NUCLEAR MEDICINE AND IMAGING RESEARCH
(Instrumentation and Quantitative Methods of Evaluation)

PROGRESS REPORT
FOR THE PERIOD JANUARY 15, 1992 THROUGH JANUARY 14, 1993

R.N. Beck, M. Cooper, and C.-T. Chen

The Franklin McLean Memorial Research Institute
The Department of Radiology
The University of Chicago
Chicago, Illinois

MASTER

July, 1992

Prepared for
THE U.S. DEPARTMENT OF ENERGY
UNDER GRANT NO. DE-FG02-86ER60418

NOTICE

Neither the United States nor the Department of Energy, nor any of their employees, nor any of their contractors, subcontractors, or their employees, makes any warranty, expressed or implied, or assumes any legal liability or responsibility for the accuracy, completeness, or usefulness of any information, apparatus, product or process disclosed or represents that its use would not infringe privately owned rights.

PROGRESS REPORT

INSTRUMENTATION AND QUANTITATIVE METHODS OF EVALUATION

DOE Grant No. DE-FG02-86ER60418

Robert N. Beck, Principal Investigator

Page

RESEARCH PROJECTS

I. THEORETICAL STUDIES OF IMAGING SYSTEMS AND METHODS

I-1.	SPECT Reconstruction Algorithms for Converging Hole and Astigmatic Collimators	1
	<i>Donald L. Gunter, Charles E. Metz, and Robert N. Beck</i>	
I-2.	Utilization of Scattered Radiation in SPECT Reconstruction	7
	<i>Donald L. Gunter, Charles E. Metz, and Robert N. Beck</i>	
I-3.	Investigation of Fundamental Characteristics of SPECT	13
	<i>John N. Aarsvold, Chin-Tu Chen, and Donald L. Gunter</i>	
I-4.	Energy-Dependent Scatter Correction in PET	14
	<i>Caesar E. Ordonez, Chin-Tu Chen, Robert N. Beck, and Kenneth L. Matthews</i>	
I-5.	Compensation for Photon Attenuation in PET	16
	<i>Chin-Tu Chen, Caesar E. Ordonez, and Xiaolin Yu</i>	
I-6.	Improving the Utilization of Detector Motion in PET	19
	<i>Miles N. Wernick, Chin-Tu Chen, and Caesar E. Ordonez</i>	
I-7.	Iterative Image Reconstruction in ECT	22
	<i>Chin-Tu Chen, Caesar E. Ordonez, Miles N. Wernick, John N. Aarsvold, Donald L. Gunter, Wing H. Wong, Oscar H. Kapp, Xiaolong Ouyang, Mark Levenson, and Charles E. Metz</i>	

II. HARDWARE DEVELOPMENTS

II-1.	High-Resolution Multi-Slice PET.	25
	<i>Nicholas J. Yasillo, Chin-Tu Chen, Caesar E. Ordonez, Oscar H. Kapp, John Sosnowski, and Robert N. Beck</i>	
II-2.	Miniature Gamma Camera	32
	<i>Nicholas J. Yasillo, Robert N. Beck, Chin-Tu Chen, and Malcolm Cooper</i>	

III. QUANTITATIVE METHODS OF EVALUATION

III-1.	Methodology for Evaluation of Diagnostic Performance	35
--------	--	----

IV. KNOWLEDGE TRANSFER: EDUCATION IN QUANTITATIVE NUCLEAR MEDICINE IMAGING

IV-1.	HyperCard Stacks for Nuclear Medicine	38
	<i>Robert N. Beck, Robert Mintzer, Erma M. Peterson, Claude J. Ortega, Chin-Tu Chen, and Malcolm Cooper</i>	
IV-2.	Video Productions for Nuclear Medicine	38
	<i>Robert N. Beck, Claude J. Ortega, Chin-Tu Chen, and Malcolm Cooper</i>	

PROJECT I-1

SPECT RECONSTRUCTION ALGORITHMS FOR CONVERGING HOLE AND ASTIGMATIC COLLIMATORS

Project Leader: Donald Gunter

Annual Progress Report

One of the problems posed by the astigmatic collimator is an accurate and effective description of its imaging properties. Since the image of an object can change drastically with its position relative to the collimator, the traditional method of describing a collimator in terms of its resolution and sensitivity is inadequate and must be extended to include the effects of source position. We have developed the generalized collimator transfer function (GCTF) to describe the non-stationary effects of collimator hole pattern on imaging¹. This concept is ideally suited to deal with the non-stationary effects of convergent and astigmatic collimation.

The performance of a stationary imaging system can be described mathematically in terms of its point source response function (PSRF). The PSRF describes the image resulting from a point source located anywhere in front of the camera. The underlying assumption is that if the image of a point source is known, then the image of any extended source distribution can be reconstructed by convolution of the point source response function with the extended source distribution. The geometry of the point source imaging process is illustrated in Figure I-3.1-1.

Figure I-3.1-1

A point source is located at a height z above the point $\vec{s}$ in the imaging plane. (Throughout this section, symbols with arrows above them will denote vectors in the two-dimensional imaging plane.) Thus, the source position is uniquely determined in space by the three-dimensional vector $(\vec{s}, z)$. The image produced by this point source is described by a count density at each location $\vec{x}$ in the two-dimensional imaging plane, where an arbitrary point in the imaging plane is described by the vector $\vec{x}$. For stationary systems the imaging process is assumed to be shift-invariant; that is, the imaging process depends only on the relative positions of $\vec{s}$ and $\vec{x}$.

Consequently, the relative position vector, $\vec{r} = \vec{x} - \vec{s}$, is particularly useful for describing stationary imaging systems. This relative position vector, $\vec{r}$, gives the separation between the point of imaging, $\vec{x}$, and the point $\vec{s}$ directly beneath the source. The assumption of shift-invariance means that the PSRF is a function of only two variables, $\vec{r}$ and z . However, our goal is to analyze systems that are not necessarily shift-invariant. In order to accommodate such systems, we introduce the generalized point source response function (GPSRF). The GPSRF is defined in exactly the same way as the usual PSRF, except that it is allowed to be a function of the source position $\vec{s}$. Thus, the GPSRF is a function of the variables $\vec{s}$, z , and $\vec{r}$; namely, $g(\vec{r}, \vec{s}, z)$ where

$$g(\vec{r}, \vec{s}, z) = \frac{\left[(\# \text{ counts detected} / \text{cm}^2) \text{ at point } (\vec{r} + \vec{s}) \text{ in the imaging plane} \right]}{\left[(\# \text{ counts emitted}) \text{ at point } (\vec{s}, z) \right]} \quad (\text{I-3.1-1})$$

Like the PSRF, the GPSRF has units of cm^{-2} and is a non-negative real function. When $g(\vec{r}, \vec{s}, z)$ does not depend upon the source position $\vec{s}$, it reverts back to the normal PSRF. The importance of the GPSRF cannot be overestimated; it contains all of the information necessary to describe any imaging process, including such effects as the collimator hole pattern, the focusing properties of convergent collimator holes and the finite field of view of the camera.

The transfer function of the conventional PSRF is just the Fourier transform with respect to the relative position $\vec{r}$ in the image. The distinguishing feature of the GPSRF is that it depends upon two vectors; $\vec{r}$ and $\vec{s}$. As a result, the transfer function associated with the GPSRF requires Fourier transformations with respect to both of the vectors $\vec{r}$ and $\vec{s}$. We have called this Fourier transform the Generalized Transfer Function (GTF), G ;

$$G(\vec{v}, \vec{\omega}, z) = \int \vec{d}^2 \vec{r} \int \vec{d}^2 \vec{s} \ g(\vec{r}, \vec{s}, z) \exp[-2\pi i(\vec{v} \cdot \vec{r} + \vec{\omega} \cdot \vec{s})] \quad (\text{I-3.1-2})$$

where the two (spatial) frequency vectors, $\vec{v}$ and $\vec{\omega}$, are dual to the $\vec{r}$ and $\vec{s}$ vectors, respectively. The GTF has units cm^2 which differs from the usual transfer function which is dimensionless.

If the GPSRF is shift-invariant [that is, $g(\vec{r}, \vec{s}, z)$ is independent of $\vec{s}$], then

$$\begin{aligned} g(\vec{r}, \vec{s}, z) &= f(\vec{r}, z) \\ G(\vec{v}, \vec{\omega}, z) &= F(\vec{v}, z) \delta^2(\vec{\omega}) \end{aligned} \quad (\text{I-3.1-3})$$

where f is the conventional PSRF and F is the conventional transfer function. The transfer function F is dimensionless, while the delta function, $\delta^2(\vec{\omega})$, has units cm^2 ; so that G has units cm^2 as it should. The GTF is a complex valued function of the real variables $(\vec{v}, \vec{\omega}, z)$.

One of the major reasons for introducing the concept of transfer functions is the simple relation that the transfer function provides between the image spectrum, $I(\vec{v})$, and the spectrum of the source distribution within the object, $O(\vec{\omega}, z)$, which produces that image. That simple relation results from the fact that a shift-invariant image is a convolution integral of the source distribution with the point source response function. However, when the assumption of shift-invariance is dropped, this relationship between object and image is no longer a simple convolution integral. The explicit relation between the image $i(\vec{x})$ and the source distribution $o(\vec{s}, z)$ within the object is

$$i(\vec{x}) = \int_{-\infty}^{\infty} d^2\vec{s} \int_{-\infty}^{\infty} dz \, o(\vec{s}, z) g(\vec{x}-\vec{s}, \vec{s}, z) \quad (\text{I-3.1-4})$$

which is a complicated integral over the source distribution, and not necessarily a convolution integral. The GPSRF appears in the integral as a "propagator" which determines the probability that an emitted photon will reach the image. The image function $i(\vec{x})$ has units of counts per cm^2 , while the source distribution has units of emissions per cm^3 , and the GPSRF has units of cm^{-2} . (For most applications the source distribution is expressed in emissions per second per cm^3 ; however, for simplicity of notation we have incorporated the time of exposure into the source distribution.) The Fourier transform of the image $i(\vec{x})$ can be taken to give the image spectrum;

$$I(\vec{v}) = \int_{-\infty}^{\infty} d^2\vec{x} \, i(\vec{x}) \exp[-2\pi i(\vec{v} \cdot \vec{x})] \quad (\text{I-3.1-5})$$

