ABSTRACTS FOR SCIENTIFIC PROGRAM:

TO BE PRESENTED BY TITLE ONLY

Lung Scan: An Adjunct in the Study of Pulmonary Carcinoma by Frank H. Allen, Thomas A. Verdon, Jr. and Bruce F. Chandler, Letterman General Hospital, San Francisco, Calif.

The analysis of data accumulated from lung scans performed on 39 patients with carcinoma of the lung reveals that the positive lung scan is emerging as an index of prognosis and an adjunct for determining operability for patients.

Thirty-five male and four female patients ranging in age from 39 to 81 years with tissue confirmation of carcinoma of the lung were seen in the Radioisotope Clinic, Letterman General Hospital, during the period December 1965 to December 1967. Lung scans using 131I-labeled macroaggregated albumin were performed on these patients as part of the diagnostic investigation in addition to conventional roentgenograms and tissue studies. "Operability" for each patient was determined by the thoracic surgeons.

Analysis of data revealed that the cases could be categorized into four groups: (1) inoperable with positive scans (27 cases, 67.5%); (2) inoperable with negative scans (1 case); (3) operable with positive scans (6 cases); and (4) operable with negative scans (5 cases).

The positive lung scan appears to imply poor prognosis for patients with lung carcinoma. In the operable groups, the negative scans may be associated with a better prognosis, although we have not been able to predict precisely the clinical course of these patients.

Additional cases will expand the series as lung scans become a routine diagnostic procedure for patients suspected of lung carcinoma. As studies continue, we are evaluating further the role of the lung scan and correlating the value of the scan as a diagnostic key and its prognostic reliability. The lung scan is being used as a screening procedure for surgery. Hopefully in the future patients will be diagnosed and studied earlier in the course of the disease.

Transform Analysis of Compartmental Models by A. B. Ashare, S. M. Pizer and G. L. Brownell, Massachusetts General Hospital, Boston, Mass.

Transform techniques for analyzing multiexponential curves obtained from tracer experiments have not been shown to be of value for biological data which are generally characterized by larger error and shorter time duration than the physical data for which the transform was originally used. We have improved and adapted the Fourier transform technique of Gardner et al. (J. Chem. Physics 31:978, 1959) for biological data. An algorithm for this technique has been programmed in Fortran IV; the program is known as REVOLT (resolved exponential variables of logarithmic transforms).

The model under consideration is a sum of negative exponential terms

\[ a_j(t) = \sum_{i=1}^{N} A_{ji} \exp(-\lambda_i t) \]

where \( a_j(t) \) is the specific activity of compartment \( j \) at time \( t \), \( N \) is the number of compartments in the system and \( A_{ji} \) and \( \lambda_i \) are the parameters of the model. The result of the transform analysis is a spectrum with peaks indicating the presence of an exponential component \( \lambda_i \). The spectral peak heights are a function of the values of \( A_{ji}/\lambda_i \).

Techniques will be described to subtract the "error ripple," or side bands, from the spectrum and to alter the spectral peak-height ratios by using a multiplicative function of the time variable. We have applied this analysis to tracer data from studies in calcium metabolism and liver clearance. The values obtained from the REVOLT analysis were found to be useful.
as input parameters in a least-squares-fitting computer program. (This work was supported in part by PHS Grant GM–889–11 and PHS-GRS Allocation–67–7.)

New Developments in Total-Body Profile-Scanning Techniques for Clinical Studies by B. M. Branson, V. Dvorak and H. N. Wellman, National Center for Radiological Health, U.S. Public Health Service, Cincinnati, Ohio

Development of a versatile whole-body counter with dimensions of 8 x 8 x 14 ft and a continuous-drive profile-scanning 8 x 4-in NaI(Tl) uncollimated crystal traveling the length of the room is described. This system has made possible an intercomparison of efficiencies and geometrical relationships between the static “standard-chair position” and profile scanning. Evaluations of optimum scan length are discussed. Segmental readout of scan data demonstrates linear-body distribution of radionuclides. Studies have been made at the Nuclear Medicine Section, National Center for Radiological Health, Public Health Service, Cincinnati, Ohio, using a matrix of 1-kg, approximately tissue-equivalent, sugar-filled boxes made to represent a spectrum of human body sizes. Radionuclide sources of known amounts were placed in the boxes. Homogeneous distributions, as well as nonhomogeneous distributions, have been compared in the counting arrays described.

A new procedure for optimization of counting efficiency with profile scanning has been developed. In this approach, the midcortical plane is counted at a fixed-parallel distance from the crystal face in all individuals. This distance is 16 cm, allowing scans of most body configurations. Prone and supine scans using this fixed counting distance result in more constant counting efficiencies between individuals of different sizes. These results are compared to the widely used fixed-detector-to-bed distance. The results suggest considerably less geometry effect with approximately equal efficiencies when these profile-scanning techniques are compared to the “standard chair position.” Clinical whole-body counting which usually involves marked nonhomogeneous distribution of radionuclides can therefore be made far more accurately when these improved profile-scanning techniques are used.

Improved Procedure for the Production of Indium-Labeled Macroiron Hydroxide and Indium Colloid by F. P. Bruno, O. A. Sorsdahl and C. M. Williams, V.A. Hospital and Univ. of Florida College of Medicine, Gainesville, Fla.

The need for a multipurpose, short-lived radioisotope in generator form has led to the use of 111In-labeled compounds (Stern, Goodwin, Wagner, Kramer) for lung, liver, brain and blood-pool scanning. We have developed a modified procedure for the routine use and production of 111In-labeled macroiron hydroxide (for lung scanning) and 111In colloid (for liver scanning). Our method of formulation has several advantages over that previously described by Stern et al. It (1) is less time consuming, (2) eliminates the need of pH meters or indicator paper and (3) is a sterile system because the reaction vessel can be closed to the atmosphere. After eluting the indium generator, the lung-scanning material can be prepared in 15 min, and the indium colloid for liver scanning can be prepared in 5 min.

New Index Related to Free Thyroxine Concentration in Serum by Alfredo Cuarón and Felipe Gordon with technical assistance of Nelly Rattoni and Carmen Pinedo, Centro Médico Nacional, Instituto Mexicano del Seguro Social, Mexico City, Mexico.

