

A Combined Scintimammography / Stereotactic Core Biopsy Digital X-ray System*

A.G. Weisenberger¹, F. Barbosa¹, T.D. Green², R. Hoefler³, C. Keppel^{1,2}, B. Kross¹, S. Majewski¹, V. Popov¹, R. Wojcik¹ and D. C. Wymer³

¹Thomas Jefferson National Accelerator Facility, Newport News, VA

²Department of Physics, Hampton University, Hampton, VA

³Riverside Regional Medical Center, Newport News, VA

Abstract

Jefferson Lab, Hampton University and the Riverside Regional Medical Center are collaborating in a clinical study employing a dual modality imaging system utilizing scintimammography and digital radiography. The purpose of the study is to obtain clinical data on the reliability of scintimammography in predicting the malignancy of suspected breast lesions with the ultimate goal to reduce the number of false positives associated with conventional x-ray mammography. The scintimammography gamma camera is a custom built mini gamma camera with an active area of 5.3 cm x 5.3 cm based on a 2x2 array of Hamamatsu R7600-C8 position sensitive photomultiplier tubes. The spatial resolution of the gamma camera at the collimator surface is <4 mm FWHM and the sensitivity is 4000 cps/mCi. Preliminary results are that of the six cases that indicated a lesion with high uptake of the MiraLuma (^{99m}Tc-sestamibi) five were positive for cancer. Out of a total of 25 patients in the study, all cases negative for MiraLuma uptake were confirmed negative via the biopsy pathology. The scintimammography results indicate that the lesions become visible with the mini gamma camera within 3 minutes post injection of MiraLuma.

I. INTRODUCTION

We report on our development of a dual modality imaging system based on a custom-built, compact scintimammography gamma camera which is mounted to a Fischer Imaging Inc. [1] digital x-ray stereotactic core biopsy system. The radiopharmaceutical ^{99m}Tc-sestamibi is known to concentrate in breast tumors and has been undergoing evaluation as a means to detect breast cancer prior to biopsy [2]. The positive predictive value of standard mammography is between 10-30% [3]. Studies have shown that scintimammography has the potential to provide early indication of breast cancer and could reduce the number of needle biopsies of benign tumors [4, 5 & 6]. There have been studies involving scintimammography using conventional gamma cameras [7] and application specific systems [8]. The use of scintimammography as an aid for tumor biopsy has also been discussed [9]. Jefferson Lab, Hampton University and Riverside Hospital have built and installed a mini gamma camera into a digital x-ray stereotactic core biopsy system. The mini gamma camera is optimized for application-specific use in conjunction with a commercially available x-ray guidance system for

stereotactically guided core needle breast biopsy. Stereotactic breast biopsy is an x-ray guided method for localizing and sampling suspect breast lesions identified from a patient's mammogram.

Guided core biopsy is a relatively new procedure, which has been shown to have many advantages over surgical biopsy. In this procedure, typically performed as an outpatient, the patient lies prone on a mammography table and the affected breast is positioned in a special compression paddle that has a 5 cm x 5 cm square opening. The physician then obtains a digital x-ray radiograph of the breast and verifies precisely the position of the suspicious breast lesion. The standard x-ray tube can be positioned perpendicular to the x-ray image detector as well as +15 degrees and -15 degrees to the perpendicular. Localization of a specific lesion within a breast is based on measurements of the position of the lesion on two x-ray images (a stereo pair) of the breast taken from different angles (+/- 15 degrees). The radiologist selects the center of the lesion, mass, or calcification, and a computer generates the Cartesian coordinates of the targeted lesion. Once the stereo pair is obtained and the exact location is calculated, one of several devices is employed to obtain a tissue sample for biopsy. Only 19% of the biopsies performed on women with suspected breast cancer based on their mammograms end up being positive for cancer [10].

Our collaboration hopes to obtain clinical data on the reliability of scintimammography in predicting the malignancy of suspected breast lesions with the hope of reducing the typically large number of false positives associated with conventional x-ray mammography. The patients involved in the study have been scheduled for breast biopsy because of suspicious regions identified in their mammograms.

