scanner. In this instance, one inch of scattering material was used between the line source and collimator face. In this case, the 265-280 keV peak with the 19-hole collimator gives slightly better resolution for large structures (about ⅝ inch or bigger) than the 126-131 keV peak with *low energy* collimator. This latter combination, however, is better for smaller structures.

Results vastly superior to either of the above situations are obtained for all spatial frequencies using the combined low and high energy photopeaks and the 19-hole collimator.

R-2 *"Clinical Radioisotope Organ Imaging—Diagnostic Sensitivity and Practical Factors: Rectilinear Scanner Versus the Anger-Type Scintillation*

Camera." MYRON POLLYCOVE, MATTHEWS B. FISH, AND ARCHIE KHENTIGAN, (Nuclear Medicine Section, Clinical Laboratories, San Francisco General Hospital, Division of Clinical Pathology and Laboratory Medicine, Department of Pathology, University of California School of Medicine, San Francisco, California)

Clinical applications and use of organ radioisotope imaging is increasing at a progressively more rapid rate. Such organ imaging has been performed for the most part by rectilinear scanning. Recent development and availability of the scintillation camera warrants a comparison of these two instruments for diagnostic sensitivity and other practical aspects of clinical radioisotope organ imaging. Ninety-three patients were studied simultaneously with a three-inch crystal-rectilinear scanner and an Anger-type scintillation camera. Brain, thyroid, lung, liver and kidney radioisotopic imaging were performed using routinely available radiopharmaceuticals.

Comparisons were made in all cases with respect to the following parameters: (1) diagnostic quality of image; (2) time required for positioning of patient, adjustment of instrument, imaging, surface landmark-identification and photograph production; (3) ease of operation, and (4) completeness of study, including multiple views and rapid sequential imaging. Illustrative examples for each organ are presented.

The following results were obtained: 1. In all instances the diagnostic quality of the image obtained with the scintillation camera is equal to or superior to that obtained with the rectilinear scanner. 2. Over all time required per view with the scintillation camera is usually ¼ of that required with the rectilinear scanner. The ratio of scintillation camera time to rectilinear scanner time per standard view varies in accordance with the organ scanned: brain ½, thyroid ½, lung ¼, liver ¼, and kidneys ¼. 3. Ease of operation was equal for both instruments. 4. Completeness of study is achieved much more readily with the scintillation camera since: a) multiple views are greatly facilitated with the scintillation camera and b) rapid sequential imaging for vascular characterization is possible only with the scintillation camera.

It is concluded that the diagnostic sensitivity of the scintillation camera per view is superior to that of the rectilinear scanner. The markedly decreased time required per view permits routine complete multiple views in each case, as well as the obtaining of many more complete patient studies per day. Furthermore, rapid sequential imaging and the use of ultra short-lived isotopes are possible only with the scintillation camera.

R-3 "*Depth Discrimination in Color by Dual Channel Scanning.*" ERVIN KAPLAN, MOSHE BEN-PORATH, AND GLENN D. CLAYTON, (Radioisotope Service, Veterans Administration Hospital, Hines, Illinois)

Color print-out in clinical isotope scanning has had extensive application in which modullation of color has been by count rate. Modulation of color display by gamma energy, using several channels of pulse height analysis, has been reported by the authors. An application of dual channel pulse height display in color permits the display of lesion depth in ratios of two colors or in multicolor gradation. This process is accomplished by using two isotopes of the same element with different gamma energy of the principal photopeak, as exemplified by ^{125}I and iodine-131. Using a two-channel scanning system, the ^{125}I is printed out in one color; the second channel shows the results of ^{131} minus iodine-125. Since the ^{125}I counts at superficial depths are of considerable magnitude, the superficial ^{131}I is not registered due to the above subtraction. As the same ratios of the two isotopes are viewed at increasing depth, the ^{125}I *decreases* with distance and self-absorption in tissue equivalent material and ^{131}I counts registered *increase* with depth in a proportional manner, again because of the subtraction of iodine-125. It is possible to discriminate depths at less than two centimeter differences over a range of twelve centimeters. The differentiation at various depths is not linear. Use of other isotopes of the same element with various gamma peak energy differences will allow discrimination at various depths.

R-4 *"Current Status of Multi-Isotope Scanning by Color Modulation."* MOSHE BEN-PORATH, GLENN D. CLAYTON, AND ERVIN KAPLAN, (Radioisotope Service, Veterans Administration Hospital, Hines, Illinois)

Addition of two pulse height analyzer count rate systems with appropriate coupling to a commercial scanning device with color print out, has permitted the subtraction of one isotope from another and the modulation of color and photo print out by gamma energy. With this methodology, it has been possible to subtract interfering organs from scan images to simultaneously display up to three isotopes in individual organs and to employ the various combinations of subtraction and color modulation for organ scanning as recently reported by the authors.

These modes of operation are exemplified by subtracting or color discrimination of the liver from the pancreas using ^{198}Au and $^{75}Selenomethionine$. Hepatoma has been color discriminated in the liver in the same system. Using ^{131}I macroaggregate, the lungs can be displayed in one color contrasted with heart blood containing ^{125}I RISA, for pericardial effusion or ^{198}Au for distinguishing subdiaphragmatic abscess. The kinetics of Rose Bengal can be visualized against ^{198}Au in the liver. Two isotopes of iodine ^{125}I and ^{131}I can be used, one preceding and the other following TSH to simultaneously delineate in separate color "hot" nodules from TSH-stimulated areas of the thyroid. Differentiation of kidney parenchyma from the renal pelvis may be accomplished in two colors using ^{197}Hg chlormerodrin and ^{131}I hippuran.

Significant technical improvements in the system have resulted in elimination of scalloping by print out while scanning in one direction. The return of the detector at high speed over the same scan line does not register. A further modification permits the simultaneous image print out of one isotope in an individual color as the detector moves from left to right; as the detector returns, the other channel is activated and the second isotope is recorded in another color. This process may be accomplished by adding one pulse height analyzer count rate system to a commercial color scanner.

R-5 *"A Versatile Photoscan Analysis Instrument Produces Color Display from Black and White Pictures."* D. B. CHARLESTON, R. N. BECK, J. C. WOOD, AND N. J. YASILLO, (Argonne Cancer Research Hospital [operated by the University of Chicago for the United States Atomic Energy Commission], Chicago, Illinois)

The continued high interest level in obtaining color readouts for radioisotope scanning has led to the design of a device which bypasses the limitations inherent in producing an original scan readout in color and takes full advantage of the benefits gained from use of black and white photoscan transparencies.

A flying spot scanning system which uses a standard color television tube readout has been designed to analyze, enhance and manipulate the information content of the black and white photoscans. The system can generate color contour lines marking film density levels. Each colored contour line is independently variable over the full range of exposure density of the film from the lower fog level to the upper saturation level. In addition, the contour interval is continuously variable. A very narrow contour interval selection results in a sharp contour line, indicating a line of constant density. A wider contour interval results in a band of color which brackets an upper and lower range of exposure density to produce a color "mapping" display.

When analyzed, structures in the photoscan generate electronic frequencies relative to their spatial frequencies. Variable band pass filtering is used to display any selected range of structure size, suppressing others. Differentiation of the output signals generates a "shadow" which varies with the spatial frequencies present in the photoscan, producing a simulated three-dimensional effect enhancing high frequency spatial structure which may be hidden within the gross structure.

The system presents the diagnostician with a reasonably low priced, on-line instrument which is easy to use, takes full advantage of the simple processing and low cost of black and white film and can be used with either standard films or Polaroid transparencies. The

film to be analyzed can be compared against a calibrated step wedge of exposure densities for quantitative information.

With this system, the original scan record is not destroyed or altered in any way.

R-6 *"Scan Analysis with Color Contrast."* HIROTAKE KAKEHI, GUIO UCHIYAMA, AND OSAMU DOI, (Department of Radiology, Chiba University School of Medicine, Chiba, Japan)

A color photo-rescanner and an isobrightness color converter (closed-circuit color TV) have been developed in Chiba University Hospital, Japan. The purpose of this paper is to re-evaluate the diagnostic value of the scan records with both systems, by extracting the latent information from them.

The color photo-rescanner was devised with some improvements on the basis of that of Harris'. The photomultiplier tube as a light sensor gives the stable output and the use of color filter ring made of light metal leads to faster response. The scalloping in the rescan records are avoided by the one-way scanning without much delay. The rescan records of high fidelity were obtained with this new model.

On the other hand, under the necessity of obtaining results in a short time, the isobrightness color converter was developed combining the color contrast technique with the closed circuit television system. The first model in 1963 did not give satisfactory results because of the poor resolution. This new device is characteristic of the higher resolution, the luminance signal effect and the versatility of the color range.

The advantages of these devices are as follows;

1) Information stored in the primary scan record can be analyzed at any time without damaging the primary record.
2) The color contrast in a rescan record or in the color TV image shows small variations of counting rate better than a black and white scan does.
3) The statistical raggedness of the primary record can be smoothed to a certain degree by the analyzing devices.
4) Very dark or very faint primary scans that are not suitable for interpretation with the naked eye can be refreshed.

R-7 *"The Photographic Color Display of Scan Data—Three Years Development and Experience."* RALPH ADAMS, AND HENRY L. JAFFE, (Cedars-Sinai Medical Center, Los Angeles, California)

Following three years' development and experience with 10,000 color scans, the authors present their evaluation of the performance of a scanning accessory previously described for the display of scan information in photographic color.

The instrument displays scan information on the screen of a cathode ray tube, which is photographed in color during a time exposure through an array of color filters, which is driven from red through violet as the counting rate decreases from maximum to background, by a servo mechanism operated from the ratemeter circuit of the scanner.

Scans of models are shown to demonstrate the advantages of color scanning:

1. Color coded counting rates are estimated with an accuracy up to ± 5 percentage points.
2. Color provides somewhat more contrast than the conventional grey scale.
3. Color greatly extends the dynamic range far beyond the useful portion of the conventional grey scale. Individual background events are seen outside the active area in the presence of 200,000 counts per minute within it.

Clinical scans are shown demonstrating both optimum and poor choices of technical factors.

Friday, June 23, 1967
9:00—10:30 A.M.
Spanish Lounge

SESSION S. METABOLISM AND COMPARTMENT THEORY

Session Chairman: William H. Beierwaltes, Ann Arbor

S-1 ***"Uses of the Radioimmunoassay of Growth Hormone as a Test for Pituitary Suppression Produced by Heavy Particle Irradiation."*** ROBERT A. FINK, EDWARD MANOUGIAN, JOSEPH F. GARCIA, JOHN A. LINFOOT, AND JOHN H. LAWRENCE, (Donner Laboratory and Donner Pavilion, University of California, Berkeley, California)

Since the development of a medical facility for the utilization of the particulate beams produced by the 184-inch synchrocyclotron, work has been done dealing with the effects of heavy particle irradiation upon the function of the human pituitary. Initially, such heavy particle therapy was directed toward total ablation of pituitary function in mammary carcinoma; but, recently, it has been determined that total ablation is not necessary in treating certain diseases. Thus, the concept of "pituitary suppression" has been developed and is currently being used for the treatment of diabetic retinopathy, acromegaly, and Cushing's disease.

Originally, the effects of such heavy particle pituitary suppression have been measured by changes in target organ function and alterations in the clinical condition of the patient. Recently, however, a more objective method of determining the effects of pituitary suppression by heavy particles has been developed with the availability of a sensitive radioimmunoassay for human growth hormone (HGH), employing ^{125}I-labelled HGH and a double antibody precipitation technique. Using this assay, HGH was measured in normal subjects and in patients undergoing pituitary irradiation. Using insulin hypoglycemia and arginine infusions, an outpouring of HGH was produced, presumably mediated through the intact hypothalamico-hypophyseal axis.

In a group of normal subjects, following the induction of hypoglycemia using a modified insulin tolerance test (0.1 unit/Kg), a twenty-fold increase in the plasma HGH level was observed. In a group of patients with mammary carcinoma studied prior to heavy particle pituitary irradiation, all patients showed a significant outpouring of HGH following the induction of hypoglycemia and/or arginine infusion (30 gm.), although the degree of response was less than that of the normal subjects. This same group of patients, following pituitary irradiation, were challenged once again but, following a suppressive dose of heavy particles, it was noted that HGH secretion was markedly depressed. At the same time that these patients were demonstrating a decreased production of HGH, detectable changes in the other pituitary trophic hormones were not apparent when measured by the more standard assay methods.

In acromegaly, where the plasma HGH level is high, insulin resistance (to hypoglycemia) is a well-known phenomenon. Following surgical hypophysectomy, in most cases, insulin resistance remains as does the elevated circulating plasma HGH. Following treatment of acromegaly with pituitary suppressive doses of heavy particle irradiation, however, insulin sensitivity is recovered, and significantly lower plasma HGH determinations have been observed.

In summary, it is postulated that the ability of the pituitary gland to respond to a challenge of hypoglycemia with an outpouring of HGH is a reflection of pituitary function and, therefore, may be utilized to assess the effect of heavy particle pituitary suppression when total pituitary ablation is not desired.

S-2 ***"Methionine and Schizophrenia."*** DAVID M. ISRAELSTAM, ALONSO JOHNSON, AND HARRY SAUL WINCHELL, (Donner Laboratory, University of California, Berkeley, California)

It has been suggested that an abnormality of methylation may be involved in schizophrenia. (See work of Osmond, Smythies, Park, Friedhoff, Hoffer and others.) The S-methyl

group of the amino acid methionine is felt to be the major source of methyl groups for transmethylation processes *in vivo*. We decided to study the kinetics of this S-methyl group of methionine in normal volunteers and schizophrenic patients. We administered 25 microcuries of methyl ^{14}C-labeled methionine intravenously and monitored the $^{14}CO_2$, CO_2 and O_2 of the expired air with a breath analyzer. In the normal group, the specific activity (or $^{14}CO_2/CO_2$ curve), was found to peak at 18-25 minutes with a definite subsequent downslope seen. The schizophrenic group showed lack of this early peak and a flat or rising curve for a period of two-and-a-half hours. We therefore see an altered (slower) pattern of conversion of methyl ^{14}C-labeled methionine to $C^{14}O_2$ in schizophrenic patients than in non-schizophrenic volunteers. This data is consistent with the speculation that a rate-limiting, enzymatically-based step is delaying the conversion of $C^{14}H_3-$ to $C^{14}O_2$. The possibility of a larger methionine pool (or, more specifically, transmethylating pool), in schizophrenics which could also explain the results will be tested in the near future. In summary, this data lends support to the previously advanced, but controversial theory, of a disturbance in methylation processes in schizophrenia.