Although the concentration of free T-4 in serum is a paramount parameter for the diagnosis of thyroid disease, the methods for its determination are impractical for the clinical routine. Thus the development of a simple and rapid procedure is important.

From the law of chemical mass action it is well known that the product of free T-4 multiplied by free thyroxine-binding globulin capacity (free TBG capacity) is equal to the product of the concentration of T-4 bound to TBG multiplied by an association constant. It follows then that the concentration of free T-4 in serum is given by the ratio of T-4 bound to TBG divided by free TBG capacity and multiplied by the association constant. The in vitro binding of T-3 by serum proteins studied by gel filtration chromatography is related to free TBG capacity. The concentration of T-4 bound to TBG can be represented by the PBI concentration and this was found to be significantly correlated with the T-4 iodine concentration estimated by saturation analysis of the T-4 binding proteins of a standard stock serum. The ratio of T-4 iodine concentration to in vitro binding of T-3 by serum proteins is an index which is correlated with the molar concentration of free T-4 in serum estimated by equilibrium dialysis of diluted serum enriched with 111I-T-4. The values of this “free T-4 index” found in various groups of subjects were: (1) euthyroid subjects: 7.0 ± 1.5 (mean ± s.d.); (2) hyperthyroidism: 12.5 ± 1.3; (3) hypothyroidism: 1.9 ± 0.9; (4) nephrosis: 6.6 ± 1.9; and (5) normal pregnancy: 6.5 ± 1.9. These results prove that this procedure can be used as a routine diagnostic test. The method is fast and simple, is not exposed to error by iodide contaminants and gives very important data related to the total concentration of T-4 in serum, to free T-4 in serum and to free TBG capacity.
New Test for Border-Line Hyperthyroidism: Inhibition of Serum Thyroxine Concentration by Triiodothyronine by Alfredo Cuarón and Felipe Gordon, with technical assistance of Carmen Pinedo and Nelly Rattoni, Centro Medico Nacional, Instituto Mexicano del Seguro Social, Mexico City, Mexico.

The suppression of the thyroidal uptake of $^{131}I$ is a well-established test for border-line hyperthyroidism. However, this test is of no use in those cases with variations of the body iodide pool produced by a chronic deficiency in daily intake of iodides or by an abnormally high ingestion of iodides or other iodinated compounds such as the iodinated radiological contrast media, some antiamoebic drugs, etc. In those cases the $^{131}I$ thyroidal uptake is greatly affected. The concentration of T-4 in serum, estimated by saturation analysis of the T-4 binding proteins of a standard stock serum, is unaffected by the administration of iodides, iodinated precursors of the thyroid hormones (MIT, DIT) and iodinated radiological contrast media, and reflects the actual concentration of T-4 in serum. Daily administration of 75 µg of 1-T-3 for 10 days significantly reduces the concentration of T-4 in sera from euthyroid subjects. On the other hand, T-4 concentration is unaffected by the same treatment in sera from thyrotoxic patients. If inadequate suppression is achieved, the test is repeated with a daily dose of 100 µg of the hormone. Our results seem to indicate that this procedure could be easily used as a test for border-line thyrotoxicosis, mainly in those patients that have received a previous treatment with an iodinated compound or when it is not possible to perform the orthodox suppression test. Work is in progress in our laboratory to determine the most effective suppressive dose and the optimal duration of treatment with T-3.

Radioactive Pulmonary Emboli by Gerald L. DeNardo, George J. Duffy and Robert B. Abington, V.A. Hospital and Stanford School of Medicine, Palo Alto, Calif.

The distribution of pulmonary blood flow can be evaluated by the deliberate blockade of pulmonary capillaries with macroaggregated albumin. These labeled micro-emboli have a biological half-life in the lung of 3–12 hr with no demonstrable radioactivity remaining after 24 hr. A second type of radioactive embolism was produced inadvertently in two patients. These emboli resulted from the injection of small radioactive blood clots and had a biological half-life of 3–5.5 days. A third type of radioactive embolism occurred in one patient and was characterized by new areas of radioactivity appearing within the lungs at some time after the initial lung scan. These emboli may have been formed by adherence of the $^{131}$IMAA-blood clot admixture to a partially thrombosed vein so that organization occurred before subsequent embolization. They had biological half-lives of 10.5–23 days. One of these emboli was recovered in the lung of the patient after he had died of pneumonia.

Both types of emboli due to radioactive blood clots are a source of artificiously abnormal lung scans. Because the emboli vary in their radioactivity and distance from the detector, estimation of their size by lung scan is difficult; the embolus recovered was very small.

Experiments in vitro revealed consistently greater radioactivity per gram of $^{131}$IMAA-blood admixture than per gram of $^{131}$IMAA fluid alone. This may explain the mechanism of production of the radioactive emboli.

Although neither of the two patients developed symptoms or signs attributed to the radioactive pulmonary emboli, their occurrence should be regarded as a potential complication of lung scanning. However, this complication can be avoided.


In the therapy of thyrotoxicosis, it is customary to calculate the therapeutic dose of radioiodine according to some formula based on thyroid uptake of a tracer dose and an estimate of gland size. No formula has proved entirely satisfactory. Some patients respond as if over-treated and others as if under-treated, irrespective of the formula. The explanation for these discrepant results remains obscure although poor estimates of gland size and individual differences in radiosensitivity are often incriminated. Therefore many clinicians use an empirical dose of radioiodine rather than a calculated radiation dose for the treatment of thyrotoxicosis.

Calculating the therapeutic dose on the basis of a pretreatment tracer dose assumes that the kinetics of both doses are the same. Careful excretion and whole-body-counting data obtained on patients being treated for hyperthyroidism reveal that this assumption is not always valid in clinical practice. Whole-body retention of the therapeutic doses of radioiodine has been determined for 72 treatments given within 1 week of a tracer dose from which a thyroid uptake has been measured. The whole-body retention at 24 and 48 hr was computed from excretion data or by whole-body-counting techniques or both. Whole-body retention studies on the tracer dose were also available on 44 treatments.

