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Award Number: DAMD17-99-1-9432

TITLE: Dual Modality Imaging System for Breast Cancer Research

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REPORT DATE: July 2000

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
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REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 074-0188

1. AGENCY USE ONLY (Leave blank)	2. REPORT DATE	3. REPORT TYPE AND DATES COVERED
	July 2000	Annual (1 Jul 99 - 30 Jun 00)

4. TITLE AND SUBTITLE
Dual Modality Imaging System for Breast Cancer Research

5. FUNDING NUMBERS
DAMD17-99-1-9432

6. AUTHOR(S)
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8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSORING / MONITORING AGENCY REPORT NUMBER

11. SUPPLEMENTARY NOTES

12a. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for public release; distribution unlimited

12b. DISTRIBUTION CODE

13. ABSTRACT *(Maximum 200 Words)*

In the 25-40% of the general female population with radiodense breast parenchyma, clinically occult lesions may be invisible in the screen-film mammogram. Even if suspicious masses are detected, determination of the benign or malignant nature of a mass is often impossible from the x-ray image. There is thus a need for diagnostic procedures that can noninvasively help characterize suspicious breast lesions.

Scintimammography is an imaging technique that shows promise as an adjunct diagnostic tool in problem solving mammography, for monitoring recurrence after surgery, and in the assessment of multidrug-resistance. However, because clinical Anger cameras have only moderate spatial resolution and are difficult to position close to the breast, small lesions are difficult to detect. In addition, no direct means exists of correlating mammographic and scintigraphic information because of the significantly different shape of the breast in mammography (compressed) and scintimammography (prone, pendulant). We are developing an imaging system that overcomes these problems by combining digital x-ray mammography and gamma emission scintigraphy in a single, integrated system. The system is mounted on a standard upright mammography unit, and can easily be placed in a typical mammography room, providing accessibility even for small breast imaging clinics not associated with major medical centers.

14. SUBJECT TERMS	15. NUMBER OF PAGES
Breast Cancer, scintimammography, digital mammography, dual modality imaging	11
	16. PRICE CODE

17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
Unclassified	Unclassified	Unclassified	Unlimited

NSN 7540-01-280-5500

Standard Form 298 (Rev. 2-89)
Prescribed by ANSI Std. Z39-18
298-102

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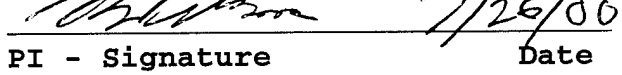

PI - Signature 7/26/00 Date

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INTRODUCTION

The purpose of the work funded by this grant is to develop a new type of dedicated system for diagnostic breast imaging that can simultaneously obtain structural information from a digital mammography detector and functional information from a high resolution gamma imaging detector.

The overall goals of the proposed project are:

a) To upgrade and optimize our test dual system,

b) To compare its performance over a broad range of phantom imaging tasks to that of the combination of film-screen mammography and scintimammography, and

c) To perform a limited clinical study in which the results of the dual modality study are compared to the results of biopsy.

BODY

As taken from the approved Statement of Work, the tasks scheduled to begin and/or be completed during the first 12 months of the grant period are as follows.:

Task 1. Upgrade digital mammography and gamma detector components of test system, Months 1-6

a) Replace current 6 cm x 6 cm spot detector with 20 cm x 30 cm full field digital mammography (FFDM) detector

b) Characterize imaging properties of FFDM detector, including linearity, dynamic range, modulation transfer function (MTF), noise power spectrum (NPS), noise equivalent quanta (NEQ), detective quantum efficiency (DQE), geometric linearity, and artifacts.

c) Replace 6 cm x 6 cm, 1.25 mm pixel detector with 8 cm x 8 cm, 2.25 pixel detector

d) Characterize detector imaging properties including sensitivity, line spread function (LSF), energy resolution, geometric linearity, and uniformity of response.

e) Modify co-registration software to accommodate new detector parameters

Task 2. Collimator optimization, Months 3-6

a) Calculate collimator efficiency, resolution for the range of object distances relevant in the dual system for several potential materials (e.g. tantalum, lead or tungsten).

b) Fabricate and evaluate small test collimators covering a limited fraction of the FOV, including slant hole collimator.

c) Build optimized high resolution and optimized high efficiency collimators for dual system.