S-3 *"Computer Analysis of Breath $^{14}CO_2$ Data."* H. S. Winchell, K. Wiley, M. Fish and M. Pollycove, (Donner Laboratory, University of California, Berkeley, California)

Subsequent to administration of many organic materials labeled with carbon-14, $^{14}CO_2$ is excreted in the breath. The shape of such breath $^{14}CO_2$ curves, as well as their amplitude, are related to the kinetics of the metabolic processes responsible for the eventual oxidation of the carbon atoms in the position labeled with carbon-14. To provide an objective method for the analysis of breath $^{14}CO_2$ data, we have devised a digital computer program for fitting a series of mathematical functions to the data by minimization of the least squares of differences. Previous experience with graphical analysis of breath $^{14}CO_2$ curves suggested that the late portion of the curve was well fit by a series of exponential terms ($\Sigma_i A_i e^{-r_i t}$). By identifying these terms with the major metabolic processes involved, and by defining $F(\tau)$ as the probability that $^{14}CO_2$ generated from such processes would be detected in the breath τ minutes after their generation, we can write the function $\left(\int_{\tau=0}^{\tau=t} F(\tau) \Sigma_i A_i e^{-r_i (t-\tau)} (d\tau)\right)$. This function is then fit to the observed breath $^{14}CO_2$ data using various forms for (F) τ. Examples will be shown for $F(\tau) =$ (delta function), $\Sigma_j A_j e^{-\alpha_j \tau}$, $\frac{e^{k\tau}}{c+e^{k\tau}}$, for data obtained from ^{14}C-labeled amino acids. When applied to $^{14}CO_2$ data obtained with #2-ring ^{14}C-labeled histidine, values for the terms A_i and r_i are obtained which clearly distinguish patients with folic acid deficiency from normal subjects or patients with pernicious anemia. This program appears to be generally applicable to a large variety of tracer kinetics problems.

S-4 *"The Rate of Medium Chain Fat Absorption in Malabsorptive Disorders."* A. D. Schwabe, V. D. Valdivieso, C. Ortega, and L. R. Bennett, (University of California, Center for the Health Sciences, Los Angeles, and Harbor General Hospital, Torrance, California)

The absorption of intraduodenally-administered glyceryl trioctanoate labeled with ^{14}C in the carboxyl position was estimated by continuously monitoring the expired $^{14}CO_2$ for 90 minutes in a ^{14}C analyzer. After hydrolysis, this medium chain lipid is transported to the liver and peripheral tissues via the portal venous system and rapidly and almost completely oxidized. From previous animal studies, it would appear that any reduction in $^{14}CO_2$ excretion after feeding this radioactive lipid is due to a retardation of absorption. In 75 control patients without clinical and laboratory evidence of malabsorption, an average of 18.6% (range 13.8-24.3%) of the administered dose of radioactivity was recovered as $^{14}CO_2$ in 90

minutes. In 21 patients with varying degrees of pancreatic exocrine insufficiency and steatorrhea, $^{14}CO_2$ excretion average 2.2% (range 0.2-11%). Following the addition of pancreatic extract, $^{14}CO_2$ excretion increased in all cases. Patients with a variety of other malabsorptive disorders, such as nontropical sprue, post-gastrectomy steatorrhea and regional enteritis, were also found to have reduced $^{14}CO_2$ excretion rates. This method has the advantage of monitoring the rate of absorption while digestion and absorption are in progress.

S-5 *"The Concentration of Radioactivity from Labeled Epinephrine and its Precursors in the Dog Adrenal Medulla."*[1]

JOSE O. MORALES, WILLIAM H. BEIERWALTES, AND RAYMOND E. COUNSELL, (Department of Internal Medicine [Nuclear Medicine], and the School of Pharmacy, University of Michigan Medical School, Ann Arbor, Michigan)

Thirty-two dogs were injected with ^{14}C-labeled epinephrine and its precursors and two different phenylethylamines. One dog was given an ^{125}I-labeled phenylethylamine. Blood samples were withdrawn at frequent intervals for the first 6 hours, the urine collected and the dog sacrificed at 6 or 24 hours. Tissue samples were obtained from 16 organs of each dog and the concentration of radioactivity determined and expressed as counts per minute per milligram of tissue. The average adrenal medulla: plasma ratio at 6 hours rose from 114 after dopa to 710 after dopamine and then fell to 125 after norepinephrine and 136 after epinephrine. Similar ratios at 24 hours could not be obtained because of low plasma activity. However, concentrations in the adrenal medulla (cpm/mg) were tyrosine 34, dopa 110, dopamine 422, norepinephrine 401, and epinephrine 243. Activity concentrations in the adrenal medulla 6 hours after the administration of ^{14}C labeled p-tyramine and phenylethylamine were low. Rapid deiodination of p-iodophenylethylamine ^{125}I precluded any distribution studies. After dopamine the average adrenal medulla: kidney ratios were 72 and 170 after 6 and 24 hours, respectively. Similarly, adrenal medulla: liver ratios were 90 and 112. The plasma concentration of ^{14}C radioactivity from dopamine fell more rapidly and to lower levels after the first hour, than after any other compounds, a more rapid urinary excretion being also found. These concentration ratios of radioactivity from labeled dopamine in the adrenal medulla are considerably higher than the concentration ratios of ^{131}I in metastases from thyroid cancer. These data suggest that similar studies after labeled dopamine in patients with chromaffin tumors would be of interest.

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[1]This work was supported by NIH Grants CA-5134-05 and CA-08429-02 and Amer. Cancer Assn. PRA-18.

S-6 *"Turnover Compartmentalization Theory."*

P.E. E. BERGNER, (Medical Division, Oak Ridge Institute of Nuclear Studies, an operating unit of Oak Ridge Associated Universities, Inc., Oak Ridge, Tennessee, under contract with the United States Atomic Energy Commission)

The classic type of compartment analysis (LFCA) is not strictly applicable when only whole-body retention of tracer is observed. A new physically precise theory has therefore been formulated. It fully appreciates the high complexity of organisms, i.e., it does not make necessary any approximations of basic physical principles (like "rapid mixing" or "homogeneity"). As a result one obtains a precise definition of the concepts *exchangeable mass* and *whole-body turnover*. The theory gives parameters, with definite physical dimensions, which can be determined also from short-term studies.

The underlying new concept is *turnover compartment*, which is defined not in classic physical or chemical terms, but in terms of the lengths of time the particles stay in the body. Whole-body retention data of calcium and potassium analyzed with the use of this concept produce detailed descriptions of the early kinetics of mother substance and characterize calcium and potassium metabolism in a new way.

S-7 *"Metabolic Systems with Re-Cycling."*[1] LENA SHARNEY, LOUIS R. WASSERMAN, AND JOHN C. STEVENSON, (Department of Hematology of the Mount Sinai Hospital and School of Medicine, New York, N. Y., and C. W. Post College of Long Island University, Department of Mathematics)

Complex physiological phenomena can often be described in terms of simple mathematical models. If a tracer quantity of a radioactive metabolic substance is introduced into a compartment containing the basic metabolite, its behavior in time may be derived from measurements of radioactivity in samples of fluids and over various organ sites. Such radioactive behavior can be approximated by sums of exponential functions which are solutions of first order ordinary differential equations with constant coefficients. These equations are mathematical analogies of mutually interchanging metabolic pools, with transfer rates corresponding to first order displacements or reactions.

The analysis of isolated or simple systems by means of the Laplace transforms does not account for a more complex situation: recycling after a "time lag." Consider the disappearance of iron from the pre-erythropoietic system and its subsequent reappearance, after time τ, in the circulating blood. The usual analysis of the pre-erythropoietic system is valid only prior to a significant return of radio-iron from either the last stages of the maturation series or from circulating red cells.

In cases of ineffective erythropoiesis or severe hemolysis the mathematical analysis can be achieved by considering a series of unidirectionally connected identical pool systems with the metabolite leaving an initial pool, I_1, of one system and entering a terminal pool, Ti + 1, of the next system. In general, we expect that the solutions of such systems would have distinct roots for the first system and roots of multiplicity i for the i^{th} system. Using the superposition principle, the solution of the original (simple) system with time lag, τ, will be equal to the solutions, $S_1(t)$, of the first system for the series, during the time $0 \leq t \leq \tau$, and to $\Sigma_1 S_1(t-[i-1]\tau)$ for $(n-1)\tau \leq t \leq n\tau$.

This approach should enable us to determine not only the magnitude of ineffective erythropoiesis and hemolysis but the correct value of RBC uptake (in the presence of the above phenomena) as well.

[1]Supported in part by USPHS Grants # AM 09564 and HE 04456 from the Institute of Arthritis and Metabolic Diseases, Grant #CA 04457 from the National Cancer Institute and the Albert A. List, Frederick Machlin and Anna Ruth Lowenburg Funds.

Friday, June 23, 1967
11:00—12:30 P.M.
Spanish Lounge

SESSION T. a) BODY COMPOSITION
b) NEW INSTRUMENTS AND TECHNIQUES

Session Chairman: Asa Seeds, Vancouver, Wash.

T-1 *"Precision and Accuracy of Assay in Whole-Body Counters of Radioactivity in Man."*[1] CHARLES E. MILLER, WAYNE KESSLER, AND ALEXANDER P. REMENCHIK, (Health Division, Argonne National Laboratory, Argonne, Illinois, Department of Bionucleonics, Purdue University, West Lafayette, Indiana, and Department of Medicine, Loyola University Stritch School of Medicine, Hines, Illinois)

A study was designed to determine the precision and accuracy of the assay of radioactive potassium in man, as a function of body size and configuration, by whole-body coun-

[1]This investigation was supported in part by USPHS Research Grant RH 00283, Division of Radiological Health, USPHS General Research Support Grant 1S01-FR-5368, and a grant from the American Medical Association Education and Research Foundation Grants-in-Aid for Research Project AMA-ERF No. 149.

ters. Thirty-six subjects, whose weight ranged from approximately 44 kg to 167 kg, were selected for assay. Several of the obese subjects were assayed at intervals as they lost weight. Their normal potassium content was assayed by three independent techniques, the Argonne tilting-chair technique and the 7 crystal-position technique which use NaI crystals and a liquid scintillation 4-pi whole-body counter. Fifty μC of ^{42}K were then administered to each subject and each subject was reassayed 40 to 50 hours later by the first two techniques and five or six days later by the 4-pi whole-body counter. All urine during this period was collected and assayed to correct for ^{42}K excreted in the urine and to calculate exchangeable potassium. Calibration factors (μC ^{42}K in body/observed counting rate) were calculated from the data for each whole-body counter technique.

A plot of the calibration factors versus weight/height demonstrates that the calibration factor is an exponential function. Significant changes in the calibration factor were observed for those subjects who lost weight. A regression line was calculated for the log of the calibration factor versus weight/height for all the subjects. The percentage deviation of the observed value from the regression line was calculated for each subject. For each technique, a second regression line was calculated for this percentage deviation versus weight/height. A significant positive regression was observed for the percentage deviation versus weight/height for the NaI crystal techniques, but not for the liquid scintillation 4-pi whole-body counter. However, the percentage deviation was less for the NaI crystal techniques. This data indicate there is a minimum uncertainty in the assay of radioactivity in man when the isotope used is relatively uniformly distributed within the body. It is evident that for non-uniform distributions, the uncertainty will be greater.

T-2 *"Body Composition in Chronic Obstructive Pulmonary Disease (COPD)."* NANCY TELFER, HARRY H. HERBST, FRANZ K. BAUR, AND M. RAY MICKEY, (Department of Medicine, UCLA School of Medicine, Harbor Hospital Campus, Torrance, and Department of Public Health and Preventive Medicine, UCLA School of Medicine, Los Angeles)

Exchangeable sodium (Na_e), potassium (K_e) and total body water (TBW), blood gases, serum and urine electrolytes were studied in 21 patients with severe COPD, documented by pulmonary function studies. Normal values for BC were predicted for each subject, using regression equations derived by Moore *et al.*

Serum Na and Cl were low; K and other electrolytes were normal. Blood gases varied widely, and mean values were of little value.

Using prediction formulas based on weight, age and sex, the Na_e was 111 ± 15%, the K_e 76 ± 16% and the TBW 93 ± 11% of the predicted values. Two explanations were considered: 1. Loss of lean tissue, i.e., loss of intracellular water and potassium with maintenance of extracellular water and sodium. 2. Failure of the sodium pump with loss of three potassium ions for each two sodium ions retained.

To evaluate these hypotheses, a hypothetical "normal" weight and BC were calculated and, using a digital computer, "lean tissue" was subtracted from the "normal" body composition until the values most closely approximating the observed values were reached.

Control subjects and patients with wasting diseases and congestive heart failure before and after diuresis were similarly compared. The results indicate that either or both postulated mechanisms may be operative.

T-3 *"Body Potassium and Lean Body Mass (LBM) in Normal, Cardiac and Endocrine Children."* RICHARD C. REBA, DONALD B. CHEEK, AND FRANK C. LEITNAKER, (Department of Radiological Science, Johns Hopkins Medical Institutions, Baltimore, Maryland, and the Division of Nuclear Medicine, Walter Reed Army Institute of Research, Washington, D. C.)

The results of total body potassium (K_t) determinations obtained by measuring ^{40}K in a total body counter are correlated with other anthropometric and biological measurements in normal and abnormal children. There is a sharp change in the slope of the arithmetic relation of K_t to height in boys at 140.5 cm, which may be related to the increased muscle growth associated with adolescence in the male.