For 12 treatments whole-body assays indicated that significantly less of the therapeutic radioiodine dose
was retained in the whole body and presumably less taken up by the thyroid gland than was measured by the pretreatment tracer study. In 11 patients the uptake of the tracer in the thyroid alone was greater than the whole-body retention of the treatment dose. In five treatments, the patients retained significantly more of the therapeutic dose than the tracer dose. If we assume that the ratio of the thyroidal to extrathyroidal pools were the same for the treatment as for the tracer dose, the thyroid gland received more radiiodine than was predicted from the tracer studies.

Where these discrepancies between the dynamics of the treatment and tracer doses exist, any radiation dose calculated on the basis of the tracer uptake data would be erroneous. Likewise, an evaluation of any treatment schedule or formula without checking on the fate of the treatment radioiodine to exclude these anomalies is apt to be misleading.

**Pulmonary-Perfusion Abnormalities in Young Women on Oral Contraceptives by N. E. Herrera, Danbury Hospital, Danbury, Conn.**

Despite the number of studies attempting to correlate the administration of oral contraceptives and thrombolic accidents, no valid conclusions about their possible relationship has been reached. The present study uses pulmonary scanning as a method for investigating thromboembolic accidents. The study is based on three assumptions: (1) Thrombosis is more common in the venous compartment of the vascular system, (2) Phlebothrombosis and thrombophlebitis are commonly associated with pulmonary embolization and (3) Pulmonary scanning with $^{131}$I macroaggregated human serum albumin is a reliable way of discovering abnormalities of pulmonary perfusion. The study includes a group of 40 women between the ages of 22 and 45 on oral contraceptives for contraception or other reasons, selected on the basis of a negative clinical history for known predisposing conditions, who became symptomatic during therapy. Findings in this group will be compared to findings in a control group of 21 patients of similar age not taking oral contraceptives who were admitted to the hospital for a variety of clinical conditions. The study has shown a statistically significant number of abnormalities of perfusion in women who become symptomatic during oral contraception. Angiographic corroboration of the findings was obtained in a limited number of cases.

**Acquisition, Processing and Utility of Digitized Data from a Multicrystal Rectilinear Scanner, by Louis Katchis, Jr., Edward M. Smith and Pablo Larrea, Univ. of Miami School of Medicine and Florida Power and Light Co., Miami, Fla.**

Quantitative organ dynamic-function studies are performed using a multicrystal rectilinear scanner, the Picker Dynapix, a multifunction computer interface system, a Kennedy incremental magnetic-tape recorder and an IBM 7040-1401 computer system plus a sophisticated software package designed around the above components. The radiation detector of the scanning system consists of 10 rectilinear NaI(Tl) crystals, each $6 \times 7/8$ in. which move in an interlaced pattern that can yield 40,000 discrete picture elements, each $2 \times 1.5$ mm. The computer-interface system transforms the output of the Dynapix into a reliable and accurate data format for recording on magnetic tape. The interface system also provides a means of sensing preselected anatomical landmarks, entering patient and procedure identification data onto magnetic tape and controlling the magnetic-tape recorder. The basic computer-software package consists of (1) data entry, error detection and coding and spatial reorganization of data, (2) seven-level, digitally processed analog map with variable upper and lower suppression levels, (3) time reorganization of scan data, (4) area integration and normalization, (5) spatial alignment of scans obtained at different times to eliminate the problems of exact repositioning of the patient and (6) statistical smoothing of scan data.

We will use the pulmonary-function studies currently being performed as an example of the application of the basic computer programs to a clinical problem. This special pulmonary package includes regional ventilation-perfusion ratio maps and wash-in and wash-out ventilation rate maps. These latter studies consist of reorganizing the scan data in both time and space and calculating the regression line to yield a value related to the volume of gas per unit time inspired or expired in a given area of the lung (2.4 x 2.4 cm).

Data is accumulated at three points per minute per lung-area studied, yielding a sufficient number of points to obtain a statistically valid slope before the equilibrium condition is reached. A data map is calculated which consists of the slopes of the wash-in and wash-out curves.

**An Evaluation of Scan Data Processing by Digital Computer by W. J. McLain, M. M. Satterfield and G. R. Dyer, Oak Ridge National Laboratory, Oak Ridge, Tenn.**

The digital computer is gradually taking its place as a useful instrument in the field of nuclear medicine. Use of the computer for processing scan data has been reported by several; however, its full potential in this application has not been evaluated. A complete evaluation of the use of the digital computer for processing scan data requires an investigation of two factors: (1) the type of processing required to provide the clinician with more accurate and meaningful results,
and (2) the hardware required to support the processing, meeting the minimum requirements of information content and scheduling. Experience has proven that the use of off-line computer systems, normally under the supervision and control of other departments of a hospital, presents delays that are prohibitive in cases of heavy patient load and when the occasional need for immediate answers arises in a clinical situation. It is for this reason that on-line computer systems, possibly controlling the scanner while processing the data, are being investigated.

Any computer system used must, of course, be able to support the data processing required without becoming so elaborate that it exceeds budgetary limitations. With this in mind, this paper presents an evaluation of scan data processing. The theoretical background for several methods of processing are presented, with examples of their use to provide a basis of comparison for information content, accuracy and resolution of results. The computer hardware required to support each method and the running times involved provide a means of determining the practicality of using each method in an on-line computer environment.

Obtaining More Uniform Sensitivity with a Scintillation Camera by Robert C. Meade, James C. Carlson and Philip P. Ruezt, V.A. Hospital and Marquette School of Medicine, Milwaukee, Wis.

This work was begun because of dissatisfaction with the count distribution over the useful crystal surface of an Anger scintillation camera. Numerous attempts to obtain a flat response with two different Anger cameras never resulted in less than a 35% variation in counts over the useful area. In addition, hot spots are obtained over the center (No. 10) photomultiplier tube and the six tubes surrounding it.

To obtain a more satisfactory result, a local tuning procedure was devised. A plastic phantom 16 in. was constructed to flood the crystal. The camera was tuned with the low energy collimator attached using a technetium source 1 in. in diam. A pinhole source used without the collimator gave comparable results. All photomultiplier tubes were tuned to within 1% of the center tube and the spectrum checked simultaneously. A deviation in spectrum always correlated with a deviation in counting rate.