Similarly, the Fourier transform of the source distribution $o(\vec{s}, z)$ gives

$$O(\vec{\omega}) = \int_{-\infty}^{\infty} d^2\vec{x} \, o(\vec{x}, z) \exp[-2\pi i(\vec{\omega} \cdot \vec{x})] \quad (\text{I-3.1-6})$$

the spectrum of the object being imaged. Using these definitions in equation (I-3.1-4), we get the relation

$$I(\vec{v}) = \int_{-\infty}^{\infty} d^2\vec{\omega} \int_{-\infty}^{\infty} dz \, O(\vec{\omega}, z) G(\vec{v}, \vec{v}-\vec{\omega}, z) \quad (\text{I-3.1-7})$$

between the image spectrum and the object spectrum. Equation (I-3.1-7) describes the imaging process in the (spatial) frequency domain and has the same structure as equation (I-3.1-4) which describes the imaging process in the spatial domain. However, if we assume shift-invariance and use the expressions in equations (I-3.1-3), then equation (I-3.1-7) can be significantly simplified to give

$$I(\vec{v}) = \int_{-\infty}^{\infty} dz \, O(\vec{v}, z) F(\vec{v}, z) \quad (\text{I-3.1-8})$$

where one of the integrals has disappeared due to the $\delta^2(\vec{\omega})$ in equation (I-3.1-3). This explains the utility of standard transfer functions in the analysis of stationary imaging processes. It also explains why the generalized transfer function has not appeared particularly useful in the past. Unless the imaging process is shift-invariant, the description of the imaging process in the spatial domain given by equation (I-3.1-4) is just as simple as the description in the frequency domain given by equation (I-3.1-7) -- but equation (I-3.1-4) has the advantage of being more intuitively clear. The reason why the generalized transfer function now appears useful is that (at least) two applications have arisen in which the non-stationary nature of the imaging process cannot be ignored, and in which the GTF provides an easy method of evaluating the imaging process. One of these applications is the evaluation of collimator hole pattern in the diagnostic images of nuclear medicine. The other application is in the algorithms used for SPECT reconstruction; in particular, algorithms for convergent, divergent, or

astigmatic collimators. The use of the GTF in reconstruction algorithms is the subject of ongoing research.

The formal definitions given above are made more comprehensible by examining the generalized transfer functions of a few idealized point source response functions. In Table I-2 #1, nine idealized collimators are described using analytic models; and the associated generalized transfer functions are exhibited. In each of these collimators a term $\theta(z)$ has been dropped from both the GPSRF and the GTF. This $\theta(z)$ term asserts that a camera only records sources located in front of the collimator, and has been dropped only to condense the table. The first five entries in the table are all shift-invariant collimators and could be described accurately with the conventional point source response function. There is really no need to use the full generalized transfer function in these cases except to illustrate the principles involved. The first entry has already been stated in equation (I-3.1-3). It demonstrates the simple property that when the GPSRF (f) is shift-invariant, the GTF is given by the conventional transfer function F multiplied by a delta function $\delta(\omega)$. The first five collimators are all of this form. The second entry represents the pathological case when no collimator is used. The third entry is a completely unphysical collimator model representing "perfect resolution" with a delta function response function. This model is used extensively in the derivation of reconstruction algorithms (e.g. the Radon transform in SPECT), even though it involves the physically unreasonable assumption of perfect camera resolution. The fourth collimator listed in the table is an idealized Gaussian collimator which attempts a more realistic representation of collimator performance by including a fixed resolution parameter σ . The fifth collimator is an even more realistic approximation of actual collimator performance; it represents a collimator response function with a Gaussian shape which widens as the source is moved away from the imaging plane. The parameter α is an opening angle which determines how rapidly the PSRF spreads as the source recedes. None of the remaining four collimators in the table are shift invariant; and consequently, all require a GPSRF to be properly described. The sixth and seventh entries in the table describe collimators which have only a finite field of view. The sixth row represents a collimator with a general (shift-invariant) PSRF f , but which is truncated so that no counts are detected outside a finite radius R . The finite radius of the camera is introduced by the θ function. As a result of this term, a source which is shifted too far from the center of the collimator will no longer be visible. This relatively minor modification destroys the shift-invariance; and as a result, the $\delta(\omega)$ term is replaced by a more complicated expression involving the first order Bessel function J_1 and the radius of the camera face R . It is significant that in the limit as the camera radius R goes to infinity, the Bessel function term becomes a delta function and the GTF reduces to the standard form presented in the first entry of the table. The seventh row represents the most physically realistic model in the table. It combines the finite field of view described by the sixth row with the angular Gaussian collimator described in the fifth row to give a reasonable model of both the collimator resolution and finite camera radius. The last two entries in the table represent collimators which cannot be described by a conventional PSRF because they exhibit a complete lack of shift-invariance. The eighth row describes an idealized model of the pinhole camera. A pinhole camera is almost the antithesis of a shift-invariant imaging system since the motion of a source shifts the image position in the opposite direction. Yet despite this fact, pinhole cameras are often useful in imaging systems for which the sensitivity is not a major concern. In this idealized model the pinhole is located a distance z_F above the origin ($\vec{s}=0$) and has radius R . The GPSRF of the pinhole collimator is constructed from four terms: the πR^2 term which gives the area of the pinhole, the ϕ term which gives the flux through the hole from the point source, the θ term which assures that the source is in front of the hole, and finally the δ^2 term which determines where the point source appears in the image. Because the δ^2 and ϕ terms are easily Fourier transformed, the GTF is easily found from the previous entries. The final entry in the table represents a convergent hole collimator. This model assumes that all the holes of the collimator are focused on the point a distance z_F above the origin ($\vec{s}=0$) in the imaging plane, and that as a consequence, the central peak of the GPSRF occurs at the point $[z_F \delta / (z_F - z)]$. The distribution is assumed to have a

Name	Parameters & Notation	Generalized Point Source Response Function (GPSRF) (cm ⁻²)	Generalized Transfer Function (GTF) (cm ²)
General Shift-Invariant Collimator	f = PSRF F = Transfer Function	$f(\vec{r}, z)$	$F(\vec{v}, z) \delta^2(\vec{\omega})$
No Collimator	None	$\phi(\vec{r}, z) = \frac{z}{4\pi} \left[\frac{z^2 + \vec{r} ^2}{r^2} \right]^{3/2}$	$\frac{1}{2} \exp \left[-2\pi z \left \frac{\vec{v}}{v} \right \right] \delta^2(\vec{\omega})$
Idealized Delta Function Collimator	\$ = Sensitivity	$\$ \delta^2(\vec{r})$	$\$ \delta^2(\vec{\omega})$
Idealized Gaussian Collimator	\$ = Sensitivity σ = Gaussian Width Parameter	$\frac{\$}{\pi \sigma^2} \exp \left[-\frac{ \vec{r} ^2}{2 \sigma^2} \right]$	$\$ \exp \left[-\pi \sigma^2 \left \frac{\vec{v}}{v} \right ^2 \right] \delta^2(\vec{\omega})$
Angular Gaussian Collimator	\$ = Sensitivity α = Opening Angle	$\frac{\$}{\pi z \tan^2 \alpha} \exp \left[-\frac{ \vec{r} ^2}{2 z^2 \tan^2 \alpha} \right]$	$\$ \exp \left[-\pi z^2 \tan^2 \alpha \left \frac{\vec{v}}{v} \right ^2 \right] \delta^2(\vec{\omega})$
Finite Field of View Collimator	f = PSRF F = Transfer Function R = Radius of the camera	$f(\vec{r}, z) \theta(R - \vec{s} + \vec{r})$	$\pi R^2 \frac{J_1(2\pi R \vec{\omega})}{\pi R \vec{\omega} } F(\vec{v}, \vec{\omega})$
Finite Field of View Angular Gaussian Collimator	\$ = Sensitivity α = Opening Angle R = Radius of Camera	$\frac{\$}{\pi z \tan^2 \alpha} \exp \left[-\frac{ \vec{r} ^2}{2 z^2 \tan^2 \alpha} \right] \theta(R - \vec{s} + \vec{r})$	$\$ \pi R^2 \frac{J_1(2\pi R \vec{\omega})}{\pi R \vec{\omega} } \exp \left[-\pi z^2 \tan^2 \alpha \left \frac{\vec{v}}{v} \right ^2 \right]$
Idealized Pinhole Collimator	R = radius of the pinhole z_p = height of the pinhole above $s=0$ in the imaging plane $R \ll z_p, R \ll z - z_p$	$\pi R^2 \phi(\vec{s}, z - z_p) \theta(z - z_p) \delta^2 \left(\vec{r} + \frac{z}{z - z_p} \vec{s} \right)$	$\frac{1}{2} \pi R^2 \theta(z - z_p) \exp \left[-2\pi \left (z - z_p) \vec{\omega} - z \vec{v} \right ^2 \right]$
Convergent Gaussian Collimator	σ = Gaussian Width Parameter z_F = Height of the Focal Point above $s=0$ in the imaging plane	$\phi(\vec{r}, z) \exp \left[-\frac{\left[(z - z_F) \vec{r} + z \vec{s} \right]^2}{2 z^2 \sigma^2} \right]$	$\frac{1}{2} \pi \sigma^2 \exp \left[-\pi \sigma^2 \left \frac{\vec{v}}{v} \right ^2 \right] \exp \left[-2\pi \left z \vec{v} + (z_F - z) \vec{\omega} \right ^2 \right]$

Table I-3.1 #1

Gaussian shape with width s . When the source is located at the focal point, the distribution is given by the geometric flux ϕ . Once again, the GTF is easily evaluated using the previous entries for the Fourier transform of ϕ and the Gaussian distribution. The converging hole collimators of this type are of great interest in nuclear medicine for possible applications to SPECT imaging and reconstruction algorithms. The convergent holes allow for increased sensitivity for small source distributions. But at present almost all the reconstruction algorithms are based on the idealized delta function collimator (in the third row of the table) which is shift-invariant. Since it is very difficult to even describe the imaging properties of a converging hole collimator without the GPSRF, we expect that the GPSRF and the GTF will play a significant role in the development of reconstruction algorithms for such non-stationary imaging systems.

During the past year we have applied the GPSRF to generate SPECT images of analytical phantoms constructed as a collection of Gaussian source distributions. Figures I-3.1 #2 and #3 show the planar images generated from a source composed of six overlapping Gaussian and viewed from two different camera positions rotated by approximately 90 degrees. This work has been submitted for presentation at the October 1992 IEEE meeting.

Figure I-3.1 #2

Figure I-3.1 #3

Submitted for presentation and publication:

Gunter, D. L. and Yu, X., "Simulation of SPECT Imaging with Converging-Hole Collimators," *IEEE Trans. Nucl. Sci.* submitted April 1992.