When one separates the sexes, body weight, total body water, extracellular volume, creatine excretion, total chloride and K_t are related arithmetically in a linear fashion. This fact implies that in the ordinary child (or adult) body fat is constant. There was a significant sex difference in the LBM (and K/LBM). This finding may reflect a difference of muscle cells relative to visceral cells between the sexes.

Children with cardiac defects were found to fall at the lower portion of the regression line for weight. Calculation of their fat content revealed less fat than in normal children. Cardiac children were also found to have less body K per unit height.

Children with a variety of endocrine disorders are also included, but the numbers in each group were generally too small to allow definite conclusions to be made; however, seven hypopituitary boys were studied before and after treatment with growth hormone. Although the average fat content did not change with treatment, there was a slight decrease in fat when expressed as per cent body weight (19.8% to 16.0%) due to growth of the LBM.

T-4 *"Measurement of Loss of Labelled Albumin in Children by Means of Total Body Counting."* M. HAYES, W. M. LARSON, JR., AND N. S. MACDONALD, (Laboratory of Nuclear Medicine and Radiation Biology; Department of Pediatrics and Department of Radiology, UCLA School of Medicine, Los Angeles, California)

Total body monitoring of ^{131}I activity after intravenous administration of labeled human serum albumin (RISA) is a practical, easy means of estimating exudative and/or metabolic losses. The sensitivity of the UCLA total body counter (TBC) permits replicate measurements during a three-week period following injection of 0.05-0.10 μC, which delivers a calculated body exposure of less than 10 mrad-an acceptable level for pediatric subjects. Thyroid uptake is blocked with Lugol's solution. The counting rate at ten minutes post intravenous injection is taken as 100% and subsequent counting rates, expressed as percentages, represent the body retention values. Semi-log plots of retention vs. time exhibit curves with two and sometimes three distinct slopes. We have found the period from 2 to 10 days to be the most useful portion. Retention values usually decrease in a single exponential fashion during this interval. Nine healthy children, ranging in age from 6 months to 12 years, displayed retention half times ranging from 8 to 13 days. This finding is somewhat shorter than the 13-18 days we have observed in normal adults. Seven ill children ranging from 18 months to 14 years of age have been tested. Initial findings included nephritis with proteinuria, hepatosplenomegaly, protein allergy, duodenal ulcer and enteropathy with edema. Half times for total body ^{131}I retention following RISA injection ranged from 2-6 days in four cases. The other three children were in the course of intensive therapeutic treatment and showed half times from 8 to 16 days. The method does not provide data with which one might estimate albumin pool sizes and rates of intercompartmental interchange. Nonetheless, the empirical value of ^{131}I (RISA) body retention half-time is a helpful measurement, particularly as a screening procedure to assist the clinician in deciding on further, more elaborate protein turnover studies.

T-5 *"A Compact Cyclotron Installation for Biomedical Uses."*[1] JAMES P. MAMACOS, PETER J. KENNY, AND JOHN S. LAUGHLIN, (Division of Biophysics, Sloan-Kettering Institute for Cancer Research, New York, N. Y.)

Small cyclotrons suitable for a compact biomedical facility are now becoming more readily available commercially. A compact installation using one of these modern cyclotrons, exclusively for biological and medical research, is described. It consists of a cyclotron room, target room, "hot" laboratory, counting room and control room in a space measuring 900 sq. ft. situated 40 feet below ground level. The cyclotron is manufactured by The Cyclotron Corporation and is capable of accelerating protons to 15 MeV, deuterons' to 7.5 MeV, helium-3 to 20 MeV and alpha particles to 15 MeV with external beam currents of 50 to 100 microamperes. The beam is directed towards solid granite and critical areas are shielded by high density (200 lbs/cu. ft.) concrete walls and ceiling with egress via a high density concrete shielding door. In order to increase the flexibility and range of the available

[1]Supported in part by AEC Contract AT(30-1)-910 and NCI Contract CA-08748.

"hot" laboratory facility, one of the two fume hoods is of the "walk-in" type. The apparatus required for each routine production method will be set up on individual heavy-duty carts and wheeled into the fume hood as required. The cyclotron installation is connected by gas lines and by pneumatic "rabbit" line with another laboratory group which includes a small "hot" laboratory, experimental laboratory to incorporate a three-dimensional digital positron camera, electronics lab, and IBM 1800 computer installation.

The cyclotron is an outstanding producer of neutron deficient radionuclides. In biological and medical research, these isotopes offer several advantages over neutron excess radionuclides as produced by a reactor. In particular, they generally decay by positron emission and the annihilation of the positron results in two gamma rays at 180° to one another. It is therefore possible to utilize two "gamma cameras" in conjunction with a computer to localize the radionuclide in three-dimensions. Such a system is being developed at this Institute. Some of the nuclides are also of unique biological importance, including carbon-11, nitrogen-13 and oxygen-15. The accelerated particles and neutrons will also be used directly in various radiobiological studies.

T-6 *"Radioiodine-125 Radiation Sources."* WILLIAM G. MYERS, (Medical Biophysics Radiology Department, Ohio State University Health Center, Columbus, Ohio)

Iodine-125 decays solely by electron capture with 60-day half-life. Characteristic 27.2-31.7-keV Te K X-rays constitute 95% of the "hard" photons emitted; the remainder are unconverted 35.4-keV γ-rays. Of the 144±6 photons/100 disintegrations, 78% are 27.4-keV Te K_α X-rays with calculated 1.7-cm narrow-beam half-thickness and experimental 2.3-cm broad-beam half-thickness in water. Preliminary studies with ~ 4 mC in a 2-mm-diam plastic tube 50 cms above a cadaver hand resting on non-screen film gave a good radiograph in 20 hours. Calculations based on this "Curie-minute" (Ci-min) source at one-half meter indicated the potential feasibility of making much stronger I-125 machines which require no electric power; and that are small, light and portable for convenient and unique applications in medicine, science and industry.

Subsequently there became available a 0.090-inch-diam source[1] which contained ~ 1.1 Curie when it reached this laboratory. It was enclosed within ~ 0.033-inch-thick Al capsules that could be slid readily from behind a lead shield into "on" position behind the 5-mil-thick steel window of a radiographic exposure device.[2] These safety features reduced the initial output rate ~ ten-fold so that the "effective" strength was only ~ 0.11 Ci of I-125, or ~ 27-fold greater than that of the first source. Leaded gloves and apron absorbed most of ^{125}I-photons.

Radiographs made at 50 cm were comparable to those obtained with conventional Röntgen-ray machines. The factors were: human hand bones in a plastic phantom—15 Ci-min with high-speed films and screens, and 35 Ci-min with non-screen film in cardboard cassette; man's ankle—30 Ci-min with regular film and par-speed screen; and malignant breast, 9 cms thick—55 Ci-min with no-screen film, 250 Ci-min with "industrial" film. Excellent radiographs on Polaroid paper required 75 Ci-min for the hand phantom, thus demonstrating a no-power, no-darkroom combination.

Should 100 Curies of ^{125}I as a "point" source be encapsulated in strong Al-Be alloy not more than 1 mm thick, all of these radiographs might be made in ~ 1-15 sec, and chest films at 3 feet in ~ 5 seconds. A practicable ^{125}I x-ray machine need not weigh over a few pounds.

Kindly loaned by: [1]Isotopes Development Center, O.R.N.L.
[2]General Motors Research Laboratory.

T-7 *"Specific Activity Estimation on Targets Immersed in a Scattering Medium by External Collimator Counting."*[1] THOMAS J. CALLAHAN, AND THOMAS P. DAVIS, (Department of Radiation Biology and Biophysics, The University of Rochester School of Medicine and Dentistry, Rochester, New York)

In situations where radioisotope scanners are employed to provide data for dosimetric calculations, the primary concern is to determine the specific activity of the tumor rather

than to locate and delineate the tumor. The estimation of the specific activity of a gamma-emitting nuclide in a given target (tumor) in a matrix of normal tissue of lower specific activity is often made by means of external counting with a scintillation crystal-focusing collimator detector array.

The relationship of the detector count rate to the actual specific activity in the target was examined utilizing the IAEA (International Atomic Energy Agency) Standard Scanning Phantom as a simulated organ-tumor system. Such parameters as target size, depth, and the specific activity ratio between target (tumor) and matrix were evaluated using ^{131}I and Mercury-203. For each of the approximately 160 combinations of the above parameters, the complete gamma-ray spectrum was recorded by a multichannel pulse height analyzer, and the resulting spectrum analyzed by digital computer.

A technique was devised using mathematical properties of the resulting gamma-ray photopeaks to separate the major contributions of scatter from the non-scatter portion of the photopeak. It was found that small angle scatter can lead to substantial errors in estimation of tumor activity.

A simple procedure is proposed which eliminates substantially all of the counts due to small-angle scatter, at some sacrifice in counting statistics. Utilizing such "scatter-free" data, the relationships among the above mentioned parameters in the estimation of target specific activity by external counting methods will be discussed.

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[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.

Friday, June 23, 1967
2:00—3:30 P.M.
Spanish Lounge

SESSION U. THYROID AND THYMUS, METABOLISM, RADIOBIOLOGY AND THERAPY

Session Chairman: **Shields Warren, Boston**

U-1 *"Application of Computer Model of Iodine Metabolism in the study of Endemic Goiter."* B. MALAMOS, D. A. KOUTRAS, J. SFONTOURIS, G. RIGOPOULOS, X. A. YATAGANAS, M. BERMAN, AND R. L. VOUGHT, (Athens University Department of Clinical Therapeutics, Alexandra Hospital, Athens, Greece, and National Institute of Health, Bethesda, Maryland)

Iodine kinetics were studied in 8 goitrous and 2 nongoitrous persons from the endemic goiter areas of Greece. Following an intravenous ^{131}I tracer dose, serial measurements of the radioactivity in the thyroid gland, the plasma and the urine were obtained over a period of 14 days. The results were analysed with the computer model devised by Berman and co-workers.

The analysis showed a generally normal plasma iodide pool in litres, a markedly increased rate of iodide transfer from the plasma into the thyroid gland and a generally normal rate of renal excretion. The thyroidal iodine pool, calculated on an I intake basis (thyroidal iodine/daily iodine intake) was greatly increased in both the goitrous and the nongoitrous persons from the endemic goiter areas in comparison to U.S.A. normals. There was a significant delay in the thyroidal handling if iodine, and the fractional thyroidal secretion rate was slightly diminished. Modest decreases in the PBI levels and the thyroxine pools were served.

It is concluded that computer analysis of iodine kinetics may clarify the metabolic adaptation to iodine deficiency, as well as the occurrence of biochemical and radioisotopic evidence of iodine deficiency in nongoitrous persons living in the endemic goiter areas.

U-2 *"Radiobiologic Factors in Radioiodine-Induced Hypothyroidism."*[1] DAVID L. JOFTES, (Cancer Research Institute, New England Deaconess Hospital, Boston, Massachusetts)

Hypothyroidism consequent to thyroid radioiodine therapy is being increasingly reported. While interference with thyroid cell division by radioiodine has been suspected for many years, it has only recently been documented (Al-Hindawi and Wilson, *Clin. Sci.* 28:555, 1965; and 5th Internat. Thyroid Conf., Rome, May 1965: Joftes, 5th Internat. Thyroid Conf., Rome, May 1965). Extension of our previously-reported experiments shows that mouse thyroids retaining aproximately 2 to 10μC at 48 hours following a 25 μC dose of ^{131}I show a statistically significant reduction in the ratios of H^{3}TDR-labeled to unlabeled cells at three and seven days, compared with controls. By 56 days the effect is reversed, with a statistically significant doubling of labeled cell ratios in the radioiodine-treated group being observed. At 90 and 175 days, there is an apparent increase in labeled cell ratios of radioiodine-treated thyroids which is not statistically significant. Earlier work in this laboratory has shown that thyroid functionality is not materially affected by this dose range over similar time intervals. Therefore, hypothyroidism would not become manifest until such time as the inability to replace lost thyroid follicle cells reduces the functional volume of the gland below that necessary to make the required amounts of hormone even under TSH stimulation. The length of time would depend upon how much of a functional remnant remained following radioiodine treatment and the cell turnover time, which is believed to be quite long (Leblond and Walker, *Physiol. Rev.* 36:255-275, 1956). The increase of reproducing cells observed at 56 days in these mice is probably a compensatory response to pituitary TSH on the part of uninjured or repaired cells. It is possible to find such cells in the mouse thyroid because its small dimensions and the non-uniform distribution of the radioiodine insure that much of the radiation will be absorbed in extra-glandular tissue. This is less true of the much larger human glands, so that compensatory recovery from radiation hypothyroidism is much less likely in humans, especially since they receive much higher radiation doses.

[1]Supported by USAEC and USPHS.

U-3 *"Persistence of Chromosomal Aberrations in Chinese Hamster Thyroid Following Administration of Iodine-131."* W. MOORE, JR. AND M. COLVIN, (Research Unit, Southeastern Radiological Health Laboratory, National Center for Radiological Health, Public Health Service, U. S. Department of Health, Education and Welfare, Rockville, Maryland, and Montgomery, Alabama)

We have investigated the persistence of chromosomal aberrations in Chinese hamster thyroid cells after administering 0.01, 0.1, 0.5, and 1.0 μC ^{131}I (approximately 100 to 10,000 rad to thyroid gland) to animals 7 to 10 days old. At thirty days and one year following injection the thyroids were removed, trypsinized, and the cells grown in tissue culture for three days. The thyroid cells were arrested in metaphase, fixed, and stained for chromosomal analysis.

The rate of growth, mitosis and chromosomal damage varied with the dose and length of time after injection. There was a marked decrease in the percentage of aberrant cells found at one year as compared to the 30-day values. For instance, with the 0.01 μC dose, there were 6.6% aberrant cells at 30 days and 2.7% aberrant cells at one year. This decrease is the result of at least two factors: (1) death of some of the aberrant cells and (2) a dilution effect from an increase in the cell population as a result of growth.

At all dose levels, the percentage of thyroid cells containing aberrations was several times greater than the control values. The control values for 30 days and one year were 0.31% and 0.29% aberrant cells, respectively. For the 1.0 μC dose (approximately 10,000 rad), 92% of the thyroid cells contained aberrations at 30 days and 28% at one year.