Following this tuning procedure, a more uniform count distribution was obtained. However, increased counts were still obtained over the center seven photomultiplier tubes, and a 30% variation in counts was still present. The shielding necessary to reduce the most sensitive areas was calculated, and a shield was constructed to give optimum response. A more uniform flat response was obtained over the useful surface area with less than 15% maximum-to-minimum variation. Tuning the camera under operating conditions appears to be a sound approach. Elimination of hot spots over the photomultiplier tubes with shielding does not affect the sensitivity or resolution and eliminates false-positive results.

113mIn for Scanning Bone and Kidney by Fred S. Mishkin, Isaac C. Reese, Gonzalo T. Chua and James E. Huddlestun, Indiana Univ. Medical Center, Indianapolis, Ind.

The development of gallium citrate using the short-lived positron-emitting 68Ga as an agent for scanning bone and the kidneys led us to examine the possible use of indium for the same purpose. These elements lie in the same group of the periodic table, III B, and should behave similarly. Both radionuclides have the advantage of a short half-life allowing administration of a large amount of activity with relatively little radiation dose to the patient. The large photon yield should considerably shorten the bone-scanning procedure which is often long and tedious using the 85Sr nitrate.

Both gallium and indium are transported in the blood bound to a beta globulin. This has proven to be transferrin in the case of gallium and is presumably the same for indium. While the group at Oak Ridge has used carrier gallium to displace radioactive gallium from the serum protein onto bone matrix, we thought a more direct approach to saturating transferrin might be the direct intravenous injection of ferric chloride. Carrier-free 113mIn chloride stabilized with gelatin and sodium chloride injected intravenously into rabbits was found in the kidneys and gradually accumulated in the bone so that 1 hr later the kidneys and skeletal structures were well delineated by scanning. In the dog, the necessary blocking dose of ferric chloride was toxic, causing death probably through the mechanism of multiple pulmonary emboli. Complexing the ferric chloride with citrate allowed administration of enough ferric ion, so that carrier free 113mIn chloride stabilized with gelatin and sodium chloride localized in the bones and kidneys. A suitable nontoxic form of intravenous ferric ion could make 113mIn feasible for scanning bone and kidneys in human subjects.

Rapid Lung Scanning with a Dual 8-in. Rectilinear Scanner and 113mIn by Fred S. Mishkin and Isaac C. Reese, Indiana Univ. Medical Center, Indianapolis, Ind.

The recent introduction of 113mIn as a scanning agent and the development of a dual 8-in-crystal rectilinear scanner illustrate the advances in radio- pharmaceuticals and scanning devices which provide faster and better scans. The parallel, opposed NaI(Tl) 8 x 2-in. detector crystals are in turn backed by

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8 × 2-in. pure sodium iodide crystals used as light pipes. With the use of a 439-hole fine-focus collimator and appropriate spectrometry, a radius of resolution of approximately 0.25 in. is achieved at the focal plane 3.5 in. from the collimator surface.

We prepare the iron (indium) hydroxide particles immediately before injection following a modification of Stern’s method: 100 μg of ferric ion are added to the 113mIn Cl₂ eluted from a Sn-In generator with 0.05 N HCl. The pH is adjusted to 12 with dilute NaOH, and 60 mg of NaCl are added to salt out the particles. After shaking the suspension for 3 min, 1 ml of 10% gelatin is added as a stabilizer and the particles are autoclaved. Counts on a hemocytometer show about 60,000 particles per ml varying from 30 to 50 microns in diam.

We believe the limiting factor in the dose of the radiocolloid is the possible cardiovascular effect of the temporary pulmonary arteriolar capillary blockade; therefore we limit the injection to 2.5 cc with 150,000 particles. With this volume, the patient usually receives 2 mc of 113mIn resulting in a local dose to the lung estimated to be 1.7–2.3 rads.

We obtain counting rates of 60,000–120,000 cpn allowing speeds of 200 in./min or more. Two views of the lungs may be finished in 7 min. Usually 30 min are consumed from the time the patient is placed on the scanning table until the completed 4 views are inspected by the physician and the patient is dismissed. We have experienced no difficulty whatsoever in our first 35 patients, even those who were extremely ill. The scans are of superior quality.

Iodide and Thyroxin Dynamics in Relative Iodine Deficiency by J. Myhill, J. B. Hales and T. H. Oddie, Institute of Medical Research, Royal North Shore Hospital, Sydney, Australia and Univ. of Arkansas Medical Center, Little Rock, Ark.

The population in Sydney, Australia, is mildly iodine deficient. Whole-body-counting studies were made on 20 volunteers from this population. Measurements were made of thyroidal clearance rate, extrathyroidal clearance rate, iodide excreted, iodide intake, iodide accumulated by the thyroid, thyroxin space, thyroxin degradation rate, total thyroxin turnover rate and net thyroidal thyroxin secretion rate. These measurements were made both initially and after controlled dietary supplements of 100 and 200 μg thyroxin/day and also after 252 and 1,008 μg iodide/day. The implications of the results in relation to thyroid homostasis and iodine deficiency will be discussed.

Estimation of in vivo Digestibility and Absorption of Food by Labeling: A New Approach in Clinical Nutrition by Kunio Okuda, Yutaka Shimokawa and Isao Takara, Kurume Univ. School of Medicine, Kurume, Japan.

The nutritive value of food has in the past been estimated from its composition, but it is also related to digestibility which has not been determined in vivo. Certain foods and nutrients are poorly digested and absorbed in diseases.

Two methods have been used to determine digestibility of food with respect to a nutrient: (1) A radionutrient is incorporated in a food, fed to test subjects and the absorption compared with that of graded doses of pure radionutrient; digestibility is assessed from percentage absorption and chemically determined content of the nutrient after thorough in vitro digestion and/or extraction. (2) A small quantity of radionutrient is added to an unlabeled food, and digestion (amount of nutrient liberated in the digestive tract) is estimated from the decrease of percent absorption using a calibration curve obtained with increasing doses of pure radionutrient. It is desirable that percent absorption of the nutrient declines sharply as the dose increases and the test amount of food fall in the range. Liver with natural 60Co-B₁₂ was prepared by injections of 60Co-hydroxocobalamin to rats. Absorption of such liver fed in small quantities were 65–85% in the normal and less than 20% in patients with malabsorption. In vitro digestion showed its easy digestibility and isotopic dilution was 50–80 fold by bio- and radioassay (first method). When a small dose of 65Co-cyanocobalamin was mixed with 10 gm liver and fed, absorption of 65Co was reduced to the same level as that with 8 μg of free B₁₂, suggesting almost 100% digestion (second method). Similar studies have been carried out with 67Fe-labeled egg yolk, hemoglobin and meat using laying hens and rabbits and with several other radionutrients.

