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Progress Report

Radioisotope Studies Utilizing a Low

Level Whole Body Counter

and

Clinical Application of Activation Analysis

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- B. Changes in Thyroid Iodine Content Following I-131 Therapy

*Preprints
Removed*

A. TASK DESCRIPTION (Approach, relation to work package, in 200 words or less)

The main emphasis of these studies is the development of methods (hardware and software) for the quantitation of body and specific organ burdens of radioactivity. Current work is directed toward the evaluation of radiation dose distributions in human beings from new radioactive tracers and new procedures used in nuclear medicine. Dosimetry and clinical studies will be carried out on patients using new radiopharmaceuticals where dosimetry data are lacking.

Future efforts will be directed toward the development of systems that will facilitate the collection of dosimetry data using less specialized facilities. The availability of instrumentation and analytic techniques that provide clinical images as well as dosimetry data should enhance the rate of collection of data on human exposures in medicine and assist in the optimization of diagnostic strategies.

In parallel with these efforts, we are developing a new computer assisted technique for diagnostic decision making. The basic aim is to utilize efficiently all the available data to maximize information gain while minimizing cost factors.

B. Publications.

1. Fiscal Year 1978

Price, R. R., Touya, J. J., Branch, R., Goddard, J. and Brill, A.B. Validation of renal transit-time calculations using compartmental models and direct measurements, A Review of Information Processing Medical Imaging. Proceedings of the Fifth International Conference, A. B. Brill and R. R. Price, Editors, pp. 536-554, Vanderbilt University, Nashville, 1978.

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Patton, J. A., Price, R. R., Rollo, F. D., Brill, A. B. and Phel, R. H. Clinical and experimental results with a nine element high purity germanium array. IEEE Trans. Nucl. Sci., NS-25, No. 1, 653-56 (1978).

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C. Purpose

1. Development of methods (analytical and instrumental) for quantitation of body and specific organ contents of stable and radioactive tracers; and
2. Application of these techniques to obtain information on:
 - A. Pathophysiologic status of patients receiving established and new radiopharmaceuticals; and
 - B. Dosimetry.
3. Development of analytic techniques for efficient extraction of information from images (features), for diagnostic and therapeutic decisions.

D. Background

This contract was originally directed toward the development of low level whole body counters for assessment of fallout fission fragments from weapons testing in the late 1950's. In the late 1960's, we redesigned the data collection systems for assessment of radiation dose from radiopharmaceuticals used in nuclear medicine diagnosis and therapy. In the 1970's, high resolution solid state detectors (GeLi) were added for stable tracer studies using neutron activation analysis to obtain information without patient radiation dose. These studies involved collaboration with scientists at ORNL. X-ray fluorescence (SiLi) detectors were developed for analysis of thyroid iodine content, and high resolution emission mapping (HPGe mosaic array) investigated in collaboration with LBL and FMI.

These investigations have required quantitative measurement and analysis techniques in which computers have played a major role. We have attempted to demonstrate the advantages to be derived from the use of the CAMAC standard in nuclear medicine. These efforts have involved collaborations with LASL, FNAL, and AERE (Harwell).

The previous program will be divided into two parts:

1. An extension of the past work, emphasizing the development and application of new concepts in instrumentation and analysis to nuclear medicine and focused on assessment of the impact of new energy sources on health. This work will be conducted at BNL and is described in this document.

2. A transfer of the BCTIC operation from ORNL to Vanderbilt.

E. Progress in FY 1979

1. Dosimetry

a. Radio-iron Dosimetry

A draft manuscript has been submitted to the MIRD Committee summarizing the data we have collected and analyzed. The key tables resulting from these computations follow (Tables VI, VII, VIII), and a draft manuscript has been prepared. (Appendix A)

b. NCRP Report on Radiation Protection in Nuclear Medicine (Scientific Committee 32)

The initial review by the prime reviewers has been obtained, their comments and suggestions incorporated and the revised manuscript returned to NCRP staff for final typing and distribution to the council. The report includes tabulations of organ dose estimates from commonly employed radiopharmaceuticals based on calculations made by W. Snyder and M.R. Ford (ORNL) using biokinetic data reviewed by the committee and using MIRD data, where available. The report should be approved and published in mid 1980.