F. Literature Cited

- 1 R. N. Beck and D. L. Gunter, "Collimator Design Using Ray-Tracing Techniques," *IEEE Trans. Nucl. Sci.* NS-32, 865-869, 1985.

PROJECT I-2

UTILIZATION OF SCATTERED RADIATION IN SPECT RECONSTRUCTION

Donald Gunter

Progress Report - 1992

During the last four years we have worked extensively on an algorithm, first proposed by Don Gunter in 1983, to reconstruct the source distribution within a scattering medium from a single point of view. The fundamental idea is that images formed in various energy windows off the emission peak are a result of scattering within the body. The amount and distribution of this scattered radiation varies with the depth of the source. By comparing the images in numerous energy windows we attempted to reconstruct the source activity as a function of depth; that is, we converted the energy information into depth information and, thereby, generated the 3-dimension source distribution. All of this was done without moving the camera. Our initial results four years ago using a linear reconstruction algorithm were very disappointing. Although two channels of source depth information were recovered from the scattered radiation, the reconstruction algorithm produced a significant degradation in the resolution within the imaging plane. This loss of spatial resolution in the imaging plane made the algorithm unacceptable.

Three years ago we developed a new nonlinear algorithm which solved this problem. The solution involved coupling the information about source depth which is available only in the low spatial frequencies of the images with the detailed information about the spatial distribution of source which is available in the high spatial frequencies. Basically, the algorithm uses the scattered radiation in the low spatial frequency regime to estimate the source depth, and then uses a simple projection scheme to estimate the high spatial frequency components deep within the scattering medium. Using this algorithm we have found that two (and perhaps) three channels of depth information can be extracted from the scattered radiation generated by a ^{99m}Tc source in water.

The new algorithm does not degrade spatial resolution in the imaging plane, provides depth resolution with standard deviation of 4 cm without requiring any camera motion, and produces significant attenuation correction in the reconstructed source distribution. Although this depth resolution is still quite modest, the technique has the potential for significantly better quantitation when combined with standard SPECT reconstruction algorithms.

The performance of the new algorithm is illustrated in Figures I-3.3 #1-#3 on the next page. Figure I-3.3 #1 shows a phantom composed of four point sources imbedded in a water bath. The sources are shown as dark points within cylindrical ROIs which project vertically into the water. The point sources are located at depths 0.5, 4.5, 8.5 and 12.5 cm in the water. Figure I-3.3-#2 shows the source distribution reconstructed by the new algorithm for the phantom shown in Figure I-3.3-#1. The density of points in Figure I-3.3-#2 is proportional to the reconstructed source density. Figure I-3.3-#3 shows the reconstructed source density as a function of depth in the 4 ROIs.

The lack of depth resolution for deep sources means that the algorithm is not very useful when only one point of view is used for imaging. However, when even limited depth information is added to the normal backprojection techniques used in SPECT reconstruction, we believe that there will be a significant improvement in imaging quality and in quantitation. Our current goal is to incorporate this scattered radiation into SPECT reconstruction by using multiple energy channels to estimate source depth prior to backprojection.

Our analysis of the scattering kernels revealed a special relationship between certain depth distributions and energy spectra. Figures I-3.3-#4 through I-3.3-#7 illustrate this relationship explicitly. In Figures I-3.3-#4 and I-3.3-#5 we display a special depth distribution and the energy spectrum associated with that distribution that we have called 'channel #1'. The depth distribution is almost flat; that is, the source is distributed equally to all depths. And the energy

spectrum associated with that depth distribution is sharply peaked at the photoemission peak (140 keV); which is precisely the energy window one would associate with normal SPECT imaging. Indeed, SPECT reconstruction is normally performed using channel #1 exclusively. However, our research found a second channel of information which can be used to ascertain source depth. Channel #2 is shown in Figures I-3.3-#6 and I-3.3-#7. The depth distribution shown in Figure I-3.3-#6 is positive for shallow sources ($<4\text{cm}$) and negative for deep sources ($>4\text{cm}$). The energy spectrum associated with this depth distribution is positive above the photoemission peak and negative below the peak. Thus, scattered radiation (below the photoemission peak) produces a negative response in channel #2, and forces the source distribution deeper (as it should).

Figure I-3.3-#1 Source Distribution of a Four Point-Source Phantom with 4 ROI's indicated.

Figure I-3.3-#2 The Reconstructed Source Distribution produced by the new algorithm.

Figure 3. Source density as a function of depth in the four Regions Of Interest.

Figure I-3.3-#3

I

In normal SPECT reconstruction, the planar images are produced from the energy spectra shown in Figure I-3.3-#5. These images are then backprojected using the (uniform) depth distribution shown in Figure I-3.3-#4. In this proposal, we wish to use the information provided by channel #2. The most naive method to use channel #2 is to create planar images using the energy spectrum shown in Figure I-3.3-#7, and then backproject using the depth distribution shown in Figure I-3.3-#6. This strategy has one major flaw; depth equal to zero occurs at the surface of the body. Consequently, one must know the surface of the body to implement the algorithm. We are currently examining methods of determining the body surface and incorporating this information into the reconstruction.

Figure I-3.3-#4. Depth Distributions associated with Channel #1.

Figure I-3.3-#5. Energy Weighting Functions associated with Channel #1

Figure I-3.3-#6. Depth Distributions associated with Channel #2

Figure I-3.3-#7. Energy Weighting Functions associated with Channel #2

F. Literature Cited

1. D. L. Gunter, K. R. Hoffmann and R. N. Beck, "Three-Dimensional Imaging Utilizing Energy Discrimination I," *IEEE Trans. Nucl. Sci.* **NS-37**, 1300-1307 (1990).

During the past year two publications have been appeared which document this research:

2. D. L. Gunter, "Three-Dimensional Imaging Utilizing Scattered Radiation," *Conference Record of the 1991 IEEE Nuclear Science Symposium and Medical Imaging Conference, November 2-9, 1991, Santa Fe, New Mexico, USA*, 1948-1952, 1991, and
3. D. L. Gunter, "Three-Dimensional Imaging Utilizing Energy Discrimination. II," *J. Opt. Soc. Am.* **A9**, 903-923, 1992.

PROJECT I-3
INVESTIGATION OF FUNDAMENTAL CHARACTERISTICS OF SPECT

Project Leader: John N. Aarsvold

Chin-Tu Chen and Donald L. Gunter

This project was not pursued because of the budgetary constraint. It will be pursued in the future when funding or other support becomes available.

PROJECT I-4

ENERGY-DEPENDENT SCATTER CORRECTION IN PET

Project Leader: Caesar E. Ordonez

Chin-Tu Chen, Robert N. Beck, and K. L. Matthews

A. Introduction

In conventional PET imaging, energy discrimination is implemented during data acquisition. Energy discrimination is done by setting lower- and an upper-cutoff values for energies of photons to be accepted as "good" events. The acquisition-energy window is set to a range that is narrow enough to reject as much scattered photons as possible, but at the same time wide enough to provide acceptable total tomograph sensitivity. In general, the energies of scattered photons are lower than the photopeak energy (511 keV). In this "one-window" acquisition mode, no distinction is made between unscattered and scattered photons, although the energy information is available to distinguish between the two.

We propose to utilize this additional information in the following manner. Instead of using a single energy window, we use a number of smaller energy sub-windows. In the simplest case, we can divide the energy spectrum of each photon into two sub-windows: a region around the photopeak, and a scatter window. Coincidence data will then naturally fall into one of four possible energy combinations: photopeak-photopeak, scatter-scatter, photopeak-scatter, and scatter-photopeak. Thus, it might be possible to isolate the scatter component by using multiple-energy windows.

B. Theoretical development

We denote by $H(\mathbf{x}, \mathbf{y}; E_1, E_2)$ the scatter distribution function (SDF) associated with a line or point source located at $\mathbf{y}$. Let E_1 and E_2 represent the energies of the two coincident photons. The explicit dependence on the location of the line or point source indicates that the SDF is in general not shift-invariant. In an extended distribution, each source location will have an associated scatter response. The scatter component can be estimated via the following integral equation:

$$S(\mathbf{x}; E_1, E_2) = \int P(\mathbf{x} - \mathbf{y}; E_1, E_2) H'(\mathbf{y}; E_1, E_2) d\mathbf{y}, \quad [\text{Eq. 1}]$$

in which $P(\mathbf{x}; E_1, E_2)$ denotes the measured projection data. The true coincidence component can then be obtained by subtracting the estimated scatter component from the measured data, i.e.,

$$T'(\mathbf{x}; E_1, E_2) = P(\mathbf{x}; E_1, E_2) - S(\mathbf{x}; E_1, E_2). \quad [\text{Eq. 2}]$$

Finally, the scatter-corrected data for the full data set are then constructed by adding up all the true coincidences in all energy subsets, i.e.,

$$T(\mathbf{x}) = \sum \sum T'(\mathbf{x}; E_1, E_2), \quad [\text{Eq. 3}]$$

in which the sums are carried over the energies E_1 and E_2 .

The method we propose has the advantage of utilizing the additional information provided by energy dependence of the scatter distribution function. Equation (1) indicates that the amount of scatter events estimated should also exhibit some form of energy dependence. This is reasonable: we expect to subtract more scatter events in the low-energy sub-windows than sub-windows close to the photopeak. Therefore, the correction method outlined above should, in principle, more accurately compensate for scatter by subtracting the proper fractions of scatter in the appropriate places.

C. Software development for simulation studies

We have written a C-version of a FORTRAN simulation package (SCAT2) developed in our laboratory, making modifications for handling input of medium material and atomic data. The new package, LIBSIMC [30], currently runs on the following workstations: IBM RS/6000 (IBM AIX), DECstation 3100 and 5000 (ULTRIX), and VAXstation 3100 (VAX/VMS and VAX/ULTRIX).

We have used LIBSIMC to model uniform distributions of activity, line sources in water-filled cylindrical phantoms, and point sources in water-filled spherical phantoms. All the possible photon-atom scattering interactions have been taken into account, but positron range and photon-pair non-collinearity have not been included.

The simulation output is stored directly onto 8 mm data tape in a standard format. Each tape holds up to 2.3 gigabytes of information. The following parameters are saved for each event: source position (3 words), initial direction of emitted photon (3 words), exit positions, directions, and energies of both photons (14 words), and the numbers of interactions experienced by both photons (2 words). Each tape can store about 48.5 million events. Additional storage is required if positron range (3 words) and photon-pair non-collinearity (3 words) effects are included, in which case only about 38 million events can be stored on each tape.