Sum-Coincidence Assay in Nuclear Medicine with a NaI Well-Type Scintillation Crystal, by J. Porter and P. V. Harper, Argonne Cancer Research Hospital and Univ. of Chicago, Chicago, Ill.

Institutions producing short-lived isotopes for diagnostic studies are confronted with the problem of on-location assay. In particular, although activities of pure positron emitters like 11C and 15F can be evaluated by photopeak comparison to calibrated Sr standards (0.51 Mev, 65 days), other nuclides like 32P and 125I have accompanying gamma rays that interfere with the photopeaks of the annihilation radiation both by Compton scatter in the crystal and by sum coincidence which displaces scintillation events from the photopeak. Provided the sample and Sr-standard strengths are sufficient, the comparison can be performed at some distance from the crystal since the interference from coincidence diminishes with the
inverse square of the geometry. In the present report, expressions are developed which permit absolute assay of nuclides emitting multiple coincident photons, either gamma, x-ray or annihilation, using equipment available in most nuclear-medicine laboratories, i.e., NaI well counter and single-channel pulse-height analyzer.

The following relationships exist:

Example 1: $^{99m}$Tc, E.C., $\gamma$ (I.C.) i.e., Kx, Kx

$$N = \frac{(C_1 + 2C_2)^2}{4C_3}$$

where $N$ = disintegration rate, $C_1$ = counting rate of detection of single 28-kev photons and $C_2$ = counting rate of detection of both photons.

Example 2: $^{18}$F, $\beta^+$

$$N = \frac{C_{0.51}}{4C_{0.20}} + C_T$$

where $C_{0.51}$ = counting rate of 0.51-mev photopeak, $C_{0.20}$ = counting rate of the 1.02 sum peak and $C_T$ = overall counting rate.

Example 3: $^{20}$K, $\beta^+$, EC, $\gamma$

$$N = \frac{C_{0.51}}{4C_{0.20}C_{1.00}(1 - \alpha)} + C_T$$

where $\alpha$ = fraction of disintegrations going into positron emission (as opposed to EC). When the sample is being counted in the presence of contaminating radioactive species, $C_T$ can be evaluated only with difficulty. In most instances, however, an alternative but more complicated relation exists whose independent variables do not include $C_T$. Such relationships can be used in any situation in which the photopeaks are not too close together.

For this evaluation the data were obtained with three collimated detectors, two placed opposite the previously determined renal sites and one centered over the manubrium. The information collected was recorded through three printing scalers activated at 10-sec intervals.

The method of analysis depends on subtraction of the extrarenal radioactivity as monitored by the sternal detector from the recorded renogram. This requires the application of a calibration factor relating the level of blood radioactivity recorded by the sternal detector to that over each kidney area at the endpoint of initial rise. The resultant curve (derived renogram) consists of an ascending limb that describes a linear increase of the counting rate and a descending limb which is a single exponential function of time. This derived renogram is thus reduced to two parameters: the time for radioactivity to reach half the peak value (1/2 $T$) and the radiohippuran disappearance half-time ($T_{1/2}$).

The values of these two parameters obtained in nine normal subjects showed a narrow range, indicating a high degree of resolution that would help in identifying any departure from normality. The results obtained in five cases of nephrectomy support the basis of this method of analysis. After removal of the kidney the entire dynamic tracing recorded by the renal probe should be accounted for by extrarenal factors. This proved to be the case except for some accumulation of radioactivity in the urinary bladder. The results of the 24 patients studied were variable and dependent on their diseases. (Supported by Grant HE-06304 from the National Heart Institute, National Institutes of Health, U.S. Public Health Service.)

Quantitative Analysis of the Radiohippuran Renogram by Subtraction of Extrarenal Radioactivity by MUHAMMAD A. RAZZAK, ROBERT E. BOTTI, WILLIAM J. MACINTYRE and WALTER H. PRITCHARD, Case Western Reserve Univ. School of Medicine, Cleveland, Ohio.

Although radioisotope renography has been in use since 1956, there has been no over-all agreement about its quantitative analysis. The hippuran renograms represent an integrated response to changing radioactivity levels within the kidneys as well as different levels of activity in the blood which perfuses these organs and other tissues within the area monitored by the detector. Therefore, for the proper analysis of such tracings, accurate corrections for the extrarenal factors must be applied.

Pancreatic Scanning: Cleveland Clinic Experience by A. RODRIGUEZ-ANTUNEZ, T. A. EGGLESTON and E. J. FISON, Cleveland Clinic, Cleveland, Ohio. As a follow-up of our preliminary report to the Society in 1965, this paper will cover our experience with pancreas scans performed with $^{56}$Se-selenometheinone and a 3-in-crystal scanner. This report will reflect our results in about 400 cases.

It has been our experience that a good visualization of the pancreas can be obtained in a high number of cases using our protocol if the pancreas is healthy.

In cases of pancreatic disease, tumor or pancreatitis, the most common finding has been a total lack of visualization of the pancreas. Our conclusion and that of our clinicians at the present time is that pancreatic scanning may have a place in clinical practice to exclude the presence of pancreatic disease.
New Theory for Elution of $^{51}$Cr from Labeled Cells by PETER RONAI, University of Sydney, Sydney, Australia.

$^{51}$Cr is a nonspecific protein label. When used to label cells, it is given in the six-valent form (Cr VI) which is reduced inside the cell to the three-valent form (Cr III). The three-valent form then binds to the intracellular protein, specifically to the basic amino acids lysine and arginine. When used to label a protein such as albumin in vitro the attachment of $^{51}$Cr is very firm, less than 1% of the label coming off the albumin in 1 month. Yet when blood and tumor cells labeled with $^{51}$Cr lose activity relatively rapidly to the extent of about 25–30% in 24 hr in vivo. Further, the $^{51}$Cr which elutes from labeled cells is dialyzable and is not precipitated with trichloroacetic acid. A theory for $^{51}$Cr elution must therefore explain how a firm protein label which labels intracellular protein can elute rapidly from labeled cells unattached to protein.