Table VI

Average Radiation Absorbed Dose in Normal Subjects
from Radioiron (rads/mCi)

Target Organ	Source Organ				Total
	Liver	Spleen	Red Marrow	RBC*	
	<u>$^{52}\text{Fe} + ^{52m}\text{Mn}$</u>				
Liver	2.68	0.03	0.14	0.04	2.89
Spleen	0.03	16.11	0.12	0.04	16.30
Red Marrow	0.03	0.02	8.96	0.03	9.05
Ovaries	0.01	0.02	0.48	0.04	0.55
Testes	0.00	0.00	0.05	0.04	0.09
Total body	0.10	0.07	0.47	0.03	0.67
	<u>^{55}Fe</u>				
Liver	60.2	0	0	3.8	64
Spleen	0	267	0	4.0	271
Red marrow	0	0	6.0	3.8	9.8
Ovaries	0	0	0	4.0	4.0
Testes	0	0	0	3.8	3.8
Total body	1.5	0.7	0.1	3.8	6.1
	<u>^{59}Fe</u>				
Liver	127	1.7	0.8	15.9	145
Spleen	3.3	463	0.8	15.0	482
Red marrow	3.1	1.7	18.5	14.1	37
Ovaries	2.7	0.9	2.2	15.0	21
Testes	0.7	0.2	0.3	15.0	16
Total body	6.3	3.3	1.5	13.2	24

* Dose from RBC activity outside of the liver and spleen. Total body "S" values used.

Table VII

Average Radiation Absorbed Dose in Abnormal Subjects
from Radioiron (rads/mCi)

	$^{52}\text{Fe} + ^{52}\text{Mn}$		^{55}Fe		^{59}Fe	
	Maximum	Minimum	Maximum	Minimum	Maximum	Minimum
Liver	12.4(G)	0.397(D)	161(O)	33.7(A)	351(O)	58.9(A)
Spleen	69.0(D)	0.840(B)	1120(H)	567(F)	1720(H)	86.0(F)
Red marrow	13.3(M)	0.652(N)	151(F)	1.98(H)	176(F)	6.3(H)

Table VIII
Comparison of ^{59}Fe Dose Estimates (rad/mCi)

	(1)	(2)	(3)	(4)	(5)
Liver	83	150	100	27	145
Spleen		230	140	57	482
Red marrow	46	140	50	65	37
Ovaries	26				21
Testes	22				16
Blood			75-100	77	
Skeleton			13		
Kidneys		90			
Total body	23	30	5-35	23	24

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- (2) Hine GJ, Johnston RE: Absorbed dose from radionuclides. J. Nucl. Med. 11, 468-469, 1970 (letter)
- (3) Garby L, Nosslin B: Radiation Doses from Radioactive Substances in Substances in Medical Use. Stockholm, Swedish National Institute of Radiation Protection, 1969 (a compilation)
- (4) Cloutier RJ, Edwards CL, Snyder, WS: Radiation doses from radionuclides in the blood. In CONF-691212, 1970, pp. 325-345
- (5) This article

2. Prediction of Radiation Sensitivity of the Thyroid During I-131 Therapy

Information of iodine uptake, the effective half-time of its retention in the thyroid and thyroid mass are used in calculating the amount of I-131 to be administered to patients in the treatment of hyperthyroidism. A major variable, however, which we have not yet learned how to assess and use in planning therapy is radiation sensitivity of the thyroid.

In previous work on iodine kinetics, we evaluated iodine metabolism in large numbers of patients during treatment of thyrotoxicosis and have determined model parameters which are reasonable predictors of absorbed radiation dose to the thyroid, given knowledge of thyroid gland size.