An "event" can either be a coincidence or a singles event. There is an option of storing one or both types of events. Saving both coincidence and singles events is useful in investigating tomograph count rate capabilities and sensitivity performances. At the present time, there is no user interface available for modifying object distributions: one has to be coded for each case considered.

As a preliminary step to studying the scatter distribution function, we have used a simulated line source in a water-filled cylindrical phantom to generate two-dimensional energy spectra of detectable coincidence photons. No explicit modeling of the detection system has been done, except for the effects of finite energy resolution which was taken to be 25% for all energies. The spectra exhibit strong energy-dependence, and show a very natural separation of events corresponding to true (both photons unscattered) and scattered (one or both photons scattered one or more times) events.

On the fastest workstation in our laboratory (IBM RS/6000 Model 730), the simulation of a 20-cm diameter by 13.2-cm axial length cylindrical phantom required 50 hours to generate roughly 20 million coincidences (no singles), all detectable by a cylindrical tomograph 60 cm in diameter and 15 cm in axial extent.

PROJECT I-5

COMPENSATION FOR PHOTON ATTENUATION IN PET

Project Leader: Chin-Tu Chen

C. E. Ordonez and Xiaolin Yu

A. Image registration

CT/MR and PET images usually are not in registration spatially because of differences in the imaging setup. Table 1 compares CT, MR and PET imaging parameters that are used regularly for brain studies in our institution. In addition, because the patient orientations in CT/MR and PET scanners are not the same, slice centers are positioned differently relative to the patient's anatomy.

	CT	PET VI	MR
Matrix Size	256x256	100x100	256x256
Pixel Size	0.9-1.1 mm	2.7 mm	0.9-2.34 mm
Slice Thickness	2-8 mm	14 mm	2-8 mm
# of Slices	15-25	5	15-100
Gantry Angle	17-20°	0	0

Table 1. Comparison of CT, MR, and PET imaging parameters.

For application of the new idea of using structural information from CT or MR images in PET image reconstruction for attenuation correction, image registration is required as a first step so that one can obtain a corresponding anatomic map for any selected PET image plane. We chose to use the surface-matching technique developed in our laboratories for image registration because this method is retrospective and accurate. After the PET and CT/MR scans are registered, we reslice the CT/MR images along the planes of the PET images. The differences in slice thickness and slice separation, as well as in image resolution between various image modalities are to be considered.

B. Derivation of attenuation maps from CT images

The pixel densities of CT images are a function of the attenuation coefficients of tissues at the X-ray energies used for CT. In order to obtain the attenuation coefficient maps for PET images by using the resliced CT images, we need to consider the difference in the characteristics of X-ray beams for CT and the photon energy for PET. The CT images that we use are produced by a broad spectrum of X-ray energies generated at 125 kVp. The X-ray beam is heavily filtered and has a half-value layer of 6 mm of aluminum. The mean effective energy is about 70 keV. In PET, annihilation photons for coincidence detection have a monochromatic energy of 511 keV.

The CT images that we normally see in clinical applications are histogram-equalized images because of the need to show subtle differences in attenuation coefficient in various tissues. The pixel intensities of the original CT image are proportional to the attenuation coefficients of various tissues. Differences in attenuation coefficients of various brain tissues are very small; therefore, the original CT image without any histogram equalization is almost uniform within the brain tissue. We use the histograms of the resliced CT structural templates to study the distribution of pixel values for brain tissues and bone. The attenuation coefficient

maps at 511 keV for PET are produced after rescaling of the pixel intensities by consideration of the energy difference between CT and PET.

When the correlated CT structural templates and the rescaled CT attenuation coefficient maps for 511 keV for PET are compared, the latter have less contrast; this corresponds to the much higher photon energy used in PET (1, 2).

C. Derivation of attenuation maps from MR images

MR images represent signals that are fundamentally different from the attenuated radiation in the case of X-ray CT. Pixel intensity in MR images is based on the combination of tissue-related parameters, which include hydrogen proton density, spin-lattice relaxation time T1, and spin-spin relaxation time T2. The specific type of RF pulse sequence used in generating a particular MR images determines the weight of each parameter in pixel intensities representing that combination. Because of the multiparameter characteristics of MR images, we cannot obtain attenuation information on various tissues directly from these images. Yet, because the attenuation coefficients are almost uniform within the brain and the value of attenuation coefficients are known, we can use the well-accepted assumption that attenuation within the brain is uniform to derive attenuation coefficient maps from the structural information in MR images.

When MR images are used, we delineate regions of brain tissue and bone by employing segmentation schemes. New pixel intensity values that are assigned to these regions are equal to the corresponding known values of attenuation coefficients. The pixel densities of MR images are, therefore, transformed into attenuation coefficients in regions of bone and brain tissue.

D. PET image reconstruction

Emission imaging with positron annihilation requires compensating for the attenuation effect in image reconstruction. The probability of two annihilation photons being detected is described by

$$\text{Probability} = \exp \left(\int -u(s) ds \right),$$

where $u(s)$ are the attenuation coefficients and the line integral of the attenuation coefficients is along the ray that two photons travel. To derive the quantitative regional physiologic or functional information and to reconstruct PET images accurately from the measured data, one should correct the measured emission projection data by dividing these data by the above probability function which represents the effect of attenuation.

When PET transmission images are used for attenuation correction, the measured emission projection data are divided by the measured transmission projection data, which are normalized to a set of transmission measurements without the subject in place. The final emission image corrected by the transmission projection data contains noise from both the measured emission projection data and the measured transmission projection data.

The equivalent attenuation coefficient maps for 511 keV photon energy which are derived from either CT or MR images are almost noise-free compared to PET transmission images. These maps are reprojected to produce the probability functions for each PET emission projection profile. PET emission images are then reconstructed from the attenuation corrected projection profiles with the standard filtered backprojection algorithm.

When PET images corrected by the PET transmission image are compared to those corrected by the rescaled CT attenuation coefficient maps, the latter exhibit higher image contrast than do the former (1, 2). The same conclusion can be drawn from studies involving the spatially correlated MR images.

E. Evaluation of improvement

The ratio of the percentage standard deviation (% SD) and image contrast of regions of interest (ROIs) at the same locations of two images were evaluated. For a PET image corrected by the PET transmission image, compared to the PET image of the same slice corrected by the CT image shown on the images of Fig.4, from left to right, the range of ratios of % SD is 1.02 to 1.10, 1.10 to 1.30, 1.30 to 1.50, and above 1.50 (1, 3). Similar results were obtained for a PET image corrected by the PET transmission image as compared to the corresponding PET image corrected by the MR image. The ratio of image contrast of an ROI in the grey matter to that in the white matter of a PET image corrected by the rescaled attenuation coefficient maps derived from the CT or MR images is about 30% higher than that of an image corrected by the PET transmission image (2, 3).

The initial results from a brain study showed that the new approach can eliminate the need for the acquisition of PET transmission scans and improve image contrast with significant reduction in the noise level. The method potentially can be extended to applications involving other parts of the body as well.

F. Recent related publication and presentation

1. Yu, X., Chen, C.-T., Bartlett, R., Pelizzari, C.A., and Ordonez, C.E.: Using correlated CT images in compensation for attenuation in PET image reconstruction. Presented at the SPIE's Optical Engineering Midwest Conference, September 27-28, 1990, Chicago, Illinois, USA, In: *Proceedings of SPIE Conference*, Vol. 1396:56-58, 1990.
2. Yu, X., and Chen, C.-T.: Compensation for the effect of photon attenuation in PET with the use of the correlated structural images. Presented at the 76th Scientific Assembly and Annual Meeting of the Radiological Society of North America, *Radiology* 177(P): 169, 1990.
3. Yu, X., and Chen, C.-T.: Applying correlated CT and MR images of the brain in compensation for attenuation in PET image reconstruction. Presented at the 33rd Annual Meeting of AAPM, July 21 - 25, 1991, San Francisco, California, *Med Phys* 18(3):649, 1991.

PROJECT I-6

IMPROVING THE UTILIZATION OF DETECTOR MOTION IN PET

Project Leader: Miles N. Wernick

Chin-Tu Chen and Caesar E. Ordonez

A. Progress summary (7/15/91-7/14/92)

We first proposed a superresolution concept for PET in our DOE renewal application of last year. Since then, we have implemented the technique in software and have performed several simulation studies that demonstrate the potential value of the proposed method in substantially improving the image quality obtainable by PET. The fundamentals of the approach and initial simulation results were reported in a paper to appear later this year in *Journal of the Optical Society of America A*. In subsequent publications and presentations we described various extensions of the method and showed that the superresolution method was robust to various misspecifications of the system spatial response functions which are inevitable in a practical implementation.

In February of this year, two of us (Wernick and Chen) filed an application with the U.S. Patent Office entitled, "Method for Recovering Signals in Tomographic Measurement Systems," in which we describe various configurations of the superresolution approach as it applies generally to tomographic imaging systems. Various kinds of detector system motions were considered as well as various configurations of the algorithm. The methods described may be useful in a number of situations, but the preferred embodiment detailed in the application refers to the use of signal recovery to exploit the extra information reported by a wobbling PET system.

In the past year, we began collaborations on fundamental signal recovery issues relating to this project with Dr. Henry Stark, Chairman of the Electrical Engineering Department at the Illinois Institute of Technology (IIT). Dr. Stark is recognized in the electrical engineering field for his work in image restoration and reconstruction. Funding for our collaborative work has not been requested from the DOE; however, basic results obtained in those efforts, regarding convex projections and the wavelet transform, are expected to be very valuable to this project.

B. Preliminary results

In PET, the measurements obtained by the imaging system are typically used to form a matrix of projection values (sinogram), from which the image is reconstructed, most commonly by the method of filtered backprojection. To facilitate the reconstruction step, the sinogram is usually defined as a uniform rectangular array of values that represent uniformly spaced points in a polar coordinate system. In traditional processing schemes, the non-uniformly spaced samples provided by the imaging system are assigned to the uniform grid points of the sinogram in a process known as gridding or rebinning.

In PET, tomographic projection measurements are made by pairs of detector elements, typically oriented in a ring. In conventional rebinning methods, the gamma-ray emissions observed by a pair of detectors are assumed to have taken place along the infinitesimal line segment connecting the centers of the detectors. Polar coordinates describing the orientation of that line segment are used to associate the observed gamma-ray counts to a grid point in the sinogram. When the exact coordinates correspond to a location that falls between grid points, interpolation is usually used to distribute the counts to the nearest elements of the grid. The implicit assumption of this approach to sinogram computation is that the detector elements are of infinitesimal spatial

extent (a particularly bad approximation for PET systems) and that no other blur mechanisms are in effect.