II. DETECTOR SYSTEM

The custom built mini gamma camera with an active area of 5.3 cm x 5.3 cm is based on a 2 x 2 array of Hamamatsu [11] R7600-00-C8 position sensitive photomultiplier tubes (PSPMTs). Each of the R7600-C8 PSPMTs has a minimum effective area of 22 x 22 mm². The PSPMT has 4x + 4y cross plate anodes such that each PSPMT has 8 outputs. A Jefferson Lab constructed charge division circuit is used to combine the signals from all of the PSPMTs, resulting in a total of four outputs (two in x-direction and two in y-direction).

*The Southeastern Universities Research Association (SURA) operates the Thomas Jefferson National Accelerator Facility for the United States Department of Energy under contract DE-AC05-84ER40150.

Optically coupled to the array of PSPMTs via a light guide is a Bicon [12] scintillator array which is a 16x16 matrix of 3mm x 3mm x 6mm NaI(Tl) crystal scintillator pixels in which each element is separated by a 0.3 mm light diffusing septum. The light guide serves to optically mix the light to facilitate light sharing across PSPMTs so that the crystal matrix can be imaged without breaks because of dead space between the individual PSPMTs. The final image is formed by mapping the data identified to belong to a particular crystal element into that crystal's appropriate pixel in the final image. A separate energy window is also defined for each crystal element. Several larger prototypes of this type of camera were tested at the University of Virginia Medical Center ([13] & [14]). (See Figure 1 for a schematic diagram of the mini gamma camera.)

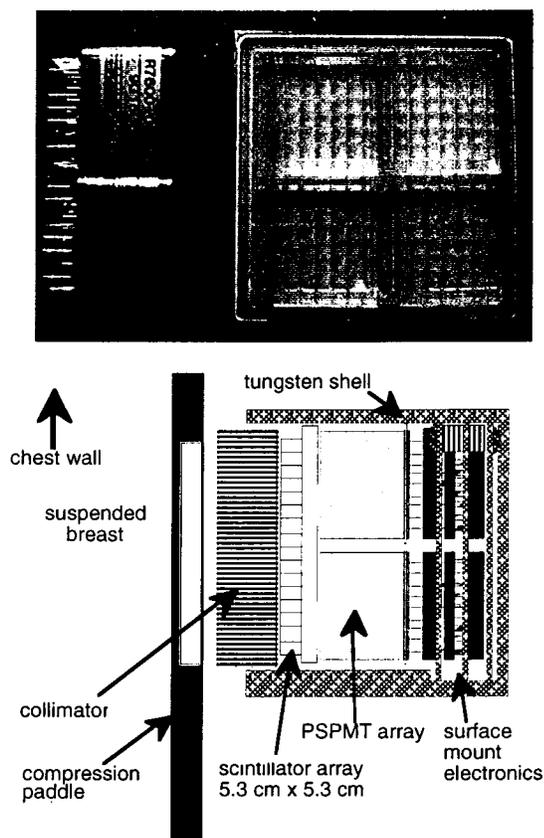


Figure 1: The top photo shows two of the PSPMTs and the NaI(Tl) crystal array with the light guide in place. The bottom figure is a schematic of the mini gamma camera detector head.

With a high sensitivity lead collimator, the computed resolution of the gamma camera at the collimator surface is 3.8 mm FWHM as confirmed by phantom measurements. The gamma camera sensitivity is 4000 cps/mCi. As mentioned above, the compact gamma camera is attached to a Fischer Imaging Inc. digital x-ray stereotactic biopsy system that is housed at Riverside Diagnostic and Breast Imaging Center.

The data acquisition system is based on an Apple Macintosh G3 workstation installed with a National

Instrument's Inc. [15] four channel ADC PCI card model PCI-6110E that is controlled by a software product called Kmax from Sparrow Corporation [16]. The system is capable of saving the imaging data in list mode for later replay. The final image overlay of the Fischer digital x-ray image and the gamma-ray image is achieved using the software application IDL [17] also running on the Macintosh.

A photograph and schematic diagram of the clinical setup is shown in Figure 2. During the positioning of the patient and the acquisition of the digital x-ray views, the mini gamma camera is usually removed from the system.