To evaluate thyroid sensitivity, we sought to find and measure a parameter that reflects damage to the thyroid. The rate of loss of iodine from the gland immediately following therapy is due to altered rates of release from the gland and by diminution of uptake. We have now measured the iodine content of the gland after therapy by means of x-ray fluorescence scanning in a large number of patients in an attempt to determine if the later incidence of hypothyroidism can be predicted from early changes in iodine content after therapy. We measured iodine content and other thyroid function parameters in 52 patients who received radioiodine therapy. These patients were studied at monthly intervals following I-131 therapy with serial, quantitative fluorescent scans and radioimmunoassays. All patients showed a steep decline in iodine content between the second and third month post-therapy.

The major finding of interest from these studies is that those patients who were destined to become hypothyroid had lower iodine content values at the 2-3 month interval than other groups. From inspection of the data, we chose a value of 2 mg as the level for making predictions on the outcome of therapy. Applying this separation criterion to the 43 patients in whom adequate follow-up information was available (as of June 1978) some interesting observations can be made as shown in the lower section of Table V. Of the 21 patients who had iodine contents of 2 mg or greater at the 2-3 month interval, only 3 became hypothyroid within 12 months. The remaining 18 either remained euthyroid or relapsed into hyperthyroidism within 12 months. On the other hand, of the 22 who had iodine contents of less than 2 mg at 2-3 months post-therapy with I-131, 18 became hypothyroid. Thus, this is a clue deserving further study to determine whether this predisposes the patient to develop hypothyroidism and, if so, by what mechanism. A manuscript summarizing the present status of this project, in preparation for submission for publication, is attached as Appendix B.

Table V

Relationship of Low Iodine Content to Early Hypothyroidism

<u>Thyroid Iodine at 2-3 Months</u>	<u>Hypothyroid Within 12 Months</u>	<u>Euthyroid at 12 Months or Relapse Within 12 Months</u>	<u>Total</u>
< 2 mg.	14	2	16
≥ 2 mg.	3	13	16

Updated to 16 June 1978:

< 2 mg.	18	4	22
≥ 2 mg.	3	18	21

Inadequate Followup: 9

E. Technical Progress (cont'd)

3. Instrumentation Projects

a. Digital Computer Interface for a Longitudinal Tomographic Scanner for Human Dosimetry Studies

SCANNER DESCRIPTION

The PHO/CON-192 Multiplane Imager is a tomographic scanning system developed by Searle Radiographics. It consists of two high performance gamma cameras, each with its own focussed collimator (Fig. 1). The cameras are supported by a moving

Figure 1.

PHO/CON-192 Multiplane Imager showing upper and lower cameras and the stationary bed.

frame so that one camera is located above and one below a stationary bed. The cameras are moved together in a rectilinear raster by the drive system, maintaining their relative positions throughout the scan. Vertical displacement of each camera can be adjusted individually. Scanning is controlled by the internal electronics of the PHO/CON. Tomographic images are reconstructed by dedicated hardware. Tomographic images of six different planes for each detector are produced on standard x-ray film. The separation between each plane and the distance from the collimator face of the first plane are specified for the upper and lower cameras prior to the start of the scan.

COMPUTER SYSTEM AND RECONSTRUCTION METHODS

The PHO/CON has been interfaced to a PDP-11/34 computer in our laboratory. A digital interface (Fig. 2) containing analog-to-digital convertors, timing and control, multiplexing, and line driving circuits has been developed. This interface encodes scan system moving frame (bed) coordinates, camera coordinates derived from the analog camera voltages, an upper/lower detector flag, and an isotope one/two flag into a 16 bits-per-word data stream which is transmitted to a DMA port in the PDP-11/34. List mode data are collected from the scanner and stored immediately on disk with no processing. Large amounts of data at high speed can be accepted and stored.

Figure 2.

PHO/CON data encoding and collection hardware block diagram.

A PDP-11/55 computer is used to reconstruct the images because of its larger memory, higher processing speed, and high quality display processor on which the reconstructed images can be viewed.