An alternative approach, which forms the basis for the proposed research, is to account for the blur mechanisms inherent to the system by viewing the problem in the context of signal recovery. Each measured value reported by the imaging system is the result of a roughly linear operation and can be described approximately by a linear equation. The set of measurements reported by the imaging system can, therefore, be used to construct a system of linear equations where each equation corresponds to one measurement and each unknown corresponds to the value of a sinogram element. Our initial studies have demonstrated that, where motion of the detection system is feasible, solution of the system of equations produces an estimate of the sinogram that is potentially much more accurate than that obtainable by simple interpolation methods.

The prime importance of detector motion to this approach can be understood in various ways; the following is an intuitive explanation. When the detection system is allowed to move, extra measurements can be obtained. The additional measurements can be used to construct an expanded system of equations which can, in principle, be solved for a larger number of unknowns (the values of the sinogram elements). The possibility of solving for a larger number of unknowns permits the sinogram to be represented on a finer grid, which corresponds to a higher spatial resolution.

In the proposed method, once the projection matrix has been recovered, the image is reconstructed by filtered backprojection. By confining the signal recovery procedure to the creation of the projection matrix, the benefits of signal recovery are obtained while retaining the speed advantage that filtered backprojection offers for the reconstruction step. In initial simulation studies, the proposed method added only a few seconds to the usual time required to produce an image; thus, superresolution is obtained without the prohibitive computational burden normally associated with complex signal recovery procedures.

In the preliminary investigations, a rough model of the PETT VI tomograph was used to test the feasibility of the proposed method in computer simulations. Simulated measurements of a phantom object were computed and Poisson noise was introduced to model the effect of photon statistics. The result of each measurement was then represented by a linear equation, in which the unknown variables represent the values of one projection profile at regularly spaced locations, and the coefficients represent the values of the pertinent spatial response function sampled at the same locations.

Once obtained, the equations were solved by the method of projections onto convex sets (POCS), an iterative signal recovery technique. POCS is a very efficient method for solving sparse systems and has been shown to provide good results in many image restoration and reconstruction problems. In our studies, the introduction of the signal recovery process in place of the traditional rebinning step added only a few seconds to the total time required to produce an image from the raw data.

The results of the superresolution technique for the simulated phantom were quite spectacular – much better than we predicted. The superresolution technique outperformed traditional rebinning by bilinear interpolation at all noise levels. In the idealized noise-free case, the extra information resulting from detector motion proved sufficient to perfectly reconstruct the object. At the other extreme, very promising results were obtained with as few as 50K simulated photoevents.

The equations used in the signal recovery technique make use of the spatial response functions of the imaging system. The initial feasibility studies were produced under the rather unrealistic assumption that the response functions are perfectly known. In reality, there will be a certain amount of inaccuracy in their measured or computed estimates. To simulate the effect of

such misspecifications, we performed an additional study in which we introduced random errors into the widths of the spatial response functions used to recover the sinogram. A data set comprising 1M simulated photoevents was used, and the FWHM of the response functions were randomly varied so that each response function estimate was stretched (or narrowed) by a different amount. The reconstructions obtained were largely unaffected by errors of up to 30% but begin to degrade significantly at the 50% level.

In another study, again using 1M photoevents, the spatial response functions were randomly shifted to simulate the effect of random errors in their positioning. The standard error in the random shifts of the response function estimates from their correct positions ranged from 0mm to ± 5 mm. Again, the results appear to be very robust to reasonable errors in the response function estimates.

Our preliminary studies produced very promising and exciting results. The effects that we expected to pose the most difficulty – noise and response function misspecifications – appear to be less troublesome than we initially supposed. While we do not expect to obtain such extraordinary results in a practical implementation, the simulation results are sufficiently impressive to warrant a thorough investigation of the foundations and applications of this technique.

In our simulations, the incorporation of the superresolution algorithm added only a few seconds to the total time required to reconstruct an image. Thus, it appears to avoid the common criticism that complicated reconstruction methods require unrealistic computation times.

C. Publications and patents related to this project (7/15/91 - 7/14/92)

Patents

M.N. Wernick and C.-T. Chen, U.S. Patent application (pending), "Method for Recovering Signals in Tomographic Measurement Systems," Ser. No. 832,863, filed February 7, 1992.

Publications and presentations

M.N. Wernick and C.-T. Chen, "Superresolved tomography by convex projections and detector motion," J. Opt. Soc. Am. A **9** (1992); in press, scheduled for September issue.

M.N. Wernick and C.-T. Chen, "Superresolution in positron emission tomography," Proc. SPIE **1731** (1992); in press.

M.N. Wernick and C.-T. Chen, "Sinogram resolution recovery using information gained through detector motion", Proc. SPIE **1660** (1992); in press.

M.N. Wernick and C.-T. Chen, "High-resolution PET from low-resolution measurements," Annual Meeting of the Association of University Radiologists, Chicago (1992).

D. Yang, H. Stark, N.P. Galatsanos, M.N. Wernick, and C.-T. Chen, "Fast positron emission tomography and techniques for noise amelioration and resolution enhancement," Technical Digest, O.S.A. Topical Meeting on Signal Recovery and Synthesis, New Orleans (1992).

PROJECT I-7

ITERATIVE IMAGE RECONSTRUCTION IN ECT

Project Leader: Chin-Tu Chen

*Caesar E. Ordonez, Miles N. Wernick, John N. Aarsvold, Donald L. Gunter,
Wing H. Wong, Oscar H. Kapp, Xiaolong Ouyang, Mark Levenson, and Charles E. Metz*

A. Bayesian image reconstruction

A series of preliminary studies has been performed in our laboratories to explore the use of *a priori* information in Bayesian image restoration and reconstruction. One piece of *a priori* information is the fact that intensities of neighboring pixels tend to be similar if they belong to the same region within which similar tissue characteristics are exhibited. This property of local continuity can be modeled by the use of Gibbs priors, as first suggested by Geman and Geman. In their investigation, they also included "line sites" between each pair of neighboring pixels in the Gibbs prior and used discrete binary numbers to indicate the absence or presence of boundaries between regions. These two features of the *a priori* model permit averaging within boundaries of homogeneous regions to alleviate the degradation caused by Poisson noise. With the use of this Gibbs prior in combination with the technique of stochastic relaxation, Geman and Geman demonstrated that noise levels can be reduced significantly in 2-D image restoration.

We have developed a Bayesian method that utilizes a Gibbs prior to describe the spatial correlation of neighboring regions and takes into account the effect of limited spatial resolution as well (1-6, 10, 11, 13-16). The statistical framework of the proposed approach is based on the data augmentation scheme suggested by Tanner and Wong. Briefly outlined here, this Bayesian method is based on Geman and Geman's approach with the following new features:

- (1) *Square-root transformation for photon counts:* We proposed to reparameterize the Poisson intensities by use of their square-roots in order to approximate the likelihood function by a Gaussian likelihood. This approximation greatly simplifies the incorporation of likelihood function with the Gibbs distributions. Reparameterization on the square-root scale also stabilizes the variance for the gamma family of distributions.
- (2) *Continuous values for "line sites":* Geman and Geman proposed to use "line sites," inserted between regular pixel-intensity sites, as indicator variables that take the value zero when the neighboring pixels lie within the same region, and the value one otherwise. In determination of a point estimate of the image, this discreteness of "line site" values causes severe computational difficulties. We proposed to modify the model by employing continuous values in the interval $[0,1]$ for the "line sites" in order to alleviate this problem.
- (3) *Expanded neighborhood systems and incorporation of the effect of limited spatial resolution:* Degraded spatial resolution is one of the most detrimental factors that limit the quality of images. In the context of the incomplete data problem, the effect of limited spatial resolution can be incorporated directly into the probability density functions that describe the relationship between image cells and detector bins. We make the important observation that it is desirable to expand the neighborhood systems beyond the range of the point spread function (PSF) to enhance the edges and to correlate pixels at greater distances that are related because of the limited spatial resolution.

(4) *Iterative conditional averages (ICA) method:* We proposed a variation of the method of iterated conditional modes (ICM) that was suggested by Besag. In this new method, samples are no longer actually drawn from the predictive and posterior distributions. Instead, the mean value of the conditional likelihood at individual sites is iteratively selected until the algorithm converges. As a result, the ICA method requires less time for each iteration and fewer iterations to converge.

(5) *Incorporation of prior information derived from correlated CT and MR images:* We developed new methods that incorporate the prior boundary information derived from the spatially-correlated structural images such as those acquired by CT or MRI (3, 5, 11, 15, 16). ECT images can be registered in 3-D space by employing a surface-fitting technique that was developed previously in our laboratories. Using the coordinate transformation parameters derived from this fitting procedure, anatomical templates that correspond to the functional ECT images can be resampled from the original data set. Boundaries identified in these high-resolution structural images tend to be sharper and more accurate. Incorporation of these prior boundary information into the Gibbs model can provide additional improvements in image quality.

B. Development of software libraries

We have initiated the development of several software packages for simulating PET and SPECT image data, including a module for simulation of interactions of photons with tissues and two modules for generating positron and single-photon imaging data, respectively, of various object configurations.

We have also refined our software library of ML-EM image reconstruction algorithms by implementing the method of sieve and blurring kernels and by incorporating the concept of feasible image and its associated statistical measures. We continue to refine our image reconstruction library of Bayesian methods based on improvements we have made in algorithm developments. These new features include a flexible choice of clique configurations (15, 16), improved iterative schemes for updating both pixel intensity and line site values, improved forms of Gibbs prior for incorporation of prior boundary information (16). In addition, we initiated an investigation of the use of Bayesian approaches for reconstruction of data only with a limited number of projection angles (8, 9).

We have also initiated an effort to investigate systematically several backprojection and forward-projection schemes including line-length interpolation, linear interpolation, nearest neighbor, and area-weighted convolution methods (7). These various methods are also being evaluated for parallel computing implementation.

We have investigated two commercial visual processing libraries, PV-Wave and IDL, for use as the basis for our software development effort. Both packages can be used as object-oriented, high-level programming language, as well as convenient tools for building user interface and graphic interface. We have reached a decision to choose IDL because of its developers' special interest in nuclear medicine applications.