Washed $^{51}$Cr-labeled mouse peritoneal cells suspended in a balanced salt solution were dialyzed against the same balanced salt solution in vitro at 37°C for 4 hr. At the end of the 4 hr the dialysate was subjected to paper electrophoresis for 12 hr in Veronal Buffer pH 8.6. Controls run simultaneously were: free $^{51}$Cr VI, free $^{51}$Cr III, $^{51}$Cr-labeled lysine, $^{51}$Cr-labeled arginine and $^{51}$Cr-labeled peptides (obtained by tryptic digestion of bovine plasma albumin). Eluted $^{51}$Cr showed an electrophoretic pattern almost identical with that of $^{51}$Cr-labeled peptides and completely different from free $^{51}$Cr or $^{51}$Cr-labeled amino acids.

Free $^{51}$Cr VI, free $^{51}$Cr III, $^{51}$Cr-labeled peptides and eluted $^{51}$Cr were each injected intravenously into groups of mice and ecretion of label followed by whole-body counting. Twenty-four-hour excretions were as follows:

1. Free $^{51}$Cr VI 99%
2. Free $^{51}$Cr III 9%
3. $^{51}$Cr-labeled peptides 95%
4. Eluted $^{51}$Cr 96%

Eluted $^{51}$Cr therefore behaves both electrophoretically and biologically like $^{51}$Cr-labeled peptides. This is consistent with the following hypothesis of $^{51}$Cr elution.

$^{51}$Cr-labeled protein within the cell is subject to normal protein turnover. Attachment of a single $^{51}$Cr atom to several basic amino-acid residues interrupts protein catabolism at the peptide level. The resulting peptides are effectively prevented from being reused in protein resynthesis. Since they cannot be reused they are lost from the cell and rapidly excreted from the body.

Should this theory of $^{51}$Cr elution prove correct, it would seem to provide a powerful technique for studying both intra- and extra-cellular protein catabolism.

Precoronary Syndrome by GUNNAR SEVELIUS, Neurocardiology Research Center, Univ. of Oklahoma, Oklahoma City, Okla.

Sixty-one patients with past history of myocardial infarction and 60 matched controls (sex, age, race, weight, education, occupation), were seen at 6-week intervals for 7 years for psychological and sociological interviews as well as numerous physiological measurements. Cardiac output, coronary blood flow, heart volume and blood volume were determined by radio-cardiogram 1–3 times per year. Coronary blood flow and cardiac output were found to decrease while heart volume and often blood volume were found to increase 6 months or less preceding a myocardial infarct. The interviews revealed a concomitant depressive state of mind (Clyde Mood, MMPI) and a feeling of fatigue. Hemodynamically the precoronary syndrome implies subclinical heart failure. The syndrome appears to be reversible.

A prognostic index (PI) indicating a high risk for myocardial infarction within the next 6 months was derived from the arithmetic mean of the percent differences between the estimated normal values for cardiac output, coronary blood flow, heart volume, blood volume and the determined results (PI > 2 s.d. of the mean = high risk). At last standing, the 121 predictions were distributed as follows: 97 (80%) negatives, 16 (13.5%) true positives, 3 (2.5%) false negatives and 5 (4%) false positives. Thirteen of the 14 patients who developed a fatal myocardial infarct had had a preceding PI value greater than 2 s.d. The risk for myocardial infarction within 6 months was 60% when the PI value was greater than 2 s.d. and 3% when the PI was within 2 s.d. The radio-cardiogram is proposed as a rapid and simple method to use in the diagnosis of the precoronary syndrome.

Digital Ratemeter System for Rectilinear Scanning by GUY H. SIMMONS, DENES HUNKAR AND J. G. KEREIAKES, National Center for Radiological Health and Univ. of Cincinnati, Cincinnati, Ohio. A rectilinear photoscanning system is described which achieves film contrast enhancement by modulating the intensity of a light source with the signal from a digital ratemeter, thereby eliminating the RC constant associated with the analog ratemeters which are used on conventional rectilinear scanners. This improves the over-all integrity of the scan in two ways: (1) The degradation of the source information caused by the exponential response of the analog ratemeter is eliminated. This effect can be quantitated by comparing the modulation transfer functions (MTF) obtained from the line-source response functions for the two systems. The MTF vs spatial frequency curve for the digital ratemeter scanner more nearly approaches that
due to collimator effects alone than does the corresponding curve for the analog system. (2) The maximum time lag between the actual change in counting rate and the change in ratemeter response is adjustable in unit increments down to 0.01 sec for the digital system and remains constant throughout the scan. This time lag for an analog ratemeter depends on the frequency of the change in counting rate, being greater for the more rapidly changing counting rates observed for smaller lesions.

With this digital system, for a given level of statistical accuracy, the averaging time for the voltage signal which controls the degree of contrast enhancement is more easily optimized. Experimentally determined MTF curves are presented, along with phantom and patient scans.

Multifunction Digital Research Scanning System by
EDWARD M. SMITH AND LOUIS KATCHIS, JR., Univ. of Miami School of Medicine, Miami, Fla.

The Multifunction Digital Research Scanning System is a modularly constructed organ-visualization system. It is a high-speed (500 cm/min), 14-crystal, digital rectilinear scanner built as a special-purpose hard-wired computer. The two synchronous detector heads, one beneath and one above the scan table, each consisted of a linear array of seven 3 × 2-in. NaI(Tl) crystals, each crystal with its own focused collimator. Each detector can be independently moved 61/2 in. in the vertical direction. The exact position of the detectors are known at all times by the use of an absolute 13-bit shaft-angle encoder along the longitudinal axis of the scan table and a programmable Slosyn motor across the table. Anatomical landmarks may be programmed into the system and automatically recognized when the detector passes over these points. The scan field is 78 in. long by 24.5 in. wide with a position resolution of 0.14 cm. The primary scan motion is along the longitudinal axis of the table, and the detectors are indexed across the table. The scan image is built-up seven lines at a time, allowing the total scan field to be visualized with each pass of the detector. Each crystal has its own 8-bit or 12-bit counter with buffer storage. A single fast pulse-height analyzyer (200 nsec random pulse-pair resolution) is used for all 14 crystals using a time-sharing ‘‘cuing’’ technique.