Reconstruction of individual longitudinal tomographic planes is performed by backprojecting the collected events along the ray paths through the focal point of the camera in which the event was detected. During scanning, events that originate at a particular position on a plane are represented by a specific camera coordinate pair. If a fictitious line is drawn from this coordinate position back through the focal point, the plane from which the event occurred will be intersected at a point (Fig. 3). By summing all of these backprojected intersections on a plane, an estimation of the activity distribution at that plane is obtained. This is an approximation of the true activity distribution because of contributions from activity on other planes which also are summed into the image and contribute a blurring or loss of resolution to the reconstruction.

The list mode data is decoded word by word during reconstruction. The X and Y moving frame coordinates are incorporated into individual data words as the low order 12 bits and are preceded by a flag word of sixteen bits of zeros. Camera data words which follow the Y bed coordinate word contain

Figure 3.

Backprojection of an event through a longitudinal plane. A fictitious line drawn through a crystal event and through the focal point of the collimator intersects a plane of interest at a point as the crystal is moved in a rectilinear raster.

the seven bit X and seven bit Y coordinates for each camera event. Also, encoded in each camera word are flag bits representing upper or lower detector data and isotope one or two data (Fig.4). Decoding is performed by detecting the flag word as the start of a unit of data. Bit masking extracts the coordinates and flag information from the data words in the proper sequence.

After decoding each data word, the appropriate action is taken to backproject the event. The X and Y bed coordinates are mapped into the final image array. Each camera event at every bed coordinate pair is backprojected on the longitudinal tomoplanes that have been chosen for reconstruction. The current program can build as many as six 128 X 128 byte mode images simultaneously, three each for the upper and lower detectors. Reconstruction times are dependent on the number of counts detected. Typically, reconstruction times for patient studies are about the same as the collection times.

This digital backprojection reconstruction technique yields longitudinal images similar to those which are available from the PHO/CON hardware reconstruction. However, there are several advantages to the computer-generated images. Reconstruction can be done at anytime (or redone, if necessary) since the raw data is stored. This obviates the need for rescanning the patient. Any number of images at any arbitrary plane separation can be reconstructed as needed. The PHO/CON reconstruction yields six images for each detector at a constant separation. Various

Figure 4.

Digital data stream from the PHO/CON interface. Each change in a bed coordinate results in a new flag word followed by bed coordinate words and camera data at the bed coordinates.

filter and deblurring algorithms can be applied to the digital images to improve the signal-to-noise ratios and enhance the images. This is not a feature of the commercial PHO/CON system.

Backprojection can be used to produce transverse sectional images from the PHO/CON data. Transverse section images are not available from the commercial system. The algorithm used to reconstruct transverse section images is very similar to that used for longitudinal section images, the difference being that the plane of interest of the intersection of a ray path is a transverse plane rather than a longitudinal plane (Fig. 5). The transverse section images are reconstructed as 128 X 128 pixels. The vertical dimension is 34 cm with the geometric focus in the center of the image. The horizontal coordinates of the transverse images are derived from the encoder information for the X axis of the PHO/CON bed, just as are the X-coordinates of the longitudinal scan reconstruction. The vertical coordinates of the transverse images are not derived from the encoder data, but are calculated from the camera data.

Transverse images usually require post-reconstruction processing to produce a final image. Ambiguities can arise in

Figure 5.

Backprojection of an event through a transverse plane. A line drawn through a crystal event and through the focus of the collimator intersects a plane of interest at a point.

the calculation of the vertical coordinates because of round-off error. When the camera is positioned squarely over the transverse plane being reconstructed, it is impossible to position some camera events properly in the plane. These events are not used in the reconstruction. Thresholding and smoothing reduces the effects of omitting these data.

RESULTS OF DIGITAL BACKPROJECTION

Numerous phantom scans have been performed with the PHO/CON using Tc-99m. Both the longitudinal and transverse section images have been reconstructed. Patient studies have been done using Tc-99m, Ga-67, and Tl-201.

Figure 6 is a phantom constructed in our laboratory. It has an annular region surrounding a volume region. Within the volume are four separate smaller volumes. For these studies, the annulus and the four volumes were filled with Tc-99m. Figure 7 shows the results of a reconstructed longitudinal scan. Reconstruction was carried out at three levels through the phantom. Figure 7 also shows transverse sections through the phantom. The inner volumes and the vertical portion of the annulus are seen to be separated. This is the expected result because the horizontal resolution is better (about 0.6 cm) than the vertical

Figure 6.