C. Recent related publications

1. Johnson, V.E., Wong, W.H., Hu, X., and Chen, C.-T.: Image restoration using Gibbs priors: boundary modelling, treatment of blurring, and selection of hyperparameters. *IEEE Trans Pattern Analysis and Machine Intelligence* PAMI-13:413-425, 1991.

-
2. Hu, X., Johnson, V.E., Wong, W.H., and Chen, C.-T.: Bayesian image processing for magnetic resonance imaging. *Magnetic Resonance Imaging* 9:611-620, 1991.
 3. Chen, C.-T., Ouyang, X., Wong, W.H., Hu, X., Johnson, V.E., Ordonez, C.E., and Metz, C.E.: Sensor fusion in image reconstruction. *IEEE Trans. Nucl. Sci.* NS-38:687-692, 1991.
 4. Chen, C.-T., Ouyang, X., Ordonez, C., Hu, X., Wong, W.H., and Metz, C.E.: Incorporation of structural CT and MR images in PET image reconstruction. In: *SPIE Proceedings on Medical Imaging V* Vol. 1445:75-77, 1991.
 5. Chen, C.-T., Pelizzari, C.A., Wong, W.H., Levin, D., and Cooper, M.: Sensor fusion in brain imaging. *J Cereb Blood Flow Metab* 11(Suppl.2):S385, 1991.
 6. Hu, X., Chen, C.-T., Ouyang, X., and Wong, W.H.: Improvement of Bayesian reconstruction in positron emission tomography. In: *Proceedings of the 13th Annual International Conference of the IEEE Engineering in Medicine and Biology Society*, pp. 206-207, 1991.
 7. Ordonez, C.E.: Comparison of algorithms for data reprojection in emission computed tomography. In: *Proceedings of the 13th Annual International Conference of the IEEE Engineering in Medicine and Biology Society*, pp. 206-207, 1991.
 8. Kapp, O.H. and Chen, C.-T.: Reconstruction from limited projection data. *SPIE Proceedings* Vol.1660: 1992.
 9. Chen, C.-T., Kapp, O.H., and Wong, W.H.: Stochastic reconstruction of incomplete data sets using Gibbs priors in positron emission tomography. *SPIE Proceedings* Vol. 1660: 1992.
 10. Chen, C.-T., Ouyang, X., Wong, W.H., and Hu, X.: Improvement of medical images using Bayesian processing. *SPIE Proceedings* Vol.1652: 1992.
 11. Chen, C.-T., Cooper, M., Metz, J.T., Chou, J.-S., Ordonez, C.E., Yu, X., Ouyang, X., and Yap, J.T.: Improvement of quantitative analysis of PET data by incorporation of spatially-correlated CT and MR images. In: *Medical Application of Cyclotrons VI*, (L-M Voipio-Pulkki and U. Wegelius, eds.), Medica-Odontologica, Sarja-Ser.D, No. 88, Turun Yliopisto, Turku, Finland, pp. A27-A28, 1992.
 12. Brailean, J.C., Little, D., Giger, M.L., Chen, C.-T., and Sullivan, B.J.: Application of the EM algorithm to radiographic images. *Med Phys* (In press).
 13. Johnson, V.E., Wong, W.H., Hu, X. and Chen, C.-T.: Data augmentation applied to image restoration. In: *The Formation, Handling, and Evaluation of Medical Images* (A.E. Todd-Pokropek and M.S. Viergever, eds.). (In press)
 14. Johnson, V.E., Chen, C.-T., Wong, W.H., and Hu, X.: Reconstruction of PET images by Bayesian data augmentation and Gibbs priors - Part I: Basic framework. (Submitted to *IEEE Trans Med Imaging*).
 15. Ouyang, X., Wong, W.H., Johnson, V.E., Hu, X., and Chen, C.-T.: Reconstruction of PET images by Bayesian data augmentation and Gibbs priors - Part II: Incorporation of prior boundary information. (Submitted to *IEEE Trans Med Imaging*).
 16. Levenson, M., Ouyang, X., Wong, W.H., Johnson, V.E., and Chen, C.-T.: Reconstruction of PET images by Bayesian data augmentation and Gibbs priors - Part III: Improvements in Gibbs prior. (To be submitted to *IEEE Trans Med Imaging*).
-

PROJECT II-1

HIGH-RESOLUTION MULTI-SLICE PET

Project Leader: Nicholas J. Yasillo

Chin-Tu Chen, Caesar E. Ordonez, Oscar H. Kapp, John Sosnowski, and Robert N. Beck

The project to test the feasibility and to initiate the design of a high resolution multi-slice PET system has progressed in the following specific areas:

A. Detector Development and Testing

Under the last DOE contract we obtained small quantities of the necessary components (BGO crystals, light pipes, and photomultiplier tubes), to demonstrate the feasibility of constructing a Multi-Slice, High-Resolution (2.5-3.0 mm) PET system for brain research.

Figure 1. Crystal, Light Guide and Photomultiplier Configuration Drawing

The design we have been developing (Figure 1) uses 2400 BGO crystals, each having dimensions of 3 x 10 x 30 mm in a 4 ring configuration. Each BGO crystal is coupled to a single photomultiplier tube 9.7 mm in diameter. Crystals in the outer 2 rings (ring A and D) are coupled directly to side-mounted photomultipliers which are positioned at 3 different radii depending on crystal position. The inner 2 rings (B and C) of crystals are each coupled to a single photomultiplier through light guides. Light guides of 3 different sizes are used to provide the necessary geometry to couple to the inner-ring phototubes. Radial positioning of the inner-ring photomultipliers is also at 3 different radii, with each adjacent tube staggered tangentially 1/3 its diameter. Using this detector configuration, it will be possible to construct a

brain and small-animal tomograph with a 62.5 cm inner face diameter and a reconstructed field of view of 26 cm in diameter. The axial field of view will be 46 mm spread over 7 slices of approximately 6.5 mm thickness each.

We have evaluated the effects of Compton scattering within BGO crystals having varying physical dimensions by using Monte Carlo techniques and will use these results to determine adjacent ring shielding requirements. The results of the Monte Carlo simulations confirm that overall system sensitivity will remain acceptably high even with the small crystal dimensions we are proposing. The simulations indicate that the sensitivity loss incurred when BGO crystals of 3 x 10 x 30 mm are used is approximately 15% if an energy threshold of 250 keV is used.

We have continued with our program of detector development by building and testing individual detector assemblies. This work has included consideration of the mechanical requirements of the final design with emphasis on a reliable, modular detector group that can be easily replaced if necessary.

Since reliable, low-loss optical coupling between the crystals, light guides and photomultipliers is imperative, we have begun to evaluate the currently available high-strength optical cements. All detector assemblies that we have constructed to date have used silicone RTV optical compounds. While these have acceptable optical performance they have relatively low mechanical strength. We are currently evaluating the performance of two-part epoxy compounds and one component UV setting materials. In our detector configuration, three different optical coupling situations exist (depending on crystal location within the array). These are: BGO crystal to side mounted glass PMT; BGO crystal to plastic light guide; and light guide to glass PMT. Each of these optical couplings may require a different material for optimum performance.

We have just received a new optical epoxy which has been optimized for excellent optical coupling as well as high mechanical strength between the BGO scintillation crystals and the plastic light guides. We have also placed an order, and are expecting immediate delivery of some specially fabricated, 0.5 mm thick, pressure sensitive, silicone rubber, optical coupling pads. If these materials meet our performance requirements during experimental evaluating testing we may be able to make substantial improvements in the optical and mechanical design of the full detector array. If these new materials perform as expected, we will change from a design concept which requires each detector assembly (a crystal, light guide and photomultiplier tube) to be an individually removable assembly to a design which treats all of the crystals and their related light guides as one major component and that treats each photomultiplier tube as a separate removable part. By using the pressure sensitive coupling pads, instead of an optical cement between the photomultipliers and their crystals or light guides it should be possible to replace individual failed tubes without disturbing the scintillation crystal array.

We have conducted extensive evaluations of BGO detector crystals obtained from manufacturers in three different countries: China, France and the U.S.A. All material tested had generally good performance with the best results obtained from samples supplied by Solon Industries of the U.S.A.

Crystal surface-treatment testing, using crystal and light guide configurations of the same dimensions as will probably be used in the final tomograph design, has resulted in a much better understanding of the steps necessary to optimize detector performance. We have evaluated a number of surface treatments including several commercially available coatings (Solon Industries proprietary and Nuclear Enterprises paint), Chrismatec factory-applied coating on surface-etched crystals, and hand-wrapped porous Teflon membrane coverings. For our detector configuration, it appears that the best performance (as indicated by total signal output level and energy resolution) can be achieved by using crystals which are first highly polished and then wrapped with Teflon membrane. The commercial coating supplied by Solon

Industries also has good performance and may be a more appropriate choice in our tomograph design because of mechanical considerations.

Several batches of the 9.7 mm Hamamatsu photomultiplier tubes required for the High Resolution PET system have been purchased during the last year. Measured tube performance has generally improved from batch to batch with the latest tubes far exceeding the published minimum specifications for these components. This is a very positive development as the performance of the original tubes was only minimally acceptable. This development should result in generally improved tomograph performance in the areas of energy resolution (improved scatter rejection) and timing resolution (better accidental coincidence rejection).

B. Electronics Configuration and Design

After careful evaluation of the volume of circuitry required for the support electronics for a 2400 detector tomograph we have reconsidered the use of surface-mount technologies in this application. We were initially reluctant to consider these techniques because of the costs involved in design and fabrication of the surface-mount boards and the lack of availability of the special integrated circuits necessary. In addition, in-house expertise and appropriate fabrication facilities were not available on the University of Chicago campus. After due consideration of the amount of physical space required to house the necessary circuits using conventional printed circuits, we decided to explore the possibility once again of using these advanced, high density construction methods.

Application specific integrated circuits (ASICs) combining multiple discriminators and programmable support circuits, including data latches and digital to analog converters, recently have been developed for high energy physics applications. We believe these surface-mount components can be used to construct the high density, parallel electronics required for a 2400 detector tomograph.

Experimental designs for much of the tomograph's "front-end", programmable signal delay, coincidence, orbiting rod source masking, and computer interface circuitry are currently being programmed into the circuit simulation programs in a collaborative effort with experts at Fermilab. The results of these simulations will be used to insure that the proposed circuits will meet the performance requirements of the complete system at the expected counting rates.

C. Mechanical Design

We have begun to finalize some of the mechanical features of the tomograph and must complete the detailed mechanical engineering of the system before beginning. Some of the major mechanical design features which we feel should be in the system include:

1. A built in rotating-rod source with highly accurate angular position encoding. With such a source, along with appropriate electronics and reconstruction software, it is possible to eliminate much of the in-plane scatter from attenuation measurements derived from transmission scans. As a result, improved attenuation correction, and thus improved accuracy of quantitation, can be achieved.