Task 3. Phantom development, Months 7-12

a) Calculate useful range of phantom parameters (thickness, lesion sizes, etc) based on x-ray and gamma ray attenuation, detector resolution, and scatter measurements.

b) Fabricate fillable contrast-detail phantoms, chamber phantoms with removable simulated lesions, fillable vessels of various thicknesses to provide background radioactivity, etc.

c) Purchase breast equivalent mammography block phantoms with imbedded simulated lesions (CIRS, Newport News, VA)

d) Evaluate dual system performance using permutations of stacked phantoms, scatter free conditions

e) Repeat the measurements of d), but incorporating the anthropomorphic torso phantom to create realistic scatter conditions.

Task 4. Quantification of the effects of compression, Months 7-18

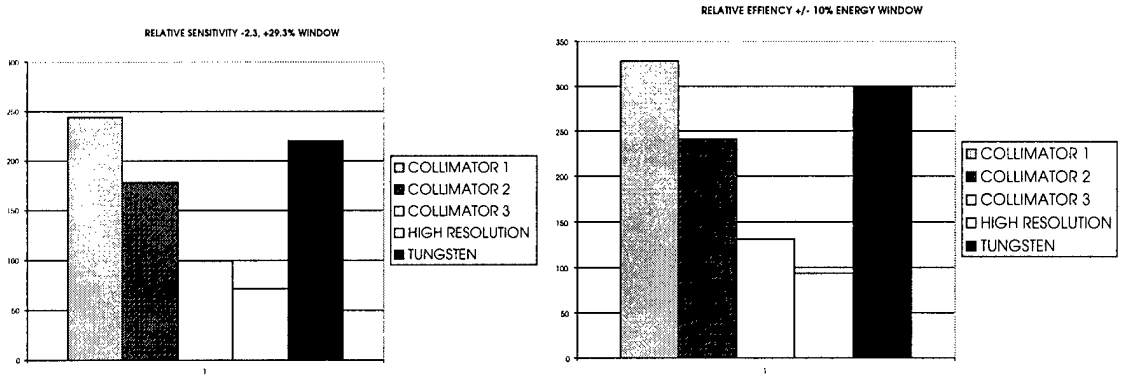
a) Use the phantoms developed in Task 3 to measure SNR, target-to-background ratio, while varying the thickness of interposed phantom material and total phantom thickness

Accomplishments

The detector upgrade of Task 1a has been done, and the measured performance (Task 1b) has been published [Williams 1999]. The upgrade of Task 1c was also implemented, and the new detector is 10 cm x 10 cm with 3 mm x 3 mm x 6 mm thick NaI(Tl) crystals. The quantities listed in Task 1d have been measured for the new detector. The sensitivity, with the current tungsten collimator, is 220 cpm/μCi, using an energy window of –2.3 %, +29.3%. The FWHM of the LSF is 3.4 mm. The FWHM energy resolution at 140 keV is 17%, geometric nonlinearity is within that attributable to crystal light centroiding, and the coefficient of variation (RMS fluctuations/average) in a raw (prior to uniformity correction) flood image is 0.053, demonstrating exceptionally good uniformity of response.