These results provide evidence that ^{131}I produces considerable damage to the chromosomes of thyroid cells in young hamsters and that some of the damage may well persist for the remainder of the animal's life.

U-4 ***"Morphological and Functional Changes in Thyroid Tissues Irradiated with Iodine-131: A scintigraphic and radiochromatographic investigation."*** **S. T. HOLAN, I. SZANTAI, M. FARCASANU, Z. URAY, AND C. GHERMA, (Clinical Radioisotope Unit, The Medico-Pharmaceutical Institute, Cluj, Romania)**

During a six-year period, a group of 430 patients with hyperthyroidism have been treated with iodine-131. Besides watching the therapeutic efficiency by means of complex clinical conditions, we have carried out scintiscans and have followed the urinary removal of amino-acids and the labelled amines in biosynthesis of ^{131}I before and after the treatment. These methods presented an interesting way to estimate the therapeutic efficiency from the morphological and functional point of view.

The scintigrams allowed us to make clear the decrease of the total volume in the regions with hyper uptake of ^{131}I in the gland and to make the difference "ex-iuvantibus" between the hyperfunctional adenomas, which after irradiation have disappeared. So, by the disappearance of the hormonal overproduction and after doing away with the exaggerated "feed back" on the TSH agent, a sound thyroid gland appeared on the scintigram, invisible before for lack of thyreostimuling hormone.

The amino-acids and amine components treated with ^{131}I (labeled by biosynthesis), have been extracted from the urine by use of ion-changing colophony (Amberlite I. R. 120). The patients have been given tracer doses pre-therapeutically as well as the therapeutic dose. Following a mean dose of 1,200 rad (beta), and after 24 hours and, even more significantly, after 48 hours, the quantity of urinary-excreted iodated aminoacids and amines decreased significantly. It seems that the absorbed dose has a radiobiological activity which also has a qualitative influence during the first 48 hours on the hormonal elaboration by the thyroid gland.

To identify qualitatively all the urinary fractions excreted, paper chromatography and autoradiography have been carried out on these radioiodinated amines and aminoacids.

U-5 ***"Experimental Studies of the Lipid Metabolism of the Thymus After Gamma Irradiation."***[1] **C. MIRAS, G. LEVIS, J. MANTZOS, N. LEGAKIS, B. MALAMOS, (Department of Clinical Therapeutics, University of Athens Medical School, Alexandra Hospital, Athens, Greece)**

Rats weighing 150 g were subjected to total body gammairradiation (^{60}Co) with doses ranging from 250 to 750 rads. The animals were killed by decapitation at different time intervals from 10 min up to 24 hours after irradiation. The thymus was immediately excised and examined by electron microscopy. The fatty acid synthetase activity was tested by incubating the cell free 600 xg supernatant with acetate-I-^{14}C or malonate-2-^{14}C and the cofactors needed for fatty acid synthesis. Total lipids were extracted, counted and separated into classes.

Irradiation with 250 rads resulted to an increased initial rate of incorporation which lasted for a period of three to five hours and showed the highest value within the first hour after irradiation. After that period the initial rate of incorporation decreased, reaching at 24 hours almost 50% of the control values obtained with thymus preparations of non-irradiated animals. Higher than 250 rads irradiation doses gave nearly similar results which are discussed.

Fatty acid esters were separated by preparative gas liquid chromatography and the data of the individual fatty acids from irradiated and control animals are discussed.

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[1]This work was supported by Contract AT(30-1)-3709 between the Department of Clinical Therapeutics, University of Athens, School of Medicine, and the U.S. Atomic Energy Commission.

U-6 ***"Short Term Results of 3500 R Iodine-131 Therapy of Hyperthyroidism."*** **J. M. KOPLOWITZ, J. T. NICOLOFF, W. H. BLAHD, AND E. M. GOLD, (Radio-**

isotope Service, Veterans Administration Center, Los Angeles, and the Department of Medicine, School of Medicine, University of Californa at Los Angeles)

In view of reports of a high incidence of hypothyroidism following ^{131}I therapy of hyperthyroidism, a preliminary study has been undertaken at the Los Angeles Veterans Administration Center to evaluate the therapeutic efficacy of a 3500 R dose. Seventeen male patients were included in the protocol, wherein each received one or more such doses as calculated by a modified Quimby formula. This group is undergoing long term surveillance for the ultimate incidence of hypothyroidism. The more immediate results as observed from a minimum interval of time of eight months to a maximum of 18 months are as follows.

Three became euthyroid with a single treatment (1.59 mC, 2.05 mC, and 1.0 mC ^{131}I) within four months and one more seems to be near normal (1.75 mC). Two patients are euthyroid after two doses each and achieved a euthyroid state after 7½ and 10 months respectively (total amounts, 7.3 mC and 3.9 mC). One person became permanently hypothyroid within four months after a treatment of 1.56 mC.

Ten subjects remained hyperthyroid after the initial administration of radioiodine and all have received from two to five additional doses at approximately three-month intervals. Two of these individuals were retreated with arbitrarily large quantities of ^{131}I because of clinically urgent indications and have been withdrawn from the study. Of the remaining eight patients in this group, three are improved and five remain significantly thyrotoxic.

Because of the clinical complications encountered and difficulty in management of prolonged hyperthyroidism in a high percentage of subjects, it has been our impression that the 3500 R ^{131}I schedule is unsatisfactory for routine use in our patient population.

U-7 *"Studies on the Treatment of Hyperthyroidism with Iodine-131."* KANJI TORIZUKA, TORU MORI, JUNJI KONISHI, RIKUSHI MORITA, KEN HAMAMOTO, TSUNESUKE KUSAKABE, TADASHI MIYAKE, AND MASAICHI FUKASE, (Second Division of Internal Medicine and Central Clinical Radioisotope Division, Kyoto University Medical School, Kyoto, Japan)

In 1965, statistical studies on the effects of treatment of hyperthyroidism with ^{131}I were made of 3,666 cases in 19 university hospitals in Japan. The average number of treatment was 1.4, and the mean total dose was 7.6 mC. Excellent effects of this treatment were seen in 73.3% of the cases, improved in 17.5% and hypothyroidism developed in 3.5%. From the comparison of administered doses of ^{131}I among these groups, any significant differences were not observed. Then, to find the factors related to the sensitivity to irradiation, the relation among the histological findings of thyroid tissues obtained by needle biopsy, serum LATS activities, thyroid autoantibodies and the effects of ^{131}I treatment were studied. Thyroid autoantibodies in serum were studied by the tanned red cell hemagglutination test (TRC) and complement fixation test (CF).

Lymphoid cell infiltration in thyroid tissue was observed in most cases. Good correlations were found between serum LATS activities and the proliferative changes of thyroid follicles and between the grades of lymphoid cell infiltration into thyroid and the titers of TRC antibodies. The cases with the low grade of proliferative change of thyroid follicle showed excellent results from ^{131}I treatment and all the cases that developed into hypothyroidism had moderate or severe lymphoid cell infiltration in their thyroid tissues and higher TRC titers in their sera.

The chronological alterations of titers of thyroid autoantibodies, serum LATS activities and histological changes in light and electronmicroscopic observations of thyroid tissue were investigated up to 10 years after ^{131}I treatment. In most cases of cured and hypothyroid group, serum LATS activities and titers of CF antibodies were elevated transiently after ^{131}I treatment, while in the improved or unchanged group they were not. The relations among these alterations and histological changes will be presented.

Friday, June 23, 1967
4:00—5:30 P.M.
Spanish Lounge

SESSION V. THYROID SCANNING AND DIAGNOSTIC PROCEDURES

Session Chairman: Basil Malamos, Athens, Greece

V-1 *"Early Thyroid Uptake Measurements Using the Gamma Scintillation Camera—1600 Channel-Analyzer."* DANIEL PALOYAN, KENNETH O. HENDRICKS, ALEXANDER GOTTSCHALK, AND PAUL V. HARPER, (Argonne Cancer Research Hospital [operated by the University of Chicago for the United States Atomic Energy Commission] and the Departments of Surgery and Radiology, University of Chicago, Chicago, Illinois)

Measurement of the early thyroid uptake-rate of pertechnetate-99m appears to be a sensitive method of detecting hyperthyroidism, because pertechnetate is trapped by the thyroid in a manner closely resembling iodide. The principal difficulty with these measurements is that they must be made against a high, rapidly varying neck background. Thigh background is unsatisfactory because of marked differences in vascularity. In the present study, these difficulties are resolved by simultaneously measuring thyroid uptake and adjacent neck background activity with the camera-analyzer combination.

Counts obtained from specific points in the neck are accumulated in spatially-corresponding channels in the analyzer. Measurements are started at the time of intravenous injection of pertechnetate and counts are accumulated, integrated line by line, and printed out at successive one minute intervals for 20 minutes. On completion of the test, the last collection of counts is displayed on the oscilloscope to identify channels containing thyroid and background counts, and to exclude those from the salivary glands and the great vessels. Calculation of thyroid uptake is based on similar measurements of a standard contained in a lucite neck phantom. Non-uniformity of camera response is corrected by counting a uniform sheet source.

The 20-minute pertetchnetate-99m uptake in hyperthyroid patients is consistently higher than 2% and occasionally as high as 15%, whereas euthyroid individuals have uptakes lower than 2%. The method is useful, not only because discrimination between euthyroid and hyperthyroid individuals is excellent, but also because the test is brief and results are available immediately. Finally, this method may be useful in the study of the physiology of the trapping phase of human thyroidal iodide metabolism.

V-2 *"Trapping of Pertechnetate by the Thyroid."* RICHARD A. HOLMES, WENDY A. NORTH, AND ARTHUR KARMEN, (Division of Nuclear Medicine, The Johns Hopkins Medical Institutions, Baltimore, Maryland)

Following its intravenous administration, pertechnetate ($^{99m}TcO_4^-$) is concentrated by the thyroid gland more rapidly than is iodine, but is not incorporated into organic molecules. The quantity of TcO_4^- which reflects the activity of the trapping mechanism may therefore be used as an index of thyroid function. However, its measurement in the thyroid by the methods used to determine iodine uptakes can yield erroneous results because of the contribution of extrathyroidal activity to the counting rate over the thyroid. It was measured by scanning the thyroid with a rectilinear scanner equipped with a recording ratemeter. As the focusing collimator passed over the two lobes of the thyroid, two peaks of activity were recorded. The contribution of extrathyroidal activity was estimated from the records of the scanning passes superior and inferior to the thyroid. The TcO_4^- in the gland was then estimated from the sum of the areas of the peaks minus the extrathyroidal contribution, by comparing it with the sum obtained from a scan of a phantom. This method of measuring isotope in the thyroid was evaluated in 11 patients receiving iodine-131. The values correlated well with the conventional uptakes.

The rate of increase in concentration of TcO_4^- in the thyroid was determined by disabling the indexing mechanism of the scanner and scanning across the middle of the gland repeatedly. After I.V. administration, the TcO_4^- increased for 2-3 minutes following which there was no further increase. This phenomenon indicated that what was estimated in the "30 minute" uptake was the TcO_4^- space of the thyroid rather than an "uptake" rate in the usual sense.

In a series of patients, 0.5 to 1% of the injected $^{99m}TcO_4^-$ was in the thyroid after 30 minutes. Lower values were found in patients with low ^{131}I uptakes and higher values in patients with hyperthyroidism.

V-3 *"Thyroid Uptake and Scan Using Technetium-99m Pertechnetate."* ALTON R. SHARPE, JR., CLAY T. GARDNER, JR., WILLIAM A. CASSIDA, JR., AND ELIZABETH BLAKBURN, (Department of Radiology, Medical College of Virginia, Richmond, Virginia)

The thyroidal concentration of Technetium-99m Pertechnetate has been studied in eight normal patients and in two hyperthyroid patients and thyroid scans have been obtained in two hyperthyroid patients and five euthyroid patients.

The uptake of technetium-99 pertechnetate has been correlated with the three-hours and five hour thyroidal ^{131}I uptake and with the resin T-3 uptake in the euthyroid and hyperthyroid subject. Mean thyroidal uptake of technetium-99 was 4.3% in the euthyroid group with a range from 3.0 to 9.1%. Mean uptake of technetium-99 pertechnetate in the hyperthyroid group was 18.9% with a range from 15.7 to 22.5%. Good correlation was obtained in the euthyroid and hyperthyroid group with the three-hour and five-hour ^{131}I uptake.

Thyroidal scans were performed twenty minutes following the intravenous injection of one to three millicuries of technetium-99 pertechnetate and were compared with scans obtained utilizing ^{131}I in both groups. Good delineation of the thyroid gland and definition of nodules were obtained using this dose.

Further studies are in progress to verify and extend the preliminary results obtained using technetium-99 pertechnetate.

V-4 *"The Autonomous Function of the Nodular Thyroid as Studied by Double Isotope Autoradiography."* J. MARTIN MILLER, AND MELVIN A. BLOCK, (Henry Ford Hospital, Detroit, Michigan)

The "hot" autonomous nodule identified by radioiodine scintigram is usually considered to be hyperfunctioning. The relativity of this designation can be demonstrated by a technique of autoradiography using ^{131}I and ^{125}I in the same thyroid. One isotope is used to establish the relative function of the nodule and the surrounding tissue and the other to identify the former during TSH suppression. (*J. Nuc. Med.* 7:188, 1966).

Small nodules which have not suppressed the surrounding thyroid on scintigram can be shown to function only slightly in excess of this tissue, yet retain this function during thyroxine feeding. Larger nodules with similar autonomy may be actually less functional on a unit basis and appear "hot" because of their thickness. A nodule which seems to be of decreased function on scintigram may become "hot" when surrounding tissue is suppressed. This nodule may be one with considerable functional autonomy which has been almost destroyed or a nodule with a lesser degree of autonomy that is anatomically intact. Autoradiographs labeled before and during thyroxine administration, as well as corresponding scintigrams will be presented to illustrate all of the above.

The response of the isolated functioning autonomous nodule to exogenous TSH is considered to be minimal. In the large multinodular goiter causing thyrotoxicosis, however, double isotope studies have often failed to demonstrate suppressed tissue responsible for the characteristic increase in the RAI uptake with TSH. The autonomous but poorly functioning tissue itself is therefore presumably responsible. A spectrum of degrees of functional autonomy and perhaps inversely of TSH responsiveness is suggested.