Plexiglas volume phantom. An annulus surrounding a volume which contains four smaller volumes is seen in the diagram. Each section can be filled separately.

Figure 7.

Tc-99m tomographic scans of the phantom shows three longitudinal planes and two transverse planes.

resolution (estimated at 2.0 cm). The images demonstrate the shape of the phantom.

Figure 8 shows longitudinal tomograms of a 72 hour Gallium-67 patient study. A Tc-99m sulphur colloid study was

Figure 8.

72-hour Gallium-67 and Tc-99m sulphur colloid scans. Two arbitrary planes of Ga-67 data and corresponding Tc-99m sulphur colloid liver scans are combined by the computer to form an overlay composite. This procedure can be done at any tomographic level.

collected immediately after the gallium scan without moving the patient. The sulphur colloid is seen primarily in the liver. An overlay composite image is generated by the computer. Any number of tomographic overlays at various planes could have been produced from the digital data. Positioning the sulphur colloid liver scan over the gallium whole-body scan was performed easily by the computer and display processor. Other types of processing or enhancement could have been used as needed.

Longitudinal images of the myocardium with Tl-201 from the PHO/CON are seen in Figure 9. The information was collected from the lower detector with the patient lying in the LAO position. A 15 X 15 centimeter scan was performed around the area of the heart. The high resolution collimator was used. The conventional PHO/CON images are characterized by high background content due to uptake of the isotope in other regions of the chest.

Computer reconstruction of the same longitudinal planes are also shown. These digital images are displayed in 64 X 64 pixel format and have been post-reconstruction processed to remove background. The enhancement procedures include band pass filtering, data thresholding, and background subtraction. Figure 10 shows the results of this processing.

Transverse sections through the myocardium are presented in Figure 11. These sections are parallel to the horizontal axis in the longitudinal images. The series of sections moves

Figure 9.

Tl-201 longitudinal tomograms of the myocardium at 1.5 cm separation. These images are from the standard film output.

Figure 10.

Tl-201 longitudinal tomograms of the myocardium at one centimeter separation. These are computer processed images.

anterior to posterior through the heart at 0.7 cm intervals and shows the myocardial wall and left ventricular cavity.

DECONVOLUTION DESCRIPTION

Methods of reducing the effects of background noise and off-plane blur information are being investigated. The algorithm of Chang, Macdonald and Perez-Mendez (1) for simultaneous multiplane deconvolution has been applied to

Figure 11.

Tl-201 transverse tomograms of the myocardium at 0.7 centimeter separation. These are sections moving from anterior to posterior.

phantom studies performed with the PHO/CON. Using system theory, one can determine the response of a linear system to any arbitrary input by convolving the input signal with the impulse response of the system. If the impulse response of the imaging system is its point spread function, the convolution of a known distribution with the point spread, assuming linear behavior, will give the output image of the system. Conversely, if the corrupted output image is available as in a clinical scan, in principle it is possible to deconvolve the output image and the point spread function to get an uncorrupted true activity distribution. This technique works perfectly with noise-free ideal images and point spread functions, but not as well with real data. Real images must be low pass filtered to reduce noise contributions. Applying this theory to multiple planes from a tomographic scanner simultaneously yields images with improved signal-to-noise ratios and reduced off-plane contributions. However, problems with noise components can distort the final images.

RESULTS OF DECONVOLUTION

Images of a phantom consisting of the numbers one, two and three separated by 1.5 cm in air are shown in Figure 12. The longitudinal tomographic sections are reconstructed at the plane of each number. Blur artifacts from the other planes are seen in each image. Processing with the algorithm of Chang, et al., yields three images in which the background blur information is reduced in each image (Fig. 12). One problem with the method is the occurrence of mottling which is seen in the processed images. This is due to the noise components of the images becoming larger than the image information at some spatial frequencies. The result is imperfect reconstruction at points in the image.

Figure 12.