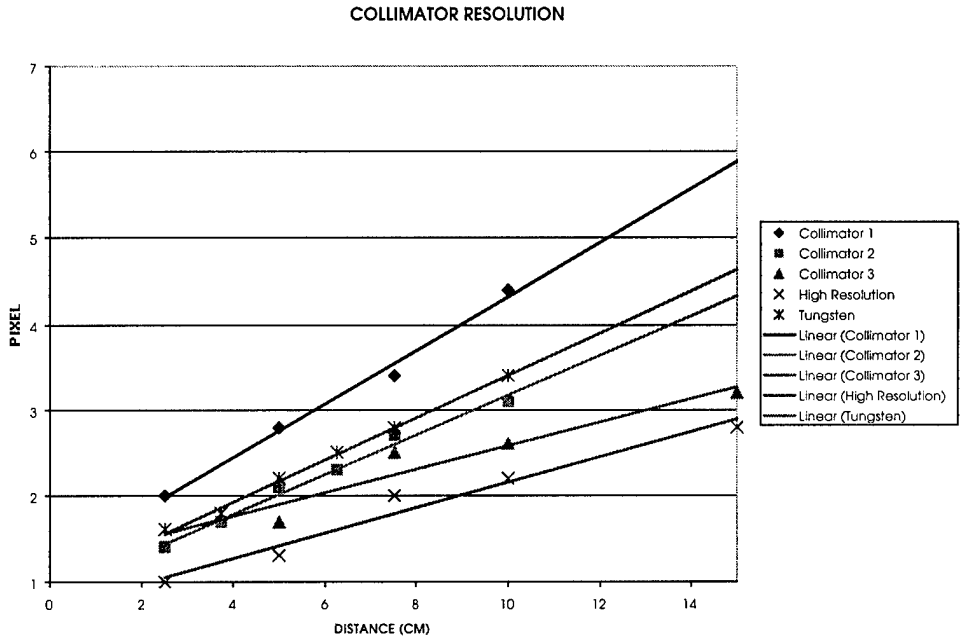
Task 2, evaluating gamma camera collimators, has been completed. Several different lead collimators with different hole dimensions, as well as an etched tungsten collimator were evaluated. The following describes the collimator parameters and summarizes the results of sensitivity and spatial resolution measurements:

	+/-10 WINDOW	-2.5, +30% WINDOW
COLLIMATOR 1	328cpm/μCi	244cpm/μCi
COLLIMATOR 2	242cpm/μCi	178cpm/μCi
COLLIMATOR 3	131cpm/μCi	99cpm/μCi
HI RESOLUTION	93cpm/μCi	72 cpm/μCi
TUNSTEN	299cpm/μCi	220cpm/μCi



Collimator Type	Hole Diameter (mm)	Septal Wall (mm)	Collimator Height (mm)	Expected Sensitivity (cpm/μCi)	Measured Sensitivity (cpm/μCi)
Coll. 3	1.397	0.203	27.000	219	131
Coll. 2	1.575	0.267	21.006	446	242
Coll. 1	1.778	0.305	19.990	627	328
High Res.	1.243	0.241	27.904	179	93
Tungsten	*1.25	0.25	17.8	544	299

**** Tungsten collimator is cast with square holes***



Task 3, the development of specialized phantoms, has thus far resulted in the following types of phantoms:

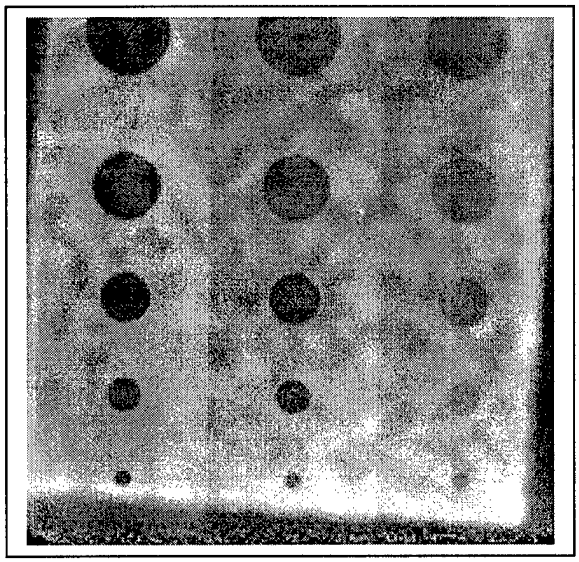
1) An acrylic dual modality contrast detail phantom, permitting a range of target size and contrast for both x-ray attenuation and gamma emission

2) A 3-layer fillable gamma phantom, permitting simulated lesions of various sizes to be placed at any of several locations at three depths in a background of 99m-Tc solution.

3) A series of compressible phantoms made of gelatin, and containing simulated lesions made of 99m-Tc doped Agarose.