V-5 ***"Data Blending with Technetium-99m in Evaluation of Thyroid Anatomy by Scintillation Scanning."***[1] **H. L. Atkins, and R. F. Fleay, (Medical Research Center, Brookhaven National Laboratory, Upton, Long Island, New York)**

A series of patients is presented in whom scintillation scans of the thyroid were performed with technetium-99m as pertechnetate during the evaluation of the functional state of the gland. Because of the high count rates possible, excellent statistical data were obtained during the scanning procedure (SD $<\pm$ 2%); thus making it possible to use data blending to advantage.

In a small gland such as the thyroid, pattern recognition can be very difficult when the raster effect and random background densities create "noise," thus disturbing the perceptual process. Data blending, despite a theoretical loss in resolution, makes recognition of the pattern less difficult. This blending is demonstrated by comparison of scans done in conventional and data-blended methods.

The evaluation of thyroid anatomy included analysis of relative size of the two lobes. This evaluation was extremely close to a previously-published series utilizing iodine-131. The right lobe was frequently larger than the left. Other items noted were the incidence of isthmus visualization, pyramidal lobes, tapering of the poles and incidence of nodules. Examples of the anatomical variations are given.

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[1]Research supported by the U.S. Atomic Energy Commission.

V-6 ***"Scanning Patterns in Chronic Thyroiditis."*** **Jorge Franco, Nancy J. Condy, and Marion Coppler, (Radioisotope Laboratory, O'Connor Hospital Medical Center, San Jose, California)**

In the course of the study of 210 consecutive patients referred for laboratory thyroid workup and scanning, a distinctive pattern became associated with histologically–proven chronic thyroiditis of the Hashimoto's type.

This pattern, observed in six adult female patients, considered of an asymmetrically enlarged nonnodular thyroid gland with diffuse decrease in activity of the enlarged lobe.

R.A.I. 24-hour uptake, T_3 and P.B.I. values were generally normal. Antibodies to thyroglobulin, as demonstrated by the tanned sheep erythrocyte agglutination method, were present in all six patients at titers of 1:32,000, or higher. Grossly, the glands had the classical glistening tan moist firm appearance.

Microscopically, there was dense diffuse and nodular lymphocytic infiltration with presence of true germinal centers and relatively rare plasma cells. Focal areas of eosinophilic acinar cell hyperplasia were also noted. Fibrosis was relatively unimportant.

Since this scanning pattern of diffuse decrease in activity of an entire lobe has only rarely been associated with malignancy and high titers of thyroglobulin antibodies are rare outside of Hashimoto's thyroiditis, we feel that this association is almost pathognomonic of Hashimoto's thyroiditis.

V-7 ***"A Comparative Study of the Resin Uptake of Radioactive Triodothyronine and Other Radioiodine Tests in the Differential Diagnosis of endemic Goiter and Other Thyroid Diseases."*** **David Martínez Villaseñor, (Hospital General de la Ciudad de México y Comisión Nacional de Energía Nuclear, México, D. F.)**

The object of the present study was to determine which of the routinely used radioiodine tests can help establish the functional status of patients coming from endemic goiter areas.

In our laboratory we found that a majority of these patients clinically borderline or euthyroid cases have a 24-hour thyroid uptake and a 24-hour conversion ratio corresponding to the values observed in hyperthyroid patients. In a series of 1000 cases in which 4554 studies were performed, we found that the triiodothyronine resin-uptake test gave much better infor-

mation about thyroid function than the other two methods employed, either separately or combined.

The thyroid suppression test was not as useful as T_3 resin-uptake to distinguish the endemic-goiter patients with high uptake from the hyperthyroids, although most of the endemic-goiter cases that failed to be suppressed were classified as what we would consider having pre-toxic autonomous-functioning nodules. Thyroid scanning did not offer reliable information to be able to establish diagnosis in doubtful cases.

It was noted that T_3 resin-uptake is not a convenient method for separating hypothyroid from euthyroid patients; although, as other authors have observed, we found the test very useful in patients receiving iodinated compounds. We suggest the use of triiodothyronine resin-uptake, combined with other radioiodine tests, especially for radioisotope laboratories dealing with a high incidence endemic-goiter population. No one single test can help establish a reliable diagnosis of thyroid disease, whether it be endemic goiter or any other thyroid functional disturbance.

Friday, June 23, 1967
9:00—10:30 A.M.
Georgian Room

SESSION W. RADIATION BIOLOGY AND ANALYTICAL METHODS

Session Chairman: **John H. Lawrence, Berkeley**

W-1 *"Age Factors in the Induction of Mouse Leukemia."*[1] SHIELDS WARREN, AND OLIVE GATES, (Cancer Research Institute, New England Deaconess Hospital, Boston, Massachusetts)

This work is designed with references to the validity of the current assumption that mammals are more susceptible to induction of leukemia during the intrauterine and neonatal periods. We have carried out a series of experiments involving the exposure to gamma radiation of mice throughout pregnancy and neonatal period. The radiation source was a cobalt-60 wire placed in the body of the mother. The experimental mice were of two kinds, RAP with high incidence of spontaneous leukemia and Ajax with low. For comparison we have used the incidence of leukemia in unirradiated mice and mice exposed from conception to death to low-level ambient gamma radiation. We have separated intrauterine irradiation from a neonatal period of radiation of equal length by transferring young of source-bearing mothers to foster mothers without sources at the time of birth and vice versa. Since there may well be different factors involved in leukemia of differing cell type, the leukemias induced have been differentiated histologically.

Only those mice living over 150 days are included, as our earliest case of leukemia developed at 155 days. Thus far, about 500 experimental animals have been studied and the results tabulated below. Estimated doses ranged from 170 to 1500 rads. These preliminary data do not suggest heightened susceptibility to leukemogenesis from this type of exposure to continuous gamma radiation during embryonic and neonatal life.

PER CENT OF ANIMALS WITH LEUKEMIA

Strain	Ajax	RAP
Control	0	25
Low-level chronic radiation	0	55
Intrauterine radiation	7	15
Neonatal radiation only	0	20
Combined intrauterine and neonatal radiation	2	30

[1]Supported by U. S. Public Health Service Grant FR 5591 and by U. S. Atomic Energy Commission Contract AT(30-1)-3777 with the New England Deaconess Hospital.

W-2 ***"Abnormalities in Histidine Metabolism Following Radiation."*** **T. M. Ngo, H. S. Winchell, S. Landaw, and J. H. Lawrence, (Donner Laboratory, University of California, Berkeley, California)**

The pattern of appearance of $^{14}CO_2$ in the breath following administration of #2 ring $^{2\text{-}14}$C-labeled histidine has been shown to be dependent on the availability of tetrahydrofolic acid (THF). We demonstrate abnormalities in such appearance of $^{14}CO_2$ in the breath of rats subsequent to total body radiation and postulate that the abnormalities are related to radiation inactivation of THF or the processes required for its production. Twelve Buffalo rats were given 5μC of #2 ring-C^{14}-Histidine I.V. and the appearance of $^{14}CO_2$ in the breath was measured continuously for 80 minutes. Prior to radiation, in each animal the time at which maximum rate of $^{14}CO_2$ excretion occurred (T.max.) was in the range of 12 to 12.5 minutes and the average per cent of ^{14}C excreted as $^{14}CO_2$ in the 80 minutes was 1.177 ± .008%. Three groups of two animals each were given 200, 400 and 600 R and repeat studies were performed 20 minutes 2, 5, 8, 11, 15, 23 and 30 days after radiation. T. max. was significantly prolonged immediately after radiation at each dose level. Maximum prolongation in T.max. was reached at 5 to 8 days and these values returned to near normal by 15 days. A delayed diminution of the per cent ^{14}C excreted occurred on the fifth to eighth days, returning to the normal range by the fifteenth day. The extent of abnormalities seen appeared to be dose dependent and independent of the time course of bone marrow cell damage. These results suggest a mechanism for radiation induced abnormalities in "1C" metabolism, particularly as related to nucleic acid synthesis.

W-3 ***"The Role of Energy Metabolism in the Repair of Radiation Injury by L Cells."***[1] **Glenn V. Dalrymple, J. L. Sanders, Max L. Baker, and J. L. Schrantz, (Departments of Radiology and Physiology of the University of Arkansas Medical Center and the Radiology Service, Veterans Administration Hospital, Little Rock, Arkansas)**

During the past decade, several studies have suggested that radiation produces an alteration of energy metabolism. Because this earlier experience indicates that radiation may produce these changes in the intact animal by abscopal mechanisms, we have used cultured mammalian cells (L cells) to avoid abscopal influences.

Single cell experiments of two types were performed. In the first group of studies, the cells were preincubated with 10^{-4} M dinitrophenol (DNP) before irradiation with spaced doses for determination of cell survival curves. Since DNP uncouples oxidative phosphorylation, it produces a depression of intracellular adenosine triphosphate (ATP), the final common carrier of biological energy. For the second group of single cell experiments, the cells were irradiated with 500 rads of $CO^{60}\gamma$ radiation and DNP was then added at intervals after exposure.

Biochemical studies were also performed with irradiated L cells. At intervals after irradiation, measurement of respiration was made with an oxygen electrode. The levels and the incorporation of $^{32}PO_4$ and Glycine-1-^{14}C into DNA, RNA, protein and the acid soluble fraction (which contains the intracellular nucleotides-including ATP) were determined.

The comparison of the cell survival curves with the biochemical data will be discussed.

[1]Supported by NASA Grant No. NGR 04001-014.

W-4 ***"A Numerical Method for Estimating the Parameters of Post-Irradiation Cell Survival Curves."***[1] **James H. Meade, Jr., and Glenn V. Dalrymple, (The Departments of Biometry, Physiology and Radiology, University of Arkansas Medical Center, and the Department of Radiology, Veterans Administration Hospital, Little Rock, Arkansas)**

An important consequence of irradiation is that injured cells loose their ability to perform sustained and repeated mitoses. In the usual experiment, known numbers of cells are seeded onto petri dishes. These dishes are given graded single doses of radiation and

the cells then allowed to grow long enough to produce macroscopic colonies. The results are scored by determining the surviving fraction (the ratio of the number of colonies on the irradiated plates to the number of colonies on the non-irradiated control plates) as a function of radiation dose. The surviving fraction (y) as a function of dose (x) is given by:

$$y = 1 - (1\text{-}e^{-\frac{x}{\beta}})^{\alpha}$$

where alpha and beta are the two non-linear parameters to be estimated. This paper describes the use of a numerical method to estimate the parameters of the above equation by least squares. It requires the use of a small scale computer. The primary advantage of this method is that objective estimates of the parameters are obtained without the use of transformations.

[1]Supported by NASA GR-04-001-014 and NIH FR-00208-01.

W-5 *"RBE of Negative Pion Beams in the Bragg Peak Region."* W. D. Loughman, (Donner Laboratory, University of California, Berkeley, California)

The search for more effective modes of radiotherapy has stimulated interest in beams of negative pi-mesons. This subnuclear particle, like other charged particles, gives up a significant fraction of its kinetic energy in the terminal portion of its range, yielding the familiar "Bragg peak" on a diagram of energy loss per unit path length vs total path length. Unlike many other particles with therapeutically useful range in tissue and a Bragg peak, negative pions also interact with atomic nuclei at the end of their range. The resultant nuclear fission produces a number of short-range highly ionizing particles whose energy adds to that produced by "Bragg peak"–type effects. Early investigations suggested that a beam of negative pions with the Bragg peak region centered in a tumor should show a high ratio of tumor dose to surrounding tissue dose. The high LET particles produced in the peak region should also produce effects greater than an equivalent dose of X-rays. Therefore, the peak region of negative pion beams should have a high relative biological effectiveness (RBE).

Using an *in vivo* mammalian cell system, the RBE for polyploidy induction of fractions of a π^- beam have been determined, in which plateau, or preterminal, π^- beam RBE = 1, compared to Co-60 gamma rays. Peak region π^- beam RBE = 2.15. For pion effects only in the peak region, RBE = 2.37. For "stars" only, RBE = 3.64. This latter value represents an estimated upper limit to π^- RBE for polyploidy induction. From theoretical considerations, it is believed RBE values for cell-killing may be higher than those found for polyploidy induction. The low ratio of surface dose to depth dose displayed by these beams, coupled with the relatively high peak region RBE demonstrated in these experiments, indicate π^- beams may be more useful in tumor radiotherapy than any other form of external radiation currently available.

W-6 *"Double Isotope Dilution Derivative Assay of Plasma Testosterone."* Mario Sparagana, (Radioisotope Service, Veterans Administration Hospital, Hines, Illinois)

Isotopic techniques have facilitated measurement of trace substances present in biological fluids and are often used when conventional chemical techniques lack adequate sensitivity.

The present analysis for plasma testosterone employs testosterone-4-C^{14} (58 mC/mM) as marker steroid to correct for losses and acetic-H^3 anhydride (100 mC/mM) as deriving reagent for mass measurements. Addition of testosterone acetate carrier after acetylation assists in recovery during purification, which is achieved by several thin-layer separations and a final gas chromatography step. Testosterone acetate in the gas chromatographic effluent is collected and the H^3 and C^{14} present are counted in a liquid scintillation spectrometer set for double label counting.

Mean plasma testosterone for normal males was 0.59 μg% and for normal females 0.09 μg%. Accuracy of the procedure was established by recovery of known amounts of testosterone added to normal saline and plasma. Absolute recovery during the entire procedure was about

15% and analytical recovery was quantitative. Specificity was assured by multiple chromatographic purification steps and arrival at constant H^3/C^{14} ratios.

The method is being applied to studies of androgen status in normal humans and in a number of pathological conditions including various endocrinopathies, hypogonadal and virilized states, cirrhosis of the liver and carcinoma of the prostate and breast.