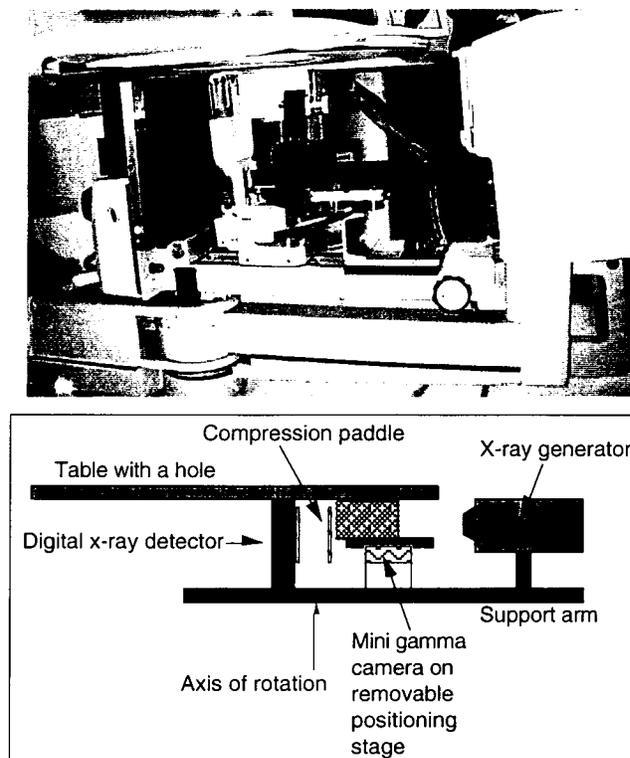


Figure 2: The top photo shows the mini gamma camera (white rectangular box) in place in the Fischer core biopsy table. The schematic on the bottom indicates the geometry of the arrangement.

III. METHOD

As mentioned above, the women included in this Riverside Regional Medical Center IRB approved study were individuals who have been scheduled for breast biopsy because of suspicious regions identified on their mammograms. As is the case in all stereo biopsy procedures, these volunteers were scheduled for a pre-op procedure one or two days prior to the actual biopsy operation. On the pre-op visit the patient is normally positioned on the stereo table, the breast compressed and three digital x-ray views are obtained: a straight-on scout view and two stereo views (+ and - 15 degrees). These views are taken to plan for the actual biopsy procedure. The study patients, while still under compression, are then injected with 25 mCi (925 MBq) of ^{99m}Tc-sestamibi which Dupont markets as MiraLuma and imaged for 10 minutes first with our mini gamma camera and after with the standard Toshiba model

GCA-901A gamma camera equipped with a high resolution collimator. Initially, the image acquisition with the mini Jefferson Lab gamma camera was started within 1 minute after the total dose was injected. However, we have found that if a tumor is present it becomes visible rapidly and peaks within three to four minutes of the injection of the dose. The mini gamma camera image acquisition is started just seconds before the dose is injected. The data acquisition system is capable of storing the time stamped event data in list mode for later replay to obtain a dynamic imaging record of the uptake of the Dupont radio-pharmaceutical MiraLuma in the area being imaged. This has allowed us to replay the data at any chosen time interval to investigate possible characteristic differences of the dynamic nature of the MiraLuma uptake for different types of tumors.

IV. CLINICAL STUDIES

Presently we have had approximately 25 study patients. Of those, there have been five cases where there has been a positive result from the mini gamma image which revealed a "hot spot." In these cases the mini gamma camera region of maximum MiraLuma uptake was well correlated with the region of interest from the digital x-ray. Of these five cases there was one case where the region of interest on the digital x-ray correlated to an enhanced uptake of MiraLuma but the biopsy revealed the lesion was benign (see Figure 4). Also, in one case, a region of enhanced uptake of MiraLuma was found un-correlated to the region of interest and the biopsy revealed that it was non-malignant and classified as focal intraductal hyperplasia. There have been no cases where the mini gamma camera returned a negative result and the tissue biopsy revealed cancer; in other words, there have been no false negatives.