We have also purchased a set of x-ray mammography block phantoms from CIRS Corp. Measurements using these and each of the above phantoms have been performed and are ongoing. Below is an example dual modality image of the contrast-detail phantom.

Finally, Task 4 involves quantification of the effects of compression. Part of the results of this work will soon be published in the Conference Record of the upcoming IEEE Nuclear Science Symposium/Medical Imaging Conference in Lyon, France, October 2000. A summary paper, submitted to the meeting, is included in the appendix. The full paper will appear in the Conference Record.



KEY RESEARCH ACCOMPLISHMENTS

- Upgraded dual modality x-ray and gamma ray detectors, with measured performance meeting design specifications
- Optimized gamma camera collimator
- New types of phantoms for evaluation of factors determining lesion contrast in breast scintigraphy
- Quantification of the effects of breast compression on lesion contrast in breast scintigraphy

REPORTABLE OUTCOMES

Publications

"A system for dual modality breast imaging", A.R. Goode, M.B. Williams, P.U. Simoni, V. Galbis-Reig, S. Majewski, A.G. Weisenberger, R. Wojcik, M. Stanton, W. Phillips, A. Stewart, Conference Record, IEEE NSS/MIC, 1999.

"Optimization of dedicated scintimammography procedure using small detector prototypes and phantoms", S. Majewski, E. Curran, C. Keppel, D. Kieper, B. Kross, A. Palumbo, V. Popov, A.G. Weisenberger , B. Welch, R. Wojcik, M. B. Williams , A. R. Goode, M. More, and G. Zhang, Conference Record, IEEE NSS/MIC, 2000.

Related Grant Funding

The Susan G. Komen Breast Cancer Foundation
'Novel System for Dual Modality Breast Imaging"
#99-003050
MB Williams, PI, 20% time commitment
12/31/99 to 12/30/01
$101,955 (total direct, year 1)
$108,457 (total direct, year 2)
$247,281 (total)

Graduate Degrees Supported by This Award

Mitali J. More, MS Biomedical Engineering (summer 2001)

Vrushali Dabak, MS Biomedical Engineering (summer 2002)

CONCLUSIONS

Research is under way to develop a new type of dual modality system for breast cancer diagnosis. Thus far, the principle effort has been towards hardware optimization and development of appropriate test tools for realistic simulated breast imaging. Even at its present stage of development, the device constitutes an integrated system for combining functional and structural information regarding normal and pathological breast structures. Future development of more sophisticated image acquisition techniques, including multiple view acquisition, and alternate breast compression schemes, will further enhance the diagnostic capabilities of the system. It is anticipated that, compared to current non-integrated imaging procedures, breast lesions that are smaller and of a wider variety can ultimately be reliably characterized.

REFERENCES

1. "Analysis of the Detective Quantum Efficiency of a Developmental Detector for Digital Mammography", MB Williams, PU Simoni, L Smilowitz, M Stanton, WC Phillips, and A Stewart, Med. Phys., 26(11) (1999) 2273-2285.

APPENDICES

1. "A system for dual modality breast imaging", A.R. Goode, M.B. Williams, P.U. Simoni, V. Galbis-Reig, S. Majewski, A.G. Weisenberger, R. Wojcik, M. Stanton, W. Phillips, A. Stewart, Conference Record, IEEE NSS/MIC, 1999.
2. "Optimization of dedicated scintimammography procedure using small detector prototypes and phantoms", S. Majewski, E. Curran, C. Keppel, D. Kieper, B. Kross, A. Palumbo, V. Popov, A.G. Weisenberger , B. Welch, R. Wojcik, M. B. Williams , A. R. Goode, M. More, and G. Zhang, Conference Record, IEEE NSS/MIC, 2000.