W-7 ***"Uniform Dose for Photoactivation Analysis of Iodine."*** **JOHN A. CARDARELLI, ELISABETH S. DELL, RAYMOND D. COOPER, AND BELTON A. BURROWS, (Evans Memorial Department of Clinical Research, the University Hospital, Inc., the Radioisotope and Medical Service, Boston Veterans Administration Hospital, the Department of Medicine, Boston University Medical Center, Boston, and the U. S. Army Laboratories, Natick, Mass)**

For studies of iodine kinetics in normal subjects and in patients with thyroid diesase, a sensitive, specific and precise method of determining iodine in biological samples is necessary. Previous work has shown that ^{126}I can be produced from ^{127}I by photoactivation. The (γ, n) reaction was obtained by using a 22 MeV linear accelerator and converting the electrons with a tungsten target. The dose rate of the photons on center line of the beam was found to be in the order of 10^6 R/min at 10 cm. In a study of reproducibility and sensitivity of ^{126}I measurement in various samples, it became necessary either to measure accurately the dosimetry of individual samples or to deliver uniform dose rate to them.

Three experiments were performed. In the first, using glass planchets in rouleau formation and perpendicular to the beam, we observed a large variation in dose rate between each planchet.

In our second experiment, suggested by others, we placed our samples in ordinary test tubes and irradiated them in front of the beam, rotating them on a 45 rev/min turntable. However, because our samples were bunched together, variations of up to 20% in dose rates between samples were observed.

In our third experiment, the possibility of using as external dosimeters the glass test tubes which contained the samples was explored. Liquid samples containing KI in plastic or glass tubes and internal solid standards of copper wire or of tin foil were prepared. The test tubes were arranged in a circle in a gallon-size can and rotated during irradiation. The radioactivity of the unselected glass tubes (mainly ^{22}Na) showed less than 10% variation. For various reasons, the measurements of the internal standards gave less reproducible figures. We concluded that glass test tubes of uniform composition would make accurate dosimeters.

Friday, June 23, 1967
11:00—12:30 P.M.
Georgian Room

SESSION X. LUNG, I

Session Chairman: **Henry N. Wagner, Baltimore**

X-1 ***"A Multifaceted Approach to Quantifying Pulmonary Physiology: The Autofluoroscope."*** **J. GOODRICH, D. SABISTON, R. JONES, R. ALLGOOD, AND A. WYRICK, (Duke Medical Center)**

A study of pulmonary vascular supply, ventilation space, gas diffusion rate and the alteration of these by acute pulmonary arterial occlusion has been approached using the digital autofluoroscope. The unique capacity of this instrument to obtain kinetic measurements from a uniform array of zones through an organ or region has made this study feasible. In addition, static (pre-set count) data acquisition and oscilloscope display was recorded on polaroid film and correlated with dynamic data and rectilinear scan records. In this pilot study, six mongrel dogs averaging 35 lbs. were subjected to inhalation of ^{133}Xe and breath-held for 60 seconds before release while serial 1 second count accumulations were recorded on the computer

type tape. Next, the respiratory exhaust of an intravenous injection of ^{133}Xe saline was recorded and finally an I.V. injection of ^{99m}Tc MAA was made and recorded as it perfused the pulmonary vascular bed. After 90 seconds of kinetic recording, a static accumulation to a pre-set 1,000 counts in a channel was obtained, placed on the tap for computer analysis and photographed for comparison with the rectilinear scans obtained at the conclusion of the autofluoroscope measurements. For each tracer administration the dynamic count rate data from each lung, regions within the lungs and the cardio-pulmonary complex were transcribed from the tape to a strip chart recorder and compared with the cardio-green recordings. From this comparison there is a good indication that a valid cardiac output measurement may be made using the ^{99m}Tc MAA injection. Therefore, the digital data obtained from regions of the tracer-perfused lungs may be quantified and expressed as values for regional blood flow. Alterations of these physiologic parameters following acute pulmonary artery occlusion will be analyzed from the computer readout of taped data.

X-2 *"Lung Scanning in the Detection of Regional Alterations of Ventilation/Perfusion Ratios."* FELIX J. PIRCHER, (Radioisotope Service, Veterans Administration Hospital, Houston, Texas)

Inhalation and perfusion scans were carried out in over 100 patients with lung disease. The procedure was as follows: 4-6 millicuries of ^{99m}Tc-labeled human serum albumin were nebulized and inhaled over a period of 20 to 30 minutes. Within two hours after the inhalation, a scan of the patient's chest was obtained. Following it, the scan was repeated with the patient in the same position shortly after the I.V. injection of ^{131}I-labeled albumin macroaggregates. Areas of deficits of particle retention were then located on both scans and compared with one another. We noticed that diseases such as emphysema, tuberculosis, pneumonia, certain forms of neoplasms and cystic fibrosis and other such diseases produced areas of deficits of injected as well as inhaled particles. In other forms of lung diseases, however, areas of perfusion deficits showed a normal deposition of aerosol particles and, vice versa, areas of ventilation deficits a normal retention of injected particles. These discrepancies in particle retention seemed to represent regional alteration in V/Q ratios. Increased ratios, i.e., decreased retention of injected and normal retention of aerosol particles were found in patients with pulmonary emboli, in one patient with congenital hypoplasia of the left pulmonary artery and in some patients with neoplastic lung lesions. Decreased ratios, i.e., decreased retention of aerosol and normal retention of injected particles were found in patients with bronchial asthma, in one patient with bronchiolitis obliterans and in one out of five patients with cystic fibrosis. Bronchogenic carcinoma often produced extensive deficits in perfusion as well as in ventilation. Occasionally, recovery of ventilation was noticed in these areas after radiation therapy while perfusion deficits remained unchanged. In patients with bronchial asthma, treatment produced recovery of ventilation only in areas that appeared to be perfused. Restoration of perfusion was so far observed only in areas affected by pulmonary emboli.

X-3 *"Measurement of Regional Pulmonary Ventilation with Radioxenon and the Anger Camera."* E. L. SURPRENANT, L. R. BENNETT, M. M. WEBBER, AND A. F. WILSON, (University of California, Center for the Health Sciences, Los Angeles, California)

The distribution of pulmonary ventilation can be accurately determined by obtaining serial images of the lung with the Anger Camera while a subject is breathing radioxenon gas. This technique requires a minimum of equipment and is easily applicable to routine clinical use where an instrument such as the Anger Camera is available.

A closed system containing 6 liters of room air and 5 mc ^{133}Xe was constructed from a conventional *water* spirometer. The subject breathes this mixture while serial images of his lungs are obtained with the Anger Camera. Once equilibrium is established, he breathes room air and serial images are obtained during this "washout" phase. Lung regions which ventilate poorly are late in concentrating radioxenon, but retain radioactivity during the "washout."

This method demonstrates regional pulmonary ventilation. Combined with similar studies following the intravenous injection of macroaggregated radioalbumin, a useful estimate of ventilation-perfusion ratios for individual lung segments is obtained.

Studies were obtained on subjects with intrathoracic tumors, asthma and pulmonary emboli.

X-4 *"The Inhalation Scan in Emphysema (A Measure of Non-Functioning Lung)."* E. K. Dore, N. D. Poe, and G. V. Taplin, (The Nuclear Medicine Department, Long Beach Memorial Hospital and the Laboratory of Nuclear Medicine and Radiation Biology, UCLA School of Medicine)

The inhalation scan in emphysema is a semi-quantitative measure of non-functioning lung. The per cent of total lung which lacks radioaerosol deposition agrees closely with the per cent of total lung which is occupied by residual air (RV/TLC). The inhalatory scan correlates better with the pulmonary function value (RV/TLC) than does the perfusion examination.

Inhalation lung scanning separates emphysema patients into a minority whose aerosol deposition mimics the distribution of arterial perfusion and a majority with a tendency to central hilar deposition. In the latter type, the inhalation scan may be helpful in predicting the patient's response to medical management and/or his prognosis regarding the natural courses of the disease.

X-5 *"Comparison of the Pulmonary Distribution of Xenon-133 Solution and Iodine-131 Macroaggregated Albumin."* Gerald L. DeNardo, Jerome S. Brody, Paul J. Leach, Donald J. Bowes, and Jon B. Glazier, (Nuclear Medicine Service, Veterans Administration Hospital, Stanford School of Medicine, Palo Alto, California)

A profile scanner with four detectors was used to compare the pulmonary distribution of 133 Xe solution and ^{131}I macroaggregated albumin (IMAA) after intravenous administration. Six normal subjects were studied in the supine and upright positions. For each radiopharmaceutical, the blood flow to each lung and to each of twenty lung zones was measured.

In the supine position, both Xenon and IMAA showed 52 per cent of total pulmonary blood flow in the right lung and 48 per cent in the left lung. In the upright position, Xenon showed 50 per cent in each lung, whereas IMAA showed 48 per cent in the right lung and 52 per cent in the left lung.

In the supine position, the distribution of pulmonary blood flow to each lung zone was approximately equal by the two methods, although the IMAA method resulted in slightly greater values to the lowest zones of the right lung. This fact could be due to liver radioactivity.

In the upright position, the gradient of blood flow from lung apex to lung base was slightly greater with the IMAA method when compared with the Xenon method. Various technical and physiological explanations for this difference will be discussed.

We conclude that the two methods measure the same parameter and provide approximately the same results in normal subjects. This study provides additional validity to each of these methods of measuring pulmonary capillary blood flow.

X-6 *"Correlation of Pulmonary Scanning and Angiography in Embolic Disease of the Lung."* Leonard M. Freeman, Melvin N. Zelefsky, Chien-Hsing Meng, and Neville Kaplan, (Department of Radiology, Albert Einstein College of Medicine, Bronx, New York)

A combined diagnostic approach of lung scintiscanning and pulmonary angiography was employed in 18 patients clinically suspected of having pulmonary embolism. Including fol-

low-up studies, a total of 35 scan examinations and 20 angiograms were performed on these patients. In almost all instances, both anterior and posterior scans were performed. If time allowed only for a single view, experience showed that the posterior study was preferable.

The procedures were found to be quite complementary and should not be considered competitive. The ease of performance and innocuous nature of the lung scan makes it the procedure of choice for screening purposes. The presence of an infiltrate on chest x-ray does not contraindicate scanning, since in most instances showers of emboli occur and cause multiple perfusion defects throughout both lungs. Peripheral emboli beyond the tertiary and quaternary branches of the arterial tree are generally best detected on the lung scan.

The presence of blebs, bullae or other emphysematous changes on the chest roentgenogram usually makes angiography the procedure of choice. Specific anatomic localization of emboli can be better supplied to the surgeon with pulmonary angiography. Occlusion of a vessel or demonstration of an intraluminal filling defect are the only diagnostic angiographic features of pulmonary embolism, although some less specific observations, such as relative lucency in the lung field and segmental slowing of the circulation, may also suggest the diagnosis. Selective arteriography will enhance diagnostic accuracy.

Since none of the patients in this series required surgical intervention, valuable information concerning the natural history of pulmonary embolism and infarction in man was obtained by following these patients serially with chest roentgenograms and scans. The usual course was rapid, often daily improvement associated with either recanalization, dissolution or peripheral dispersion of the clots. In other instances, areas of embolism not apparent on the initial studies were detected at a later time. In occasional cases, the embolized areas remained unchanged in appearance on the follow-up studies suggesting organization of the clot.

X-7 *"Misinterpretation of Lung Scans in the Diagnosis of Pulmonary Embolism."*

NORMAN D. POE, EARL K. DORE, LEONARD A. SWANSON, AND GEORGE V. TAPLIN, (Laboratory of Nuclear Medicine and Radiation Biology, University of California at Los Angeles; Harbor General Hospital, Torrance, California and Memorial Hospital, Long Beach, California)

As lung scanning becomes more widely utilized in the diagnosis of pulmonary embolism, "false positive" scans are being reported with increasing frequency. Actually a "false positive" scan is a euphemism for a misinterpreted scan and can result from poor techniques, improper correlation with clinical information, or failure to recognize that a number of physiologic and pathologic conditions can produce regional pulmonary ischemia identical to that found in pulmonary embolism. With thoracic surgeons attempting pulmonary embolectomy with greater frequency and enthusiasm, incorrect diagnosis of embolization in acutely ill patients may lead to unwarranted and disastrous surgery.

The posture of the patient at the time of tracer injection has a significant influence on the distribution of the injected particles. In the erect position blood flow to the upper lungs is normally reduced, but this is the best position for identifying basilar lesions. In the horizontal position, a more equal distribution of aggregates throughout the lungs is produced, but basilar emboli are more difficult to detect. Other conditions that secondarily alter pulmonary arterial perfusion are obesity, cardiomegaly and congestive heart failure, and pulmonary hypertension.

Ischemia on the scan alone is insufficient evidence on which to base a diagnosis of pulmonary embolism. However, the etiology of the ischemia in most lung diseases is apparent on the chest radiograph. An exception is emphysema, which may cause ischemia without characteristic x-ray changes. Serial scanning may support embolism by demonstrating rapid restoration of blood flow which is uncommon with emphysema.

Occasionally the scan may fail to indicate the extent of a major embolic process. This situation can occur when large emboli partially occlude the pulmonary arteries bilaterally. If the clinical findings suggest greater involvement than the scan, pulmonary angiography is definitely indicated. However, in the great majority of cases, a properly interpreted lung scan will demonstrate pulmonary embolization as effectively as any test now available.

Friday, June 23, 1967
2:00—3:30 P.M.
Georgian Room

SESSION Y. a) LUNG, II
b) THERAPEUTIC APPLICATIONS OF RADIOISOTOPES

Session Chairman: George V. Taplin, Los Angeles

Y-1 *"Indium-113m Labeled Iron Hydroxide Particles for Lung Scanning."* DAVID A GOODWIN, HOWARD S. STERN, AND HENRY N. WAGNER, JR., (Division of Nuclear Medicine, The Johns Hopkins Medical Institutions, Baltimore, Maryland)

The measurement of regional pulmonary arterial blood flow by radioisotope scanning after the injection of radioactive particles is useful in the diagnosis of several pulmonary diseases in physiological studies of the pulmonary circulation. Indium-labeled iron hydroxide particles offer certain advantages over ^{131}I-labeled macroaggregated albumin (MAA). Indium-113m decays with a half-life of 1.7 hours and emits 390 KeV gamma rays and no beta rays, a mode of decay that results in a low radiation dose to the patient.