Multiplane simultaneous deconvolution of PHO/CON images using the algorithm of Chang, et al.

CONCLUSIONS

A Searle PHO/CON-192 multiplane imager has been interfaced to a PDP-11/34 computer. Digital data collected during scans can be backprojected to produce multiple tomographic planes in longitudinal and transverse sections. Digital collection and reconstruction allows image formation and image enhancement that is not available from the commercially available instruments. Further, post-reconstruction processing using the simultaneous multiplane deconvolution algorithm of Chang, et. al, has been applied to phantom studies. Iterative forms of this method are being investigated.

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E. Technical Progress (cont'd)

3.b. Microprocessor Controlled Whole-Body scanner for Human Dosimetry Studies

Due to increasing difficulty in maintaining the PDP9 computers which have been used to control and collect data from research scanner instrument in the low-level whole-body counter, we have designed and have constructed a microprocessor controlled interface to operate the low-level whole-body counting facility. This system is based upon an LSI 11 controlled autonomous CAMAC crate connected to a dual floppy disk drive. The LSI 11 contains 32,000 words of solid state memory and the entire system resides in the CAMAC crate. The low-level whole-body counting system is controlled through an output register which generates a command which in turn operates a control register, which controls the mechanical motion of the scanner in the low-level whole-body counting facility. The status of the limit switches and the hand control buttons are returned to the LSI 11 computer through an input register in the CAMAC crate. The incremental encoders attached to the lead screws of the scanner, used to monitor the X and Y position of the scanner, are fed back to the LSI 11 through a encoder follower CAMAC module. The scanner will operate under computer control, and data will be collected from both the upper and lower probes through standard nuclear electronics located in a NIM bin in the same electronic rack which holds the CAMAC crate control system. The system is designed to collect up to 4 input channels of data from each detector during its scanning motion. These data are normally stored in memory during the scan, however, for large area scans where large amounts of data are collected these data can be buffer stored on the floppy disks during data acquisition. These data can then be sent after data collection is finished to the departmental PDP1155 or to the central computing facility containing a PDP10 computer. These data are sent through an asynchronous communication port using communications protocols already implemented, and in routine use for communication between

these computers. The system has been built and we are currently awaiting delivery of some parts needed for the scanner interface, at which point the system will be installed and the PDP9 removed from service. The module designed for this work could be used to drive a scanning bed, such as is now available in many laboratories. With stationary opposed detectors, such a system would provide a general purpose scanning capability for routine and research studies. Since no U.S. manufacturer currently manufactures a scanner, this may be of general interest to other nuclear medicine research groups.

STEEL ROOM INTERFACE PARTS LIST

Integrated Circuits

1-13	SPX74A1		
27-34, 37-40	(Spectronics)		
14, 15, 22	75451B or 75452B	Vcc = 5	Gnd = 4
23, 25, 26	(See Note 1 on drawing)		
16, 17, 19			
35, 36	74LS14	Vcc = 14	Gnd = 7
18	74LS158	Vcc = 16	Gnd = 8
20	74LS08	Vcc = 14	Gnd = 7
21	74LS02	Vcc = 14	Gnd = 7
24	75468		Gnd = 8

Transient Suppressor

1N5658A (General Semiconductor)

Resistors

2.4K	17 on logic board 8 on line board
1.0K	8 on logic board 4 on line board
150	13 on logic board 8 on line board
390	4 on logic board

Connectors

J1, J6	DB25
J2	6 terminal
J3	8 terminal
J4	10 terminal
J5	5 terminal
J7	To be specified

Power Requirements (Maximum):

Vcc (line board) 418ma
Vcc (logic board) 653ma
Vk (logic board) 340ma (5 Volts)
Vcc + Vk 993 ma

Computer/Line Interface

J6

Remote Command Drivers

J6

Limit Switch Drivers

J7

IC 24 75468

P2 of 2	Drawn: S D Wilson	Date: 4 Sept 79
	Checked: D. B. P. Wilson	Date: 5 Sept 79
STEEL ROOM LOGIC		
Computer/Line Interface, Clutch Drivers, Limit Switch Drivers		