OPTIMIZATION OF DEDICATED SCINTIMAMMOGRAPHY PROCEDURE USING SMALL DETECTOR PROTOTYPES AND COMPRESSIBLE PHANTOMS

S. Majewski[1], E. Curran [3], C. Keppel[1,4], D. Kieper[1], B. Kross[1], A. Palumbo[3], V. Popov[1], A.G. Weisenberger[1] , B. Welch[1], R. Wojcik[1],
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Several prototypes of dedicated scintimammography mini gamma cameras with a FOV of 4"x4" were tested for applications in dual modality breast imaging as an adjunct technique to digital mammography and as a stand-alone imager in a dedicated breast SPECT. The goal of the study was to obtain experimental data confirming selection of the imager design and of the best imaging geometry to detect small lesions labeled with Tc-99m.
The optimal design of the small scintimammography gamma camera used in these studies with an active FOV of about 10cm x 10cm is based on a 4x4 array of Hamamatsu R7600-C8 position sensitive photomultiplier tubes (PSPMTs). Optically coupled to the PSPMT array via a specially designed efficient multi-element light guide is a matrix of NaI(Tl) scintillator pixels (made by Bicron) with each element about 3mm x 3mm x 6mm in size and separated by 0.3 mm thick septa. Several variations of this basic design were used in different prototypes to detect small lesions inserted in rigid and flexible breast phantoms with and without compression and in a non-compressed breast SPECT mode with the detector rotating around the breast. Anthropomorphic torso phantoms were also employed to simulate realistic scatter radiation fields. Two data acquisition systems were used to collect and analyze the data: one based on a Macintosh G3 workstation with FERA ADCs and one based on a PC computer running Windows NT/KmaxNT software which makes use of a four channel ADC PCI card. The results confirm that the preferred imaging geometry is with the breast under compression. The two head imager design is proposed and demonstrated to increase sensitivity in detection of asymmetrically located small lesions.

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OPTIMIZATION OF DEDICATED SCINTIMAMMOGRAPHY PROCEDURE USING SMALL DETECTOR PROTOTYPES AND PHANTOMS

S. Majewski[1], E. Curran [3], C. Keppel[1,4], D. Kieper[1], B. Kross[1], A. Palumbo[3], V. Popov[1], A.G. Weisenberger[1], B. Welch[1], R. Wojcik[1], M. B. Williams[2], A. R. Goode[2], M. More[2], and G. Zhang[2]

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Imager System

Several mini gamma camera prototypes were built with an active area of 4" x 4" based on a 4x4 array of compact Hamamatsu R7600-00-C8 position sensitive photomultiplier tubes (PSPMTs). Figure 1 shows a schematic diagram of the mini gamma camera. Each of the R7600-C8 PSMTs has a transversal size of ~26x26 mm^2 and a minimum effective photocathode area of 22 x 22 mm^2. The 4x4 PSPMT array was optically coupled to a high quality 9.8 cm x 9.8 cm pixilated NaI(Tl) array from Bicron Corporation. The array is a 30x30 matrix of ~3mm x ~3mm x 6mm pixels encapsulated in a compact housing with a 5 mm thick glass window. Each pixel element is separated by 0.3 mm septa made of white epoxy diffusing walls. Intrinsic energy resolution of ~8.5% FWHM @122 keV was measured for this array using a standard PMT. A specially designed optical light guide enabled uniform response across the surface of the detector despite the dead regions between individual PSPMTs. The overall energy resolution attained, including all the uniformity corrections (PSPMT response, light guide response, dead area losses, etc), is 17.5% FWHM @ 140 keV (Figure 1). An in-house built multi-channel amplifier circuit is used to combine the signals from all of the PSPMTs resulting in a total of 2x16 outputs (16 for x-direction and 16 for y-direction). With a carefully selected parallel hole lead collimator the obtained spatial resolution of the gamma camera is under 5 mm FWHM at 5cm with sensitivities up to~300cpm/μCi, depending on the energy window employed. Two data acquisition systems were used. The first was based on an Apple Macintosh G3 attached to a mini-CAMAC crate with two 16ch FERA LeCroy ADCs. The second was built around a PC computer with two 16ch Datel PCI ADC cards. In both cases the software program Kmax from Sparrow Inc. was used.