Dual radionuclide studies may be performed with this system. The major components of the system consist of the mechanical scanning frame and position encoders, radiation detectors, coincidence circuitry and nuclear instrumentation, counters and buffer storage, anatomical landmark recognition section, arithmetic section, program control logic, system control logic system, output control logic and the output devices.

At present the output devices consist of digital cathode-ray tubes, a storage scope, an IBM I/O writer and a Kennedy incremental read-write magnetic-tape recorder. The objectives in the design of this system were to demonstrate the usefulness of designing a scanning system as a special-purpose computer to determine the most efficient and useful information-handling techniques for quantitative scanning, to evaluate what is the most efficient media and device for data storage and to develop special-purpose scanning systems.

Promotion of $^{203}$Hg-Chlormerodrin Excretion by Cold Chlormerodrin or Mercurhydrin by WILLIAM H. STRAIN, RICHARD M. PEER, MARTIN R. THOMAS, ARNOLD P. GASS AND WALTER J. PORIES, School of Medicine and Dentistry, Univ. of Rochester, Rochester, N.Y.

The excretion of $^{203}$Hg-chlormerodrin from rats is greatly increased by the intramuscular administration of cold chlormerodrin or mercurhydrin. If chlormerodrin, the more effective agent, is administered immediately after injection of the radiopharmaceutical, 90% of the radioactivity compared to controls is eliminated in 10 days. A delay of 24 hr in the administration of cold chlormerodrin reduced the excretion to only 84% in the same time interval. Mercurhydrin administration after injection of the radiopharmaceutical flushed out 67% of the radioactivity in 10 days when given immediately and 52% when administered after a delay of 24 hr. The kidney binding sites of the $^{203}$Hg seem to be primarily affected.

These results are important for the clinical use of the long-lived radiopharmaceuticals. The measurements show that a radiopharmaceutical is flushed out better by a cold preparation with the same chemical structure than by one with a different configuration. Although compounds which effectively promote the excretion of radiopharmaceuticals make it possible to use agents with long half-lives, these preparations have to be proven safe from the standpoint of FDA. Fortunately, both chlormerodrin and mercurhydrin have been used clinically for many years, and may be used to sweep out $^{203}$Hg-chlormerodrin without additional clearance from FDA. (This research was supported in part by Research Grant RH 00042, National Center of Radiological Health, U.S. Public Health Service.)

Case Report—Pulmonary Metastases from Thyroid Carcinoma Detectible Only by $^{131}$I Scans: Treatment and Response by J. E. TURNER, U.S. Naval Hospital, Philadelphia, Pa.

A 20-year-old caucasian male who developed mixed papillary and follicular carcinoma of the thyroid was
originally treated with total thyroidectomy and neck dissection. Postoperative management included replacement thyroid hormone and vitamin D to correct manifest tetany. Twenty-six months after the initial treatment, the patient presented with fatigue, vomiting and mental confusion secondary to hypercalcemia. During the ensuing hospitalization, physical examination of the chest and routine chest roentgenography were normal, but scanning with $^{131}$I revealed extensive uptake throughout both lung fields. The patient was treated with a second 200 mc $^{131}$I and a repeat scan 16 weeks later revealed no uptake above background.

Follow-ups included $^{131}$I scans at 4 and 12 months. The scan performed after 18 months again revealed extensive uptake in both lung fields. Physical examination and chest roentgenogram were again normal. The patient was treated a third time with 200 mc of $^{131}$I, and the scan became negative.

Pulmonary-function studies, including routine spirometric measurements, compliance, resistance and diffusion were conducted before and after each of the therapeutic $^{131}$I administrations. The literature has been reviewed for case reports of thyroid carcinoma with pulmonary metastases detectable by scanning but not by routine studies including roentgenography. Three other case reports have been published.

**Dynapix: A New Concept in Rapid Rectilinear Scanning**

BY THOMAS A. VERDON, JR. AND FRANK H. ALLEN,
Letterman General Hospital, San Francisco, Calif.

The Dynapix is a machine that has been developed to produce high-quality rectilinear scans in a very rapid time sequence. Ideally, we would get all the favorable qualities of rectilinear scanning performed in a time frame comparable to that of the scintillation camera. To obtain this result this machine is composed of two parts: a detector head that has 10 sodium iodine crystals moving in unison and a console that records the data from this detector head on television, magnetic tape and Polaroid film. We have used this machine to study 1,000 patients for a total of 3,000 scans. It has given high-quality scan images and diagnostic information in minutes. A review of the first 1,000 patients studied and their scans produced by this machine will be discussed, and selected examples of various scans will be shown.

**Technetium Brain Scanning—Normal and Pathologic Variations of Posterior Fossa**

BY MILO M. WEBBER,
GERALD IBA AND L. R. BENNETT, Univ. of California, Los Angeles, Calif.

Original evaluations of brain-scan results suggest that the posterior fossa is an especially difficult area. Abnormal accumulations in this region are easily missed and can not be easily differentiated from the various normal configurations in the area. This paper will present the variations of the normal configuration seen in the posterior fossa and a review of our experience. Several cases of proven pathology presenting in this region will be shown with emphasis on their differences from the normal patterns. The technique of positioning and set-up of scanning equipment will be critically evaluated. (This work was supported in part by Contract AT (04-1) GEN-12 between the Atomic Energy Commission and the University of California at Los Angeles.)

**Clinical Experience with Oblique Views in Pulmonary Perfusion Scintiphography in Normal and Pathological Anatomy**


To definitely localize perfusion defects by pulmonary scintiphography, it is desirable to visualize the defect on two or more views of the lung. The anterior and posterior views are most generally used by radioisotope laboratories. With the aid of the gamma scintillation camera, additional views can be easily and quickly obtained. We have found that oblique views of the lungs add considerable additional visualization of perfusion defects, and, in some cases, the oblique view gives us our only visualization of an otherwise missed perfusion defect. In the oblique position, overlap of activity from the opposite lung field is also avoided. Gamma camera scintiphotos and anatomical reconstructions of oblique lung views will be presented to define the normal and pathological anatomy in the anterior, posterior and oblique views of the lungs. The information was collected from a large series of patients over a 2-year period.