2. A removable septal scatter shield assembly, so that data acquisition may be done experimentally in a full solid angle scan mode. With the addition of some supplemental components to the coincidence circuits, and with the further development of full 3-D reconstruction methods, in the future it might be possible to realize a substantial increase in sensitivity of the tomograph. We feel the current design should not exclude the possibility of this future expansion if satisfactory full 3-D reconstruction algorithms are developed.

3. A central scintillation crystal/light guide array with individually removable photomultiplier tubes using pressure sensitive, optical gel pads for light coupling. If our research determines that this concept is not practical we will use our original design of modular groups of 12 or 24 detectors which can be quickly and easily removed for off-line service when necessary.

4. Internal, programmable axial translation of the complete detector array. The planned axial movement will increase the field of view of the tomograph to 13.8 cm or a total of 21 slices (with scatter reduction septa in place).

Although much of the mechanical engineering can be accomplished at the CAD/CAM facilities currently being developed on the U. of C. campus at both F.M.I. and Central Shop, we feel that a qualified outside consultant with PET mechanical design experience will be essential. We have identified such an individual and he has already been retained on a consultant basis. Work is progressing on the general mechanical configuration and on details of the multiple motion systems to be incorporated in the system. (see figure 2).

D. System Simulation

System simulation programs have been written to evaluate the changes in overall performance resulting from variations in system configuration. These programs are currently being used to estimate linear sampling requirements (numbers of wobble points and wobble diameter) for tomograph configurations having different ring and individual detector dimensions.

We have continued with our computer simulation studies to evaluate changes in overall performance as a function of variations in system configuration. In particular, we have investigated sampling non-uniformities by evaluating the non-uniformities in the sampling patterns of sinograms generated by different numbers of wobble positions for a 62.5 cm diameter ring of 600 crystal detectors, with 3.27 cm center-to-center distance between adjacent crystals.

We have also written computer programs to evaluate the expected count rates (trues, scatter, singles, and accidentals) using the analytical models of Derenzo (1975) and Tanaka, et. al. (1982). The calculations assumed a uniform distribution of activity in a 20 cm diameter cylindrical container. The programs have the option of varying the lower-energy threshold, as well as taking into account system dead-time.

We have also assessed the effects of non-uniform resolution in the trans-axial and axial directions (about 2.6 mm and 5.7 mm, respectively). This was carried out by calculating the recovery coefficients for simple geometrical objects (such as cubes and spheres) with varying sizes, and comparing these with those expected from currently existing positron tomographs. The 3D recovery coefficients (RC) were calculated in the following manner. Denote by $g(\vec{x})$ the point spread function (PSF) of a given tomograph at its center. The desired recovery coefficient is

$$RC = \frac{\iiint_{\text{object volume}} g(\mathbf{H}) d^3x}{\iiint_{\text{all space}} g(\mathbf{H}) d^3x}$$

To simplify calculations, assume that $g(\vec{x})$ can be decomposed into a product of these independent PSFs, one for each of three orthogonal directions (eg, Cartesian axes)

$$g(\mathbf{H}) = g_x(x)g_y(y)g_z(z)$$

The subscripts (x,y,z) denote different functional behaviors which likewise denote non-uniform resolution along different directions. Further assume that the individual PSFs are Gaussian functions with FWHM (resolution) R_x , R_y , R_z . In the center of the scanner, $R_x=R_y$. The non-uniform resolution is characterized by an asymmetry factor $k=R_z/R_x$.

Our results indicate that despite the relatively large resolution asymmetry, the recovery coefficients of the high-resolution system we are investigating are far better than those of systems with uniform (but poorer) resolutions in all directions.

3D Recovery Coefficients

Tomograph	R_x	R_z	R_z/R_x	Recovery Coefficient (%)			
				Cube Side Length (mm)			
				2.5	5.0	10	15
U of C Hi-Res. & Donner 600	2.6	5.7	2.19	21.7	66.6	96.1	99.8
Hamamatsu (Small Animal Only)	3.5	5.7	1.63	14.2	57.5	96.0	99.8
CTI 713 (Small Animal Only)	3.8	4.4	1.16	15.7	63.2	98.8	99.9
Headtome IV	4.5	9.5	2.11	5.8	30.4	77.1	93.7
GE(Scanditronix) PC2048	4.5	5.9	1.31	9.1	44.6	93.7	99.7
GE(Scanditronix) PC1024	4.7	10.7	2.28	4.8	26.1	71.1	90.1
GE(Scanditronix) PC4096	5.0	6.0	1.20	7.4	39.0	91.5	99.6
CTI/Siemens 951	5.0	4.8	0.96	9.1	45.2	94.9	99.9
PENN-PET	5.5	5.5	1.00	6.8	36.6	90.6	99.6
Posicam 6.5	5.8	11.9	2.05	2.9	18.1	62.1	85.8
CTI/Siemens 921 ECAT EXACT	6.0	5.0	0.83	6.3	34.5	88.6	99.3
PETT VI (Hi-Res. mode)	7.1	13.9	1.96	1.7	11.5	49.1	77.6
CTI ECAT III Model 911	8.4	15.5	1.85	1.1	7.9	38.9	69.4

Figure 3. This table compares the relative recovery coefficients of the proposed U of C High Resolution Positron Tomograph with several existing Whole Body, Brain, and Small Animal Designs. Computed percentage recovery is for cubes of specified size centered within a plane. Spatial resolution figures (all FWHM) are as published or specified in manufacturer's literature.

R_x = average in plane resolution (mm FWHM X/Y or R/T)

R_z = average axial resolution (mm FWHM)

When completed, these simulations will help determine the most uniform sampling scheme for our tomograph configuration. The count rate distribution simulations will be used to help minimize the total buffer memory requirements and to optimize the design of the coincidence circuits and the computer interface hardware.

Simulations of the various electronics sub-systems has been started using advanced hardware simulation tools such as Cadence Varilog for the major digital components and Spice for the analog front end discriminator designs.

We have evaluated the effects of Compton scattering within BGO crystals having varying physical dimensions by using Monte Carlo techniques and will use these results to determine adjacent ring shielding requirements. The results of the Monte Carlo simulations confirm that overall system sensitivity will remain acceptably high even with the small crystal dimensions we are proposing. The simulations indicate that the sensitivity loss incurred when BGO

crystals of 3 x 10 x 30 mm are used is approximately 15% if an energy threshold of 250 keV is used.

We have already written test software routines in compiled program code to measure the ability of the IBM R-6000 Model 730 to implement the (usually external) data acquisition histogramming function. Using this (not fully optimized) code we have achieved histogramming rates of 5×10^5 events per second. We expect that with machine language implementation of the histogramming and I/O code, and/or the use of later, faster CPU's it may be possible to meet our counting rate goals for this configuration without the use of external hardware histogramming buffers.

E. Significance

The design and construction of a multiple-slice, high-resolution positron tomograph will provide substantial improvements in the accuracy and reproducibility of measurements of the distribution of activity concentrations in the brain. The range of functional brain research and our understanding of local brain function will be greatly extended when the development of this instrumentation is completed. We see the development of this device as being directly in line with national priorities for the 1990s --- the Decade of the Brain.

Figure 3

PROJECT II-2

MINIATURE GAMMA CAMERA

Project Leader: Nicholas J. Yasillo

Robert N. Beck, Chin-Tu Chen, and Malcolm Cooper

A. System hardware and software

In our effort to produce a high performance miniature gamma camera we have concentrated on system simulation (including full collimator modeling), component evaluation, optical design, circuit design, and software development.

Specifically we have accomplished the following:

Detailed measurement of the optical sensitivity vs. position on the photocathode of the PSPMTs was completed. These measurements were acquired through the use of a special scanned array of pulsed and collimated light sources. These data were essential to allow us to understand the extent of spatial variation of sensitivity and geometric distortion present in the PSPMT. Also, measurements of system spatial linearity, energy resolution, and usable field of view were completed using special test scintillation crystals which provided optical access to the edges for adjustment of the edge reflectivity coefficients.

Modeling of the required resolution and accuracy of the vector correction method was accomplished and will be used in determining electronic circuit and software requirements.

A high speed Direct Memory Access computer interface was installed and tested and is meeting expected performance requirements.

Minor revisions were made to the mechanical design of the system as a result of measurements of sensitivity to magnetic fields, done during the initial development stage. Machined tungsten radiation shielding has been designed and fabrication has been completed. These parts will be used in the final clinical camera configuration.

Figure 1

Mechanical Drawing of Minicam Cross Section

June 8, 1992
N. J. Yasillo

Display routines for both real-time data-display during acquisition and for display of stored image files are complete and have been successfully tested. Control software for the high-speed parallel input interface is essentially complete. These routines are used to transfer

data between the camera circuits and the host computer. Vector correction software to correct for geometric errors in the PSPMT spatial output signals and spatial sensitivity variation has been started but is not yet completed. All software written to date has been implemented in compiled C 5.1 code.

A computer controlled mechanical stage having X, Y and rotary motions has been acquired to be used to implement automatic mapping of the spatial linearity and sensitivity error functions of each miniature gamma camera assembly. An extensive library of control software routines have been written which will allow us to accurately map the required parameters of each PSPMT/crystal assembly. Verification of performance of the stage and its control software is presently being completed. The automated mechanical stage will also be used with various test phantoms for performance evaluation of the completed camera/collimator assemblies.

Design of the front-end electronics circuits is complete and prototype circuits have been tested. These circuits seem to work well but we expect that some minor modifications may be required, such as optimization of integration time, to improve performance. Circuit board designs for the camera internal analog driver card and the analog position and energy card will soon be finalized.

B. Collimators

We believe that the miniature gamma camera can be successfully used for a variety of imaging tasks, both planar and tomographic. We listed some of them above. The objectives of these tasks vary greatly, and system sensitivity and resolution requirements are not identical for each task. Because there are a variety of tasks and requirements and because collimator design is the factor controlling system sensitivity and resolution, we have designed the camera such that collimators can be easily attached and removed. We have also begun analysis that will provide the structures of collimators appropriate for the variety of tasks.