Carrier-free ^{113m}In can be obtained from 118-day ^{113}Sn in a nuclide generator. It can be easily incorporated into iron hydroxide particles of relatively uniform size (20-40 micra), which can be sterilized by autoclaving. The final specific activity of the particles is approximately 20 microcuries/microgram. After intravenous injection, of a 2mc dose, approximately 90 per cent of the particles are trapped in the lungs. Although the radioactivity decays with a physical half-life of 1.7 hours, the particles of iron hydroxide leave the lung with a half-time of about 12 hours. Both indium and iron hydroxide are non-toxic to animals with doses of at least 10,000 times higher than those used for lung scanning in man.

We have now performed over 150 lung scans with the new agent and have compared the results obtained with ^{131}I-MAA in more than 20 patients studied with both agents. No toxic, hemodynamic or pyrogenic reactions have been observed. With the usual 300 microcurie dose of ^{131}I-MAA, the absorbed radiation dose to the lungs is about 4.5 rad per millicurie, compared to about 0.75 rad/mc with the ^{113m}IN particles. The high count rates obtained with ^{113m}In make it possible to obtain better images in less time than with the ^{113m}I-MAA. The indium particles are much less expensive and it is not necessary to administer thyroid-blocking agents, such as Lugol's solution, as in the case of ^{131}I-MAA.

Y-2 *"Lung Scanning with a High Speed 5-inch Dual Detector System."* ARTHUR A. SASAHARA, JOHN S. BELKO, AND ROBERT G. SIMPSON, (Research and Medical Services, Veterans Administration Hospital, West Roxbury, and The Department of Medicine, Harvard Medical School, Boston, Massachusetts)

Intravenous radioisotope lung scanning has rapidly gained an important role in the early diagnosis of pulmonary embolic disease. Its main virtues have been simplicity, safety, ease of performance and reasonable specificity in diagnosis. There are limitations, however, to the conventional method of single-plane scanning. The lung, unlike other organs of the body, has great depth and is therefore incapable of being fully scanned by a single detector. There are large areas of lung lying beyond the range of effective collimation which are generally undetected. Both anterior and posterior scans may be obtained sequentially to improve coverage, but only at the expense of prolonging scan duration (40-60 minutes). This problem poses a serious limitation in seriously ill patients where its application should be most useful.

By employing a high speed dual opposed 5-inch crystal scanner which permits simultaneous scanning of the anterior and posterior portions of the lungs, more complete information of lung perfusion has been obtained. The procedure, using 250-400 uC of I^{131} macro-aggregated serum albumin, requires approximately 10-14 minutes, or one-fifth of the time previously required to obtain both views. With this instrumentation, it has also been possible

to obtain simultaneous right and left lateral scans which have been especially useful in defining vasculature in the costophrenic areas as well as providing more precise localization and estimation of antero-posterior defects. In addition, small to moderate perfusion deficits in the extreme anterior or posterior regions not ordinarily detected by frontal views have been visualized by lateral projections.

Another innovation has been the use of a data-blending method for obtaining a fused image in place of the conventional slit photorecording. Electronically performed, this technique offers less random fluctuation of count-rate resulting in a reasonable relationship between counting rate and optical density.

Y-3 *"Comparison of the Anterior and Posterior Lung Scan Views in Relation to Their Individual Information Content."* JOHN A. BURDINE, AND W. MARION JORDAN, (Nuclear Medicine Division, Department of Radiology, Baylor University College of Medicine, Houston, Texas)

Although lung scanning has become firmly established as a reliable means of assessing regional pulmonary capillary perfusion in conditions such as pulmonary thromboembolism, the technique continues to undergo refinement. During the past 18 months, a considerable number of investigators stressed the opinion that significant areas of decreased isotope activity ("cold" defects) will frequently be missed if scanning is confined to either the anterior or posterior view alone. Since many patients with regional deficits in pulmonary blood flow are unable to lie prone, the anterior scan is the only view possible with the conventional scanner. To determine just how much information may be lost in such a patient, we undertook the analysis of scans from a series of 100 patients each of whom had a definite pulmonary parenchymal abnormality. An anterior and a posterior scan were performed in each of these patients and many had a lateral view as well. A variety of cardiorespiratory illnesses were represented in the group, including pulmonary thromboembolism, pulmonary fibrosis, bronchogenic carcinoma, lung abscess and lobar pneumonia. In spite of the fact that a number of these patients had fairly small areas of decreased pulmonary capillary perfusion at the extreme anterior or posterior limits of the chest, in the great majority of cases the abnormality could be seen on either the anterior or posterior scan. A geometric diagram using an appropriate iso-response curve for lung scanning is presented as a possible explanation for this finding.

Y-4 *"The Intralymphatic Administration of Radioactive Isotopes in the Overall Treatment of Malignant Melanoma."*[1] IRVING M. ARIEL, MICHAEL I. RESNICK, AND RUBEN OROPEZA, (Pack Medical Foundations, Inc., and Division of Radioisotopes, Department of Radiology, Hospital for Joint Diseases, New York)

This report details the role which the intralymphatic infusion of radioactive isotopes plays in the treatment of malignant melanoma. Three isotopes have been used: (1) yttrium 90 (^{90}y) micromicrospheres[1] (1-4 micron in diameter plastic spheres); (2) radioactive gold 198 (^{198}Au) in colloidal suspension; and (3) radioactive iodine 131 Ethiodol (^{131}I Ethiodol).

Although the malignant melanoma is a radioresistant lesion, nevertheless it is radioresponsive. The intralymphatic administration of radioactive isotopes is particularly indicated in treating those patients who have a primary lesion on the extremity, especially the distal portion (hand or foot) and in whom there is a question of metastasis to the inguinal or the axillary lymph nodes. It has been demonstrated that the performance of an incomplete operation, that is, a radical resection of the primary melanoma with either a radical groin or axillary dissection leaving the intervening lymphatic vessels intact is not without hazard. Accordingly, the following sequence of events occurs. There is a pouring out of lymph, and possibly melanoma cells, into the free tissue spaces followed by an anastomosis of the lymphatic vessels and the development of unpredictable types of collateral lymphatic circulation, with the resultant unpredictable distribution of the cancer cells. If the collateral circulation is inadequate, regurgitation of lymph occurs in the newly-formed dermal lymphatic vessels

[1]Manufactured by 3M Company, St. Paul, Minnesota.

and melanoma cells in-transit will be transported into these dermal lymphatic channels where they "take" and grow producing satellitoses.

Twenty patients with malignant melanoma were treated by the intralymphatic infusion of radioactive isotopes. After identification, the isotopes were infused via a lymphatic vessel on either the dorsum of the hand or the foot, which permits the deliverance of a satisfactory dosage of internal irradiation to either the axillary or the inguinal, femoral and iliac lymph nodes. Large dosages of internal irradiation varying from 20,000 to 40,000 rads beta can be safely obtained in the lymph nodes without deleterious effect upon the contiguous tissues, and without any alteration in lymphatic dynamics.

To date, none of the patients in this series have developed metastases. The treatment has been well tolerated, without complications, and the results appear most encouraging.

Y-5 *"Allograft Survival Following Antibody Suppression with Radioiodine-Labeled Antigen."* MILO M. WEBBER, (Department of Radiology, UCLA, Los Angeles, California)

Antibody suppression following irradiation of rabbits with the intravenous injection of particulate antigen labeled with 131 radioiodine was reported by the author in 1964. Animals who had been sufficiently irradiated failed to produce detectable antibodies to a test antigen, while stigma of total body irradiation was absent. The irradiation is delivered to the reticulo-endothelial system and its vicinity.

The usefulness of this technique of antibody suppression was then assessed in the prolongation of skin allograft survival. A/J white mice were the hosts and C/57 black mice were the skin donors. Intravenous injection of .5 mc of 131 radioiodine labeled particulate antigen (tobacco mosaic virus) was performed in a series of 20 mice. Survival of the skin allograft and growth of black hair for periods ranging to six or seven weeks were noted. The experiment was controlled by several groups of mice including those receiving 131 radioiodine intravenously. Control groups failed to show growth of hair and survival was limited to less than two weeks. The effects of whole body irradiation were absent. A marked lyphocytopenia was seen in the radioiodine-labeled antigen group and not in the others.

Y-6 *"Aminopterin—Iodine-131, a Folate Antagonist: Preparation, Distribution, and Scanning in Man."*[1] J. R. BERTINO, R. P. SPENCER, P. K. CHANG, E. LEFKOWITZ, AND D. G. JOHNS, (Yale Univ. School of Medicine, New Haven, Connecticut)

The folate antagonist aminopterin persists in liver and kidney for several weeks after administration, tightly bound to the enzyme dihydrofolate reductase. The compound 3′-^{131}I-aminopterin, which can be monitored by external scintillation counting, has been synthesized for the purpose of following its persistence in organs. The iodination of aminopterin was carried out at room temperature in aqueous solution; the product was isolated in 5-10% yield by chromatography on DEAE-cellulose. It exhibited UV-absorption, as well as chromatographic properties, identical to those of unlabelled 3′-I-aminopterin. The labelled material (specific activity 45 to 120 μC per μmole) has been administered to six patients with advanced neoplastic disease at a dosage of 2 μC/kg. The plasma disappearance rate, organ distribution and urinary excretion have been measured. By external scintillation counting, the highest levels of radioactivity were found over the liver, kidney, spleen, and thyroid. Pretreatment of the subjects with Lugol's solution prevented uptake by the thyroid, indicating that some of the compound was undergoing dehalogenation *in vivo* and that radioactivity in the thyroid represented free iodide. After an initial rapid disappearance of the radioactivity over liver and kidney, the rate of disappearance from these organs became much slower; the latter radioactivity could be displaced by unlabelled methotrexate, suggesting that it represented unchanged, enzyme-bound 3′^{131}I-aminopterin and that the drug bound to dihydrofolate reductase is only minimally subjected to dehalogenation *in vivo*. These preliminary studies indicate that tracer doses of 3′-^{131}I-aminopterin may be useful for monitoring turnover of the folate antagonist in the liver and kidney in human subjects.

[1]Supported by Grants CA 06519, CA 08010, CA 0810 and AM 09429 from the United States Public Health Service.

Y-7 ***"Comparisons of Radiocolloid Distribution Following Administration by Portal Vein and Peripheral Vein Injections."*** **NORMAN B. ACKERMAN, (Department of Surgery, Boston University Medical Center, University Hospital, Boston, Massachusetts)**

In earlier studies (J. Nuclear Med. 4:234, 1963) we demonstrated the value of therapeutic doses of ^{32}P-tagged colloidal chromic phosphate in decreasing tumor "take" in the liver of experimental animals. This radio-colloidal material, which averages in size from 0.5 to 1.5 microns is rapidly cleared from the blood by the RE system, mainly in the liver. In attempting to build up a therapeutic dose in the liver, we have become interested in comparing the uptake of radiocolloid when administered by portal vein and by peripheral vein injection. We were particularly concerned about the possibility of exposing other organs (spleen, kidney and lung) to excessive radiation following intravenous administration as compared with portal vein injection.

Sprague-Dawley rats were given 10-25 uC of ^{32}P-tagged colloidal chromic phosphate by either portal vein or peripheral vein injection. The animals were sacrificed on the fifth day and radioactivity in the livers, spleens, kidneys, lungs and hearts were counted in a well-scintillation counter. Seventeen intravenous and 15 portal vein studies were completed. Mean uptake of colloidal chromic phosphate in the liver appeared to be the same in both groups: 39.1% following intravenous injection and 40.4% following portal vein injection. The range of the liver uptake varied widely in both groups. The uptake of radiocolloid in the other organs was as follows: in the IV group, spleen 1.0% kidney 0.10%, lung 0.14%, and heart 0.03%; in the PV group, spleen 0.56%, kidney 0.10%, lung 0.06% and heart 0.03%. The differences appear to be of little significance and the results indicate that a therapeutic dose to the liver could be achieved by a simple intravenous injection without fear of excessive radiation to other organs. In addition, there would appear to be little advantage in using a portal vein route for irradiating the liver.

Friday, June 23, 1967
4:00—5:30 P.M.
Georgian Room

SESSION Z. PANCREAS, ADRENAL AND SALIVARY GLANDS, AND THE PLACENTA

Session Chairman: **Millard N. Croll, Philadelphia**

Z-1 ***"Evaluation of Pancreatic Disease by Dual Channel Scanning."*** **ERVIN KAPLAN, MOSHE BEN-PORATH, SIDNEY, FINK, GLENN D. CLAYTON, AND BURTON JACOBSON, (Radioisotope and Medical Services, Veterans Administration Hospital, Hines, Illinois)**

The visualization of the pancreas by selenomethionine-^{75} may be accomplished without interference from the hepatic image by the technique of dual channel scanning previously described by the authors. This method either subtracts the liver from the print out or simultaneously displays the liver and pancreas in separate colors. By this means, 60 patients have been studied to date, including 25 patients with normal pancreas, 11 cases of pancreatic carcinoma and 10 cases of chronic pancreatitis. Fourteen patients are awaiting confirmation of diagnosis. The normal pancreas is consistently visualized. The diagnosis of carcinoma of the pancreas made by this method was subsequently confirmed by surgery or necropsy. In three patients, the correct diagnosis was made by scanning after conventional x-ray studies were interpreted as negative. It is generally characteristic that the distribution of ^{75}Se is confined to the liver and pancreatic remnants in carcinoma of the pancreas. This distribution is not characteristic of the scans done in 10 patients with chronic pancreatitis, in which the ^{75}Se showed a marked distribution in the upper abdomen and lower chest outside the liver and pancreas. Evaluation of these three classes of patients is continuing, to verify the reliability of scanning as a specific diagnostic method.