A. Initial Cases

In the following, we highlight four cases which resulted in a positive focal uptake of MiraLuma. In each of the cases the patient was first positioned, her breast placed under compression and the technologist using the mammogram films located the suspected region with the Fischer digital x-ray system. Two stereo views (-15° and +15°) and one scout (0° to the normal) were obtained. After the radiologist was satisfied with the information required for the actual biopsy, the patient was then injected with MiraLuma and the gamma imaging started. The duration of the image acquisition for each case is 10 minutes. After the image data acquisition the patient was moved to a room housing a Toshiba standard clinical gamma camera. The patient was placed in the standard scintimammography prone position on a table with the breasts hanging dependently. The patient was then imaged again for 10 minutes with the standard clinical gamma camera.

The four images shown in each of the following (Figures 3 through 6) proceeding clockwise starting at the top were obtained with the Toshiba camera (top-left), the mini gamma camera (top-right), digital core biopsy x-ray (bottom-left), and

a co-registered overlay image of the mini gamma camera image with the digital x-ray blue image (bottom-right).

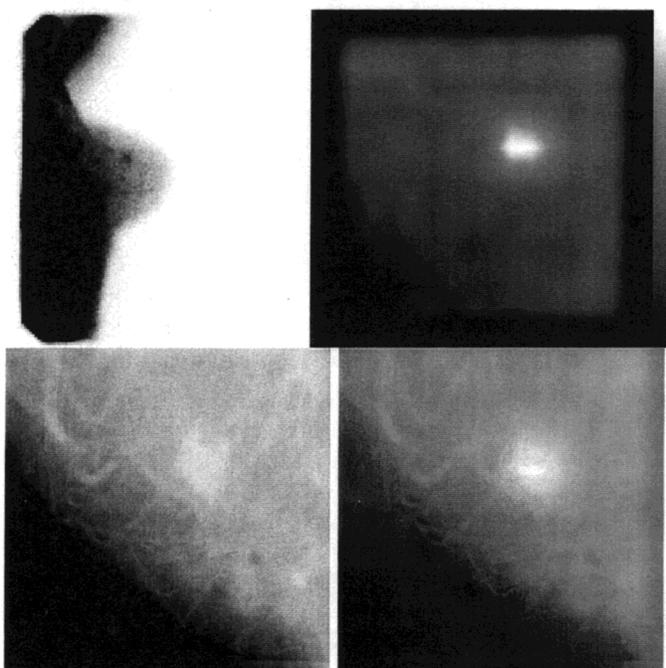


Figure 3: Case 11. A compression of 8 cm with a CC view of the right breast was used for this 175 lb., 68 year old patient. The Toshiba camera image shows only a weak evidence of lesion, the dedicated camera shows strong signal. The biopsy confirmed positive breast lesion classified as an intraductal carcinoma cribriform type.

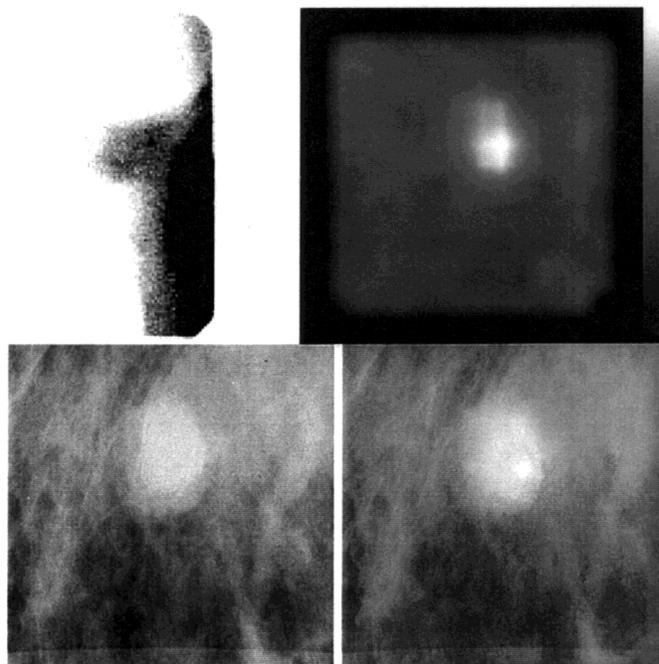


Figure 4: Case 14. A compression of 7 cm with a 60° MLO view of the left breast was used for this 196 lb., 39 year old patient. The Toshiba camera image shows evidence of a lesion, the dedicated camera shows strong signal. The biopsy returned negative for a malignancy. The benign lesion was classified as cellular fibroadenoma.