Laboratory Studies

Two distinctly different imaging geometries were compared using flexible, compressible breast phantoms made from gelatin with inserted small fillable lesions (figure 2). Realistic Tc-99m doping levels were used both in the gelatin ("healthy tissue") and lesions. Three lesion sizes (volumes) were chosen: 0.35ml, 0.6ml and 1ml. Several uptake ratios between the lesion and the surrounding "healthy" breast tissue from 3:1 to 6:1 were used. In the first imaging geometry, the breast phantom was compressed down to ~5 cm and the imaging time was 5-10 minutes. In the second case a dedicated breast SPECT imaging geometry was evaluated with the breast phantom rotated in front of the mini-camera using a computer controlled stepping motor. Over 100 projections, each collected for times from 10 to 60 seconds, were acquired in test runs with an angular step of ~ 3.5•. In the 3d image reconstruction we used a SPECT algorithm developed in IDL software by Steve Meikle of the Royal Prince Albert Hospital in Sydney, Australia. Additional studies involved comparative

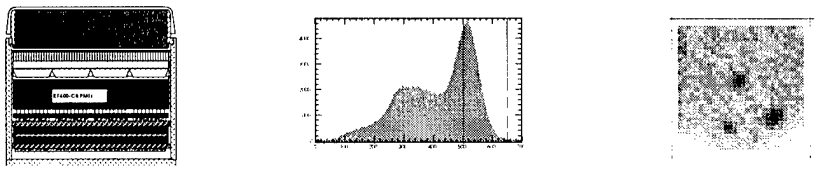

Figure1: Left: the structure of the mini gamma camera, middle: an example of the energy spectrum measured for Tc-99m with a compressed breast phantom, right: flood- and energy-corrected non-filtered image of the same phantom using a –2.5% to +30% energy window, as marked in the central energy spectrum histogram.

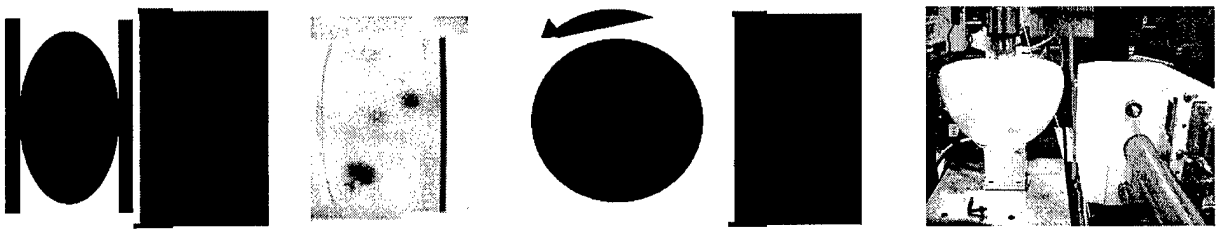

Figure 2: The left schematic drawing shows the preferred imaging geometry with breast phantom under compression. Three lesions of different sizes and the same uptake ratio of 6:1 were used. Middle-left photograph shows the actual gelatin phantom under compression. The second schematic drawing illustrates the SPECT study with the right photograph showing the breast phantom with lesions in front of the mini camera.

measurements of the resolution and sensitivity for five different collimators to select the optimal collimator for the two types of studies. One of the high efficiency collimators was custom made for us of etched Tungsten by Tecomet.

Results

Some of the early results obtained in the study (the study is continuing) are shown in the attached figures below.