**Quantitative Cinescintivideography—A New Concept for Dynamic Function Studies**

BY H. N. WELLMAN, J. MACK, D. HUNKAR AND J. KEREIAKES, National Center for Radiological Health, U.S. Public Health Service and Cincinnati General Hospital, Cincinnati, Ohio.

Widespread availability of short-half-lived radiopharmaceuticals with high photon yield and low patient dose have made rapid organ imaging feasible. Indeed, these radiopharmaceutical developments have, to a degree, stripped the capabilities of presently available imaging devices. The gamma scintillation camera, as commercially available, can provide individual Polaroid photographs of probably greater than 2–3 sec integration time. However, dynamic events of shorter duration cannot be recorded because of the short duration of oscilloscopic pulses and the inability to process photos more rapidly.
A system capable of recording frames of as short as 0.1 sec or greater has been developed using a variable retention oscilloscope, high-resolution video system and video-tape recorder. This system makes possible the recording of very rapid dynamic events in a qualitative mode. By means of the video system contrast enhancement can be superimposed as desired.

In addition to a qualitative presentation, digital data can be recorded through a unique integrating system which makes possible the intercomparison of any two selected areas of variable size within the field of view of the detector. These integrated pulses are then recorded on rapid-response strip-chart recorders or digital printers. The total system thus makes possible the recording of continuous and instantaneous events.

Preliminary clinical experience with this system will be reported including comparative carotid-cerebral flow as well as angio-cardiographic flow dynamics. Studies of the perfusion ventilatory and wash-out phases of intravenous $^{133}$Xe pulmonary function will be reviewed. Comparative renography and other studies using the qualitative and quantitative functions will be reported. Addition of a magnetic-tape system that is under development for playback of retention oscilloscopic pulses will make an even more versatile system possible.

Radioisotopic Dilution and Kidney Retention of $^{197}$Hg
BY BERGENE KAWIN, EDWARD E. WINTERS AND B. J. SAUERBRUNN, V.A. Hospital, Washington, D.C.

In many nuclear-medical laboratories $^{197}$Hg or $^{203}$Hg-labeled Neohydrin (N) is a first choice for brain-scanning studies. One major drawback to the use of radioactive N for brain studies is the irradiation dose associated with its prolonged, high retention in kidney. To help resolve the question of whether a non-radioactive mercury compound, thimerin (T), might compete effectively to modify N retention in organs, it was tested when given as an “isotopic diluent” to rats. Concentrations of $^{197}$Hg in various organs were measured 24 hr after single intravenous administration of isotopic mixtures comprised of nonradioactive T and $^{197}$Hg-labeled N. The log dose treatment levels of T used were equally spaced at intervals of 2.8, 4.0 and 5.6 mg/kg body wt with four replicates for each level. The radioisotope-assay analysis showed statistically significant downward responses to T treatment in liver, spleen, lung and femur, but not in adrenal, ovary and brain. An unexpected but definite upward trend was observed in kidney after isotopic dilution with T; $^{197}$Hg concentration linearly increased from 31 to 35% in statistically significant proportion to the T doses administered. Presumably, renal capacity for uptake and retention of $^{197}$Hg and T was so great that no effects of isotopic dilution could be demonstrated with the moderate, sublethal doses used. Compared to the positive isotopic-dilution effects observed in other organs where N has less deposition specificity, it is probable that the T treatment shifted the distribution of radiomercury to the very numerous sites available in the kidney. Because T treatment increased kidney deposition of the radiomercury, it could augment the long-term kidney irradiation exposure hazard. For this reason, the use of T with radioactive N may be questionable.

Statistical Interpretations on the Scintigrams of So- Called Nodular Goiters by HIROSHI YASUKOCHI, FUMIO KINOSHITA, DAII ISHIKAWA AND TOSHIRO YAMAZAKI, University of Tokyo, Okubo Municipal Hospital and Toranomon Hospital, Tokyo, Japan.

The thyroid scintigram is one of the most popular and valuable examinations in the field of radioisotope-distribution detection for diagnosis. Many reports on the interpretations of thyroid scintigrams have been presented. We have experienced about 7,000 cases of thyroid scintigrams at the University of Tokyo Hospital, Okubo Municipal Hospital of Tokyo and Toranomon Hospital in Tokyo. In this report about 700 cases of histologically confirmed “so-called nodular goiter” are discussed. Here the term “so-called nodular goiter” means thyroid disease that has one or more palpable or occult nodules in the gland.

The administered dose of radioiodine influences the value of interpretation. For valuable interpretations of thyroid scintigrams the lower limit of radioiodine in the glands is about 20/L$^{\mu}$Ci where L is the diameter of the scanner crystal in inches. Of course, this formula also depends on the efficiency of the collimators and/or the presentation mode of the apparatus.

Nodular goiters are histologically classified for the analysis and the frequency of them was about 40% of malignant nodules, 40% of benign nodules and 20% of chronic thyroiditis (Hashimoto) in this series.

The scintigram information analyzed for the diagnosis are position or deviation of the glands, area of the cold spots, the nature of the boundaries between nodule and other tissue and the condition of the deposit of radioisotope in the glands or tumor.

Detail numbers of each information will be presented: (1) Malignant nodules, mostly carcinoma, have large nodules and mostly a greater defect area compared with that of the palpable nodule. The margin of the defect is not expansive and the boundary is rather clear compared with that of the benign tumors. Less chance of the deviation of the glands exists compared with that of the benign tumors. (2) Benign nodules, such as adenoma or cyst, mainly have one or more small nodules. The margin of the tumor is
mostly expansive, and the boundary is relatively unclear. (3) Chronic thyroiditis (Hashimoto). This is the most difficult disease to differentiate from other nodules. The deposit is usually nonuniform and mottled in the area of disease, but serial examinations will be needed in most of the cases. As a result, we feel that skillful physicians will be able to diagnose the nature of thyroid nodule by the scintigram reading before the operation. Of course, other examinations such as palpation should not be neglected at the clinic. Lastly our opinions on comparing scintigrams from cameras and scanners and the experiences of the computerized diagnosing method of thyroid diseases will be discussed.