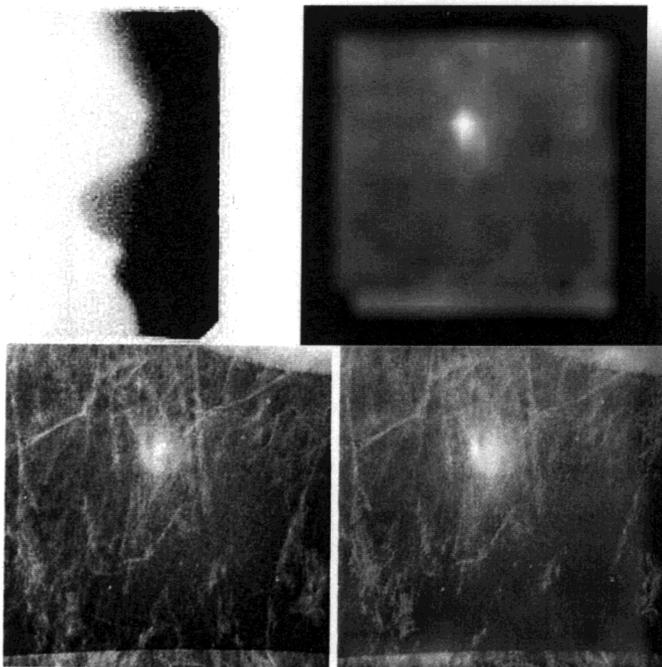


Figure 5: Case 18. A compression of 7 cm with a CC view of the left breast was used for this 180 lb., 77 year old patient. The standard camera image shows no evidence of a lesion, whereas the dedicated camera shows uptake correlated with the suspected lesion. The biopsy returned positive for a malignancy for the suspected region. The lesion was classified as invasive ductal carcinoma, well differentiated and 0.8 cm in size.

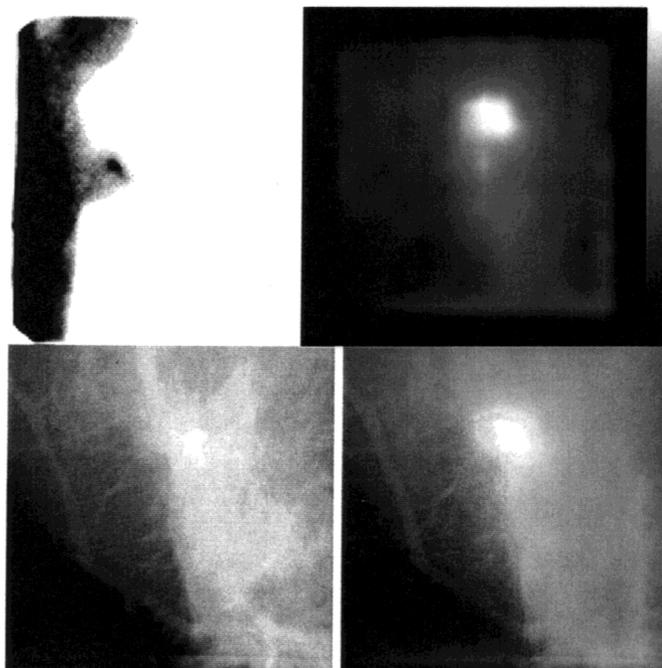


Figure 6: Case 20. A compression of 6 cm with a CC view of the right breast was used for this 192 lb., 56 year old patient. The standard camera image shows evidence of a lesion, the dedicated camera shows uptake correlated with the suspected lesion. The biopsy returned positive for a malignancy with the lesion classified as an infiltrating carcinoma, predominantly lobular and 2.8cm in size.

B. Dynamic Imaging

As mentioned above, it is possible for us to replay imaging data obtained with the mini gamma camera that was stored on the hard disk of the Macintosh G3 workstation. We have developed an analysis program using IDL that allows the user to select the time interval desired to generate a time series of images. It is also possible to select regions of interest (ROIs) to develop a time activity curve for the chosen ROI.

By replaying the event data taken during the patient study shown in figure 6 a time series of images was obtained with the mini gamma camera. This is shown in Figure 7.