Z-2 *"Animal Studies with ^{75}Se-Selenomethionine."*

GERALD L. DENARDO, LAWRENCE CROWLEY, RUSSELL PARDOE, AND RONALD WEINTRAUB, (Nuclear Medicine Service, Veterans Administration Hospital, Stanford School of Medicine, Palo Alto, California)

In dogs, the radioactivity in the pancreas, duodenum, remaining small intestine, colon, spleen, liver and blood was measured 30 minutes after intravenous ^{75}Se-selenomethionine. The radioactivity in the same organs also was measured immediately and serially for four hours after selective pancreatico-duodenal arterial ^{75}Se-selenomethionine and ^{131}I-macroaggregated albumin. These studies were done to determine the extraction efficiency of the pancreas and duodenum for ^{75}Se-selenomethionine; the relative blood flow to the pancreas and duodenum; the feasibility of pancreatic scanning after selective intra-arterial ^{75}Se-selenomethionine or ^{131}I macroaggregated albumin; and the validity of pancreatic scanning after intravenous ^{75}Se-selenomethionine.

Pancreatic extraction exceeded duodenal extraction of selenomethionine by three to four times approaching one hundred per cent. However, the total content and concentration of selenomethionine in pancreas was only 1.5-2 × greater than in the duodenum, because duodenal blood flow was approximately three times greater than pancreatic blood flow from the pancreatico-duodenal artery. Scintiscanning of the pancreas and duodenum *in vitro* revealed that the duodenal radioactivity contributed significantly to the "pancreatic" image. If these findings are applicable to human subjects, and there is no evidence to the contrary, then intestinal radioactivity could represent a serious deterrant to successful pancreatic scanning as currently performed utilizing ^{75}Se-selenomethionine. The pancreas is essentially surrounded by a "sea of radioactive gut." Radioautography revealed the selenomethionine to be located primarily in the epithelial area of the duodenum.

This method is proposed as a model to determine the ability of the pancreas to extract various radiopharmaceuticals and the effect on blood flow of various pharmacologic agents.

Z-3 *"Rapid Placental Imaging and Localization Utilizing Ionic Technetium-^{99m} Pertechnetate."*

MATHEWS B. FISH, DANIEL LAVINE, MYRON POLLYCOVE, AND ARCHIE KHENTIGAN, (Nuclear Medicine Section, Clinical Laboratories, San Francisco General Hospital, Division of Clinical Pathology and Laboratory Medicine, Department of Pathology, University of California School of Medicine, San Francisco, California)

The advent of the Anger-type scintillation camera and near-ideal nuclides such as ^{99m}Tc has made possible the ability to visualize vascular structure and certain organs by obtaining rapid sequential scintiphotographs of an isotope bolus as it passes through these structures. Utilizing this approach, a technique was developed for rapid and accurate placental imaging and localization with an Anger-type scintillation camera and the rapid intravenous injection of 300 μC of ^{99m}Tc pertechnetate ion. Sequential studies revealed that optimum placental imaging is accomplished during 30 to 90 seconds after injection. An adequate placental image persists for five minutes, thus allowing for supplementary views. Studies of pregnant and nonpregnant subjects failed to "visualize" pelvic or abdominal structures other than the placenta during a period of 10 minutes after injection of 300 μC ^{99m}Tc pertechnetate.

Utilizing this procedure, placental imaging was performed in over 50 subjects in their third trimester of pregnancy. The placenta was unequivocally visualized and localized in all cases. Close correspondence was obtained with localization performed by body surface counting after injection of ^{51}Cr-RBC. Clinical course, including caesarian-section when necessary, verified the anatomic site of placenta implantation. With this technique, posterior placentas are easily localized, twin placenta have been noted and cervical pooling of blood from placental hemorrhage has been dynamically demonstrated.

In summary, this technique affords an accurate, rapid (2-3 min), simple, readily available (ionic pertechnetate) and safe (fetal dose = 3 mrad) means of placental imaging and localization.

Z-4 *"Cardiac and Placental Scanning with Indium-113m."* HOWARD S. STERN, DAVID A. GOODWIN, AND HENRY N. WAGNER, JR., (Division of Nuclear Medicine, The Johns Hopkins Medical Institutions, Baltimore, Maryland)

The availability of short-lived Indium-113 from a generator system provides us with a radionuclide that can give a high photon yield with decreased or equivilent radiation dose in a variety of scanning procedures. For those laboratories which undertake simple techniques for radionuclide incorporation into specific compounds, technetium-^{99m}Tc)-labeled albumin has been the agent of choice for blood pool scanning.

In contrast to ^{99m}Tc albumin, which takes approximately one hour to prepare and requires many steps including millipore filtration for sterilization, carrier-free ^{113m} In eluted from a ^{113}Sn-^{113m}In generator can be stabilized with gelatin, adjusted to pH 3.5-4.0, sterilized by autoclaving and be ready for use in approximately 30 minutes. Preliminary observations of elctrophoretic patterns obtained from *in vitro* incubation of the preparation with whole blood reveal that the ^{113m}In in this form is either transferred or bound to the beta$_1$-globulin fraction of the plasma.

The blood levels of the ^{113m}In-protein complex remains high (T½ - approximately 3 hours) and, unlike ^{99m}Tc-albumin, which may accumulate in the bladder, thereby interfering with the interpretation of the placenta scan, urinary excretion of ^{113m}In is of the order of 0.06 to 0.1 per cent of the administered dose. The usual dose for satisfactory placental and cardiac scanning is 1 and 2 millicuries, respectively, which is equivalent to the dose of ^{99m}Tc-albumin.

Z-5 *"The Salivary Gland Scintigram."* MARGARET M. FLETCHER, McRAE W. WILLIAMS, AND JOSEPH B. WORKMAN, (Division of Otolaryngology, Department of Surgery and Division of Nuclear Medicine, Department of Medicine, University of Maryland School of Medicine, Baltimore, Maryland)

Scintigrams have proven to be valuable adjuncts in the study of salivary glands. Our objective was to further develop this technique and to correlate isotope uptake with salivary gland function in normal patients and in those with tumor or inflammatory disease.

METHOD

Group I—Tracer amounts of technetium-^{99m} pertechnetate were given intravenously to normal human beings and anterior and lateral scans obtained of the salivary glands, bilaterally. Routine sialography followed the salivary gland scans.

Group II—A similar program was followed in a group of patients with inflammatory disease of the salivary glands. Included were patients with obstructive sialadenitis as well as acute suppurative parotitis. Three patients subsequently underwent excision of the submandibular gland. Histologic evidence is submitted to relate ^{99m}Tc pertechnetate uptake with clinical impression in these patients. Where feasible, serial salivary gland scintigrams were obtained in the inflammatory group during the acute phase and following resolution.

RESULTS

Group I—Normal salivary glands demonstrate high concentration of ^{99m}Tc pertechnetate. Their superior and inferior boundaries are clearly outlined because of the relatively inert soft tissues which surround them. Medially, the deep lobe of the parotid can be well visualized on the frontal view.

Group II—The submandibular gland lends itself well to scanning. The amount of activity collected by the gland is directly proportional to the amount of normal tissue present histologically. Little or no uptake was demonstrated during the acute suppurative stage of parotitis, but after antibiotic therapy the gland appeared to show higher concentration than the uninvolved side.

SUMMARY

Salivary gland scanning using technetium-^{99m} pertechnetate is a useful tool in studying the extent of lesions interfering with salivary gland function. The precise etiology must be determined by correlation of the clinical picture presented by the patient with the scintigram.

Although parotid tumors have shown decreased uptake by this technique, this last is also true of inflammatory disease. In the latter condition, serial scanning can define the extent of the insult as well as the degree of recovery.

Salivary gland scanning can be performed easily and without discomfort to the patient. Compared with sialography, scanning can be done at any stage of the disease without danger of precipitating an acute inflammatory response secondary to dye injection and with comparable information.

Z-6 *"Adrenal Photoscanning with an Iodinated Analog of P,P' −DDD [2,2-bis(4-iodephenyl)-1,1 dichloroethane-^{131}I]."* WALTER DIGIULLO, (Radioisotope Service, Veterans Administration Hospital and the Department of Internal Medicine [Nuclear Medicine], University of Michigan Medical School, Ann Arbor, Michigan)

Two, 2-(4-chlorophenyl, 2-chlorophenyl) 1, 1-dichloroethane (*p,p'*-DDD) causes adrenal cortical necrosis and suppression of adrenal cortical function. To develop a method for photoscanning the adrenals in humans, the distribution of an iodinated analog of *p,p'*-DDD, 2,2-bis (4-iodophenyl)-1,1-dichloroethane-^{131}I (p,p'-DDD-^{131}I was studied in rabbits and dogs. The ratio of adrenal cortex to liver concentration of radioiodine in rabbits was approximately 4:1 and to other intra-abdominal organs 8:1.

At 24 hours, bone marrow and fat had higher concentrations of radioiodine, but other tissues were lower than they had been at four hours.

Three dogs received up to 468uC of DDD-^{131}I and were scanned with a Picker Magnascanner. The adrenals appear to have been localized by the scans in two of the three dogs. In one dog, spinal needles inserted perpendicularly into the carcass at the points of interest penetrated one adrenal and bypassed the second adrenal at one centimeter. The x-ray position of metal clips placed on the adrenals was compared with the scan image of a second dog.

Tissue assays in two dogs revealed the following ratios of tissue concentrations of radioactivity: adrenal/liver 4.8 and 7.2; adrenal/kidney 13.5 and 16.2; adrenal/muscle 10.5 and 17.0; adrenal/serum 35.6 and 46.2; adrenal/fat 0.64 to 3.8.

These results indicate that iodinated DDD analogs may be useful for adrenal photoscanning in humans. Considerations of dose requirements, toxicity, route of administration, optimal scanning interval and electronic elimination of liver background will be discussed.

Since *o,p'*-DDD has a higher relative concentration in human adrenals than *p,p'*-DDD, the iodinated analog of *o,p'*-DDD may be more desirable for adrenal photoscanning in humans. The distribution of four additional radioiodine labeled DDD analogs is being studied in animals. The synthesis and preliminary distribution data of three of these compounds will be presented elsewhere.

Z-7 *"A Progress Report on the Development of Adrenal Gland Scanning."* TERUO NAGAI, BALTZAR A. SOLIS,[1] CHANGSOON KOH,[1] MASARU HASEGAWA,[1] AND RENSUKE GOTO,[1] (National Institute of Radiological Sciences, Chiba and Daiichi Kagaku Co. Ltd., Tokyo, Japan)

This report describes our experience on animal distribution studies and clinical scanning with a new compound, ^{131}I labeled stigmasterol, of suitably high specific activity and with sufficient adrenal gland specificity to be useful for scanning.

The H-3 compound was prepared by the catalytic reduction with H-3 gas and the I-131 compound was prepared by the iodination with ^{131}NaI and chloramine-T. The cortex of the adrenal glands of mice were labeled with H-3 and ^{131}I stigmasterol, as demonstrated by whole body autoradiography. A group of rats were injected with these compounds and sacrificed at varying times. The adrenal-liver concentration ratio of the ^{131}I stigmasterol rose significantly in 24 hours after injection (1hr; 1.52, 3hr; 1.67, 5hr; 1.69, 24hr; 5.69, 48hr; 7.47). Much higher ratios were obtainable with H-3 stigmasterol (1hr; 2.52, 3hr; 2.61,

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5hr; 4.04, 24hr; 20.45, 48hr; 22.07). ACTH used to increase the target to non-target ratio of the ^{131}I compound was not effective.

To evaluate the usefulness of ^{131}I stigmasterol for scanning, rabbits were administered 50 μC of the compound and scanned with a Picker-Magnascanner V with a color attachment. The scanning indicated the deposition of radioactivity in the adrenal glands, liver and kidney. *In vitro* scanning of the extirpated organs demonstrated that the concentration in the adrenal glands was sufficient to visualize with scanning technique.

To demonstrate the value of this procedure in clinical scanning, patients with non-adrenal disease and some suspected of having adrenal disease, including hyper-aldosteronism and Cushing's syndrome, were scanned after intravenous injection of 400-800 μC of ^{131}I stigmasterol. To demarcate the kidneys, a renal scan with ^{203}Hg chlormerodrin was performed in advance. Although the clinical scanning was not regularly successful because of the uptake in the liver and the excretion of free ^{131}I in the stomach, it is our feeling that this procedure can be an approach to the development of adrenal gland scanning.

Other compounds administered were ^{14}C and ^{131}I-labeled cholesterol. Preliminary studies with ^{82}Br and ^{18}F labeled compounds will also be presented.

DR. JOHN TOTTER NAMED DIRECTOR OF AEC'S DIVISION OF BIOLOGY AND MEDICINE AS DR. DUNHAM RESIGNS

Robert E. Hollingsworth, General Manager of the Atomic Energy Commission, announced the appointment of Dr. John R. Totter as Director of the Division of Biology and Medicine, effective June 10.

Dr. Totter will succeed Dr. Charles L. Dunham, who is resigning after having served as Director of the Division since October 1, 1955. In the fall, Dr. Dunham will join the staff of the National Academy of Sciences as Chairman of the Division of Medical Sciences of the National Research Council.

Dr. Totter has been Associate Director for Research since January 1963. He came to the AEC Headquarters staff in 1962 as Assistant Director for Biological Sciences in the Division where he has been named Director.

As Director of the Division of Biology and Medicine, Dr. Totter will be responsible for planning, developing and directing the program in biomedical research with particular emphasis on the biological effects of radiation; the control of radiation and other industrial hazards associated with AEC activities; the release and environmental distribution of radionuclides and the development of peaceful uses of atomic energy in these and related fields.

Dr. Totter first became associated with the U.S. atomic energy program in 1952 as a chemist in the AEC's Oak Ridge National Laboratory, Oak Ridge, Tennessee. After four years at ORNL he became a member of the AEC's Headquarters staff in Washington in the Division of Biology and Medicine where he served until 1958. He was visiting professor at the Faculted de Medicina, University of the Republic, Montevideo, Uruguay, from 1958-1960.

Before coming to the AEC in 1962, he was a Professor and Chairman of the Division of Biological Sciences at the University of Georgia. Dr. Totter was a member of the faculty of the University of Arkansas School of Medicine from 1939-1952, and at the West Virginia University School of Medicine from 1938-1939.

He was born in Saragosa, Texas, and received his B.A. degree in chemistry and his M.A. in chemistry from the University of Wyoming and his Ph.D. in chemistry from the State University of Iowa.