Previous work on collimator design performed in this laboratory resulted in the development of a ray-tracing program for use in collimator design (Beck RN and Redtung LD, 1985) and resulted in a procedure for obtaining optimal parallel-hole collimators--those with the highest sensitivity given a desired resolution at a specified distance from the collimator face (Gunter *et. al.*, 1990). The codes also allow us to determine the resolution obtainable at other distances once the parameters for the optimal collimator have been determined and can be used assuming most of the standard collimator materials. The computer codes were developed and implemented on a Perkin-Elmer 3254. We recently updated these fortran codes so that they can be used on a variety of workstations. Computation times remain nontrivial but have been substantially reduced.

Two studies relevant to the design of collimators for use with miniature gamma cameras have recently been completed. The first study was performed to determine optimal collimator parameters (thickness, hole separation, hole size, and septa thickness) for a specified task. The second was performed to determine the optimal parameters (only thickness was variable in this study) for collimators that we could construct from two high-resolution collimator blanks to which we have access. For the second study the specified task was the same as for the first.

One conclusion of the work of Gunter *et. al.* (Gunter *et. al.*, 1990) was that among the range of collimator hole patterns commonly used the pattern comprising hexagonal holes in a hexagonal array is optimal. Thus, the first study assumed such a hole pattern and the parameters listed above were determined for the task of imaging with 3.0 mm resolution at a distance 5 cm from the collimator. The conclusions of this study are that the optimal collimator parameters are: thickness 19.0 mm, hole separation 1.2 mm, face-to-face hexagonal hole

opening 0.98 mm, and septa thickness 0.202 mm. The system sensitivity for this design, is 1.35×10^{-4} .

The second study was performed to determine the optimal thickness of two collimator blanks, one having a pattern comprising triangular holes placed vertex to side and the other having a pattern comprising square holes placed side to side. The conclusions of this study are that the optimal thickness for the triangular hole collimator is 50 mm (other parameters were hole separation 2.6 mm, face-to-vertex triangular hole opening 2.25 mm, and septa thickness 0.35 mm). The optimal thickness for the square hole collimator is 21.5 mm (other parameters were hole separation 1.2 mm, face-to-face square hole opening 1.02 mm, and septa thickness 0.18 mm). The resulting system sensitivities are 0.63×10^{-4} for the triangular hole design and 1.26×10^{-4} for the square hole design.

These results indicate that collimator assemblies fabricated from the square hole blank we currently have on hand will provide near optimal performance and those fabricated from the triangular hole blank reduced but acceptable performance for the imaging tasks of interest to us. Thus, the blanks will be used for our initial studies. However, we believe that for some applications it may be appropriate to use astigmatic collimators or pinhole apertures, and we plan to construct the camera in a way which will accommodate those options.

Figure 2 Summary of results of studies on miniature gamma camera collimator design.

The highest sensitivity for specified resolution requirements is achieved with the hexagonal hole collimator. The curves on the graph represent a comparison of resolution of the optimal collimator specified in the text to the best collimators we can obtain from collimator blanks presently available to us.

PROJECT III

METHODOLOGY FOR EVALUATION OF DIAGNOSTIC PERFORMANCE

Project Leader: Charles E. Metz

A. Introduction

Effort in this project during the past year has focused on the development, refinement, and distribution of computer software that will allow current Receiver Operating Characteristic (ROC) methodology to be used conveniently and reliably by investigators in a variety of evaluation tasks in diagnostic medicine; and on the development of new ROC methodology that will broaden the spectrum of evaluation tasks and/or experimental settings to which the fundamental approach can be applied.

Progress has been limited by the amount of financial support made available to the project. Until recently, DOE funding for this work was confined to 15% of Dr. Metz's salary. This was reduced to 5% in May 1992 to allow the support of Mr. Benjamin Herman (a student working toward the Ph.D. degree in our Graduate Programs in Medical Physics) as a Research Assistant for the project.

B. Accomplishments

B.1. Distribution of computer software for ROC analysis

Our software was distributed without charge to an additional 50 laboratories, increasing the total number of user sites to 245. Currently, six programs are available in versions for IBM-PC compatible microcomputers and for minicomputers and mainframes. The four most frequently-requested programs are available also in versions for the Apple Macintosh.

B.2. Refinement of computer software for ROC analysis

We made significant progress toward development of a single, integrated software package for ROC curve fitting and statistical testing that will accept either categorical or continuously-distributed data, thereby eliminating the current inconvenience of separate programs for these purposes. An important feature of this new software package will be its ability to read files created by the five existing programs that it integrates, each of which now uses a different format. Work to incorporate the capabilities of five of our existing programs is now virtually complete; remaining is the task of adding several new features, such as calculation and output of 95% confidence intervals for estimated differences between ROC curves as an important supplement to "p-values" (Metz, 1992b).

B.3. Development of new ROC methodology

Collaboration with Drs. Howard Rockette and David Gur at the University of Pittsburgh resulted in a publication (Rockette, Gur and Metz, 1992) which argues for the use of continuous confidence-judgment scales in image reading studies, rather than the conventional

discrete categorical scales, and shows that ROCs estimated with discrete and continuous scales are indistinguishable when discrete data are not problematic.

In collaboration with Drs. Donald Dorfman and Kevin Berbaum at the University of Iowa, we developed the theoretical aspects of a new method for evaluating the statistical significance of differences between ROC curves that are estimated from image readings by more than one reader. This method uses conventional analysis of variance (ANOVA) and "jackknifing" to implement the general statistical test first suggested by Swets and Pickett (1982), which takes both case-sample variation and reader variation into account. Although the Swets/Pickett test is widely acknowledged to be the most comprehensive to date, it seldom has been used in practice because the particular implementation which Swets and Pickett proposed usually either is impractical or requires arbitrary assumptions concerning the magnitudes of some variance and/or correlation terms. A manuscript describing the new approach (Dorfman, Berbaum and Metz, 1992) is scheduled to appear in the September 1992 issue of *Investigative Radiology*.

We continued to investigate the theoretical properties of a fundamentally new model for ROC curve fitting which assumes that diagnostic decisions are based upon the *likelihood ratio* of a quantity that arises from Gaussian distributions, rather than upon a Gaussian-distributed quantity itself. Because this alternative model ensures ROC curves with monotonic slope but allows fits that closely approximate those of the widely-accepted binormal model when data are statistically reliable, we expect that a curve-fitting algorithm based on it will prove helpful in dealing with "degenerate" data sets. Development of software for reliable implementation of the new model has been delayed by a lack of computer-programming personnel, however.

B.4. Dissemination and application of evaluation methodology

Elucidation of methodological issues that arise in practical applications of ROC analysis represents an important goal of this project. *Science Citation Index* lists more than 400 citations of our methodological and tutorial publications on ROC analysis during the three-year period 1989-1991.

When a difference between two ROC estimates is tested and is found not to be "statistically significant," one cannot conclude that no difference exists, but confusion concerning the correct interpretation of a negative result of this kind is common among individuals without formal statistical training. This misunderstanding can lead to serious practical consequences in situations where statistical significance is not found but small differences, if they really exist, are clinically important. The need for a range in which the true difference plausibly lies, given a particular set of data, is met by "confidence intervals," which can be calculated in virtually all situations to which statistical hypothesis testing applies. A manuscript recently accepted for publication in *Investigative Radiology* (Metz, 1992b) illustrates the meaning and usefulness of confidence intervals by analyses of results from a hypothetical receiver operating characteristic (ROC) experiment.

At the invitation of Dr. William Strauss, editor of the *Journal of Nuclear Medicine*, we published a tutorial commentary in which mathematical constraints on the sensitivity and specificity of "logically" merged test results are illustrated by a general computational example (Metz, 1991a). Collaboration with Drs. David Gilland and Benjamin Tsui at the University of North Carolina resulted in a publication (Gilland *et al.*, 1992) that describes the use of ROC analysis for comparison of SPECT images reconstructed by maximum-likelihood and filtered-

backprojection techniques. Other publications from collaboration with Wu *et al.* at the University of Chicago and with King *et al.* at the University of Pittsburgh are listed below.

C. Publications related to work performed in this project

- Dorfman DD, Berbaum KS, Metz CE (1992). ROC rating analysis: generalization to the population of readers and cases with the jackknife method. *Invest. Radiol.* (in press; scheduled for September 1992 issue).
- Gilland DR, Tsui BMW, Metz CE, Jaszczak RJ, Perry JR (1992). An evaluation of maximum likelihood - expectation maximization reconstruction for SPECT by ROC analysis. *J. Nucl. Med.* **33**: 451-457.
- King JL, Gur D, Rockette HE, Curtin HD, Obuchowski NA, Thaete FL, Britton CA, Metz CE (1991). Radiologists' confidence in detecting abnormalities on chest images and their subjective judgments of image quality. *Proc. SPIE* **1446**: 268-275.
- Metz CE (1991a). Constraints on the sensitivity and specificity of "logically" merged test results. *J. Nucl. Med.* **32**: 1646-1647.
- Metz CE (1991b). ROC methodology for the evaluation of PACS. In: *A New Horizon in Medical Physics and Biomedical Engineering* (H. Abe, K. Atsumi, T. Iinuma, M. Saito, and M. Inoue, eds.). Amsterdam: Elsevier Science Publishers, pp. 89-97.
- Metz CE (1992a). Evaluation of medical images. In: *The Formation, Handling, and Evaluation of Medical Images* (AE Todd-Pokropek and MA Viergever, eds.). Berlin: Springer-Verlag, pp. 277-302 (in press).
- Metz CE (1992b). Quantification of failure to demonstrate statistical significance: the usefulness of confidence intervals. *Invest. Radiol.* (in press).
- Metz CE, Shen J-H (1992). Gains in accuracy from replicated readings of diagnostic images: prediction and assessment in terms of ROC analysis. *Med. Decis. Making* **12**: 60-75.
- Rockette HE, Gur D, Metz CE (1992). The use of continuous and discrete confidence judgments in receiver operating characteristic studies of diagnostic imaging techniques. *Invest. Radiol.* **27**: 169-172.
- Wu Y, Giger ML, Doi K, Vyborny CJ, Schmidt RA, Metz CE (1992). Artificial neural networks in mammography: application to decision making in the diagnosis of breast cancer. Submitted to *Radiology* (in review).

PROJECTS IV-1 & IV-2
KNOWLEDGE TRANSFER:
EDUCATION IN QUANTITATIVE NUCLEAR MEDICINE IMAGING

Project Leader: Robert N. Beck

*Robert Mintzer, Erma M. Peterson, Claude J. Ortega,
Chin-Tu Chen, and Malcolm Cooper*

These two projects were not pursued because of the budgetary constraint. It will be pursued in the future when funding or other support becomes available.

END

**DATE
FILMED**

9 / 8 / 92