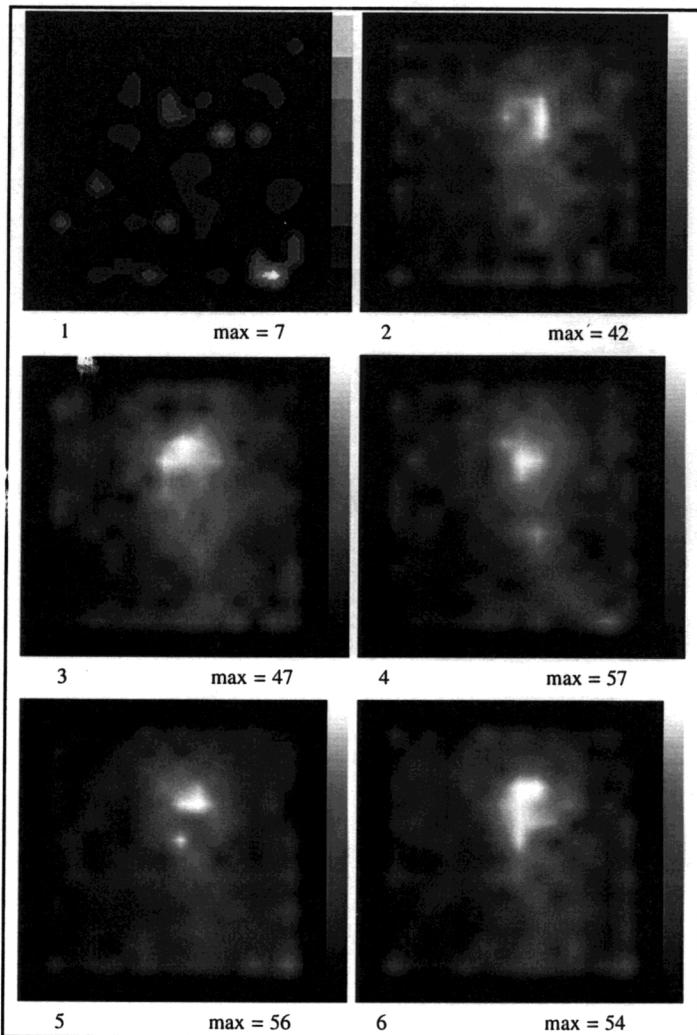


Figure 7: A time series of images obtained with the mini gamma camera for the case shown in Figure 6. Each image represents an acquisition time of 1 minute. The number of counts in the maximum pixel is indicated.

The series of images represent the first 6 minutes of image acquisition that was started just as the 25 mCi (925 MBq) dose of MiraLuma was injected intravenously into the patient's arm. Each of the images represents a new image acquisition taken every minute for time of 1 minute. It is clear from the images that the image of the tumor becomes visible within

two minutes after the injection. In Figure 8 is a plot showing the dynamic nature of the uptake of MiraLuma by the lesion that is shown in the series of images in figure 7.

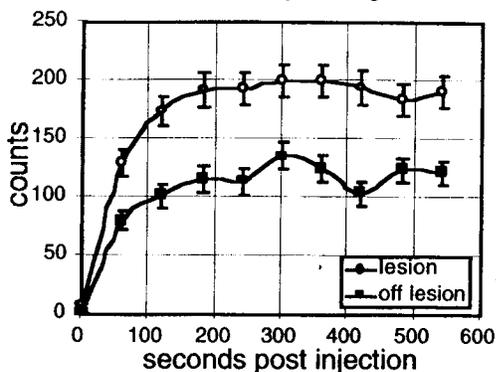


Figure 8. Time activity curve for a 1cm square region of interest centered on the lesion and one centered just to the right and completely off the lesion

V. CONCLUSION

We have described the development of a dual modality imaging system based on a compact gamma camera that is mounted to a commercial digital x-ray stereotactic core biopsy system. The system is presently being used to gather clinical data on the reliability of scintimammography in predicting the malignancy of suspected breast lesions. Preliminary results show that of the six cases which indicated a lesion with high uptake of the MiraLuma, five proved to be positive for cancer based on the pathology report. The scintimammography results indicate that the lesions become visible