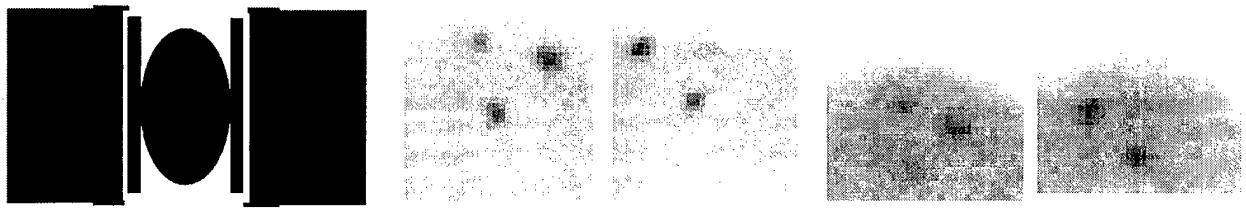

Figure 3: The left schematic drawing shows the idea of a two-gamma camera system used to simultaneously image the breast under compression to obtain a better visualization of the asymmetrically placed lesions. The situation was simulated by imaging both sides with a single camera in separate acquisitions. The two images in the middle show the effect of distance on the detection of the smallest 0.35ml lesion under 5.5 cm compression. The right two images show the same situation but under no compression (compression paddle distance of about 9 cm). Note that in the compressed case the lesions are better visible.

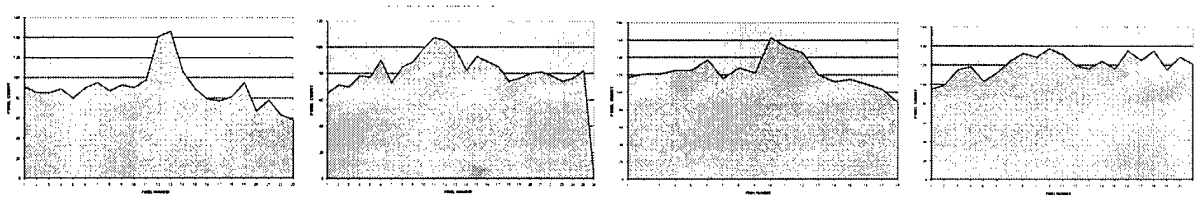

Figure 4: Profile histograms through the small 0.35 ml lesion in the phantom images from figure 3 above shown in the same order (compressed-close to lesion side, compressed-far to lesion side, non-compressed-close, non-compressed-far).

Imaging case	S/N	CONTRAST (%)
Compressed Bottom View	7.8	15
Non-compressed Bottom view	6.9	10
Compressed Top View	17.1	36
Non-compressed Top View	15.0	26

Table 1: S/N and Contrast values for the smallest 0.35 ml lesion: S/N (signal to noise) = $(N_L - N_B)/sqrt\ N_L$, CONTRAST= $100\%*(N_L - N_B)/N_B$. The highest contrast and S/N values were obtained for the compressed case with the imaging from the close distance side (top).

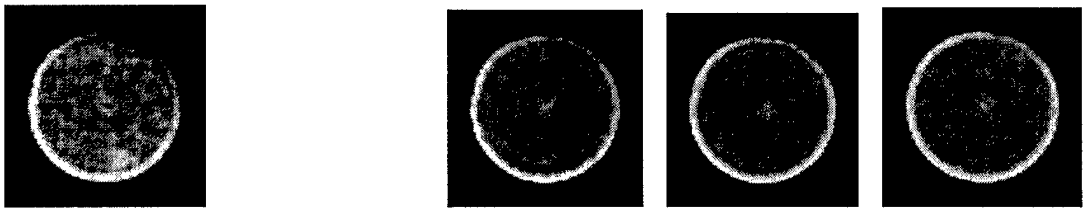

Figure 5: Reconstructed preliminary horizontal SPECT slices (perpendicular to the rotation axis) through the breast phantom show the middle size lesion (0.6 ml) in the two left images (seen at the bottom edge of the phantom), and the 1ml lesion in the central and the two right images (placed close to the center of the image). The smallest 0.35 ml lesion was not clearly visible in the corresponding slices. These results come from a different phantom than the one shown in figure 2.

Summary of results: The preliminary results of our multi-modality study confirm that the compressed geometry is best for detection of small lesions in the breast, even when compared to the dedicated breast SPECT geometry. The near-future studies will include the above-introduced method of double-sided imaging with co-registration of the two images to improve detection of asymmetrically placed small lesions and to increase statistical validity of the signal obtained from all lesions. We believe, that the added cost of the second detector head will be well justified by the increase in the detection sensitivity.

Acknowledgements: This work was supported in part by grants from the US Army MRMC (BC980469) and the Susan G. Komen Foundation (IMG-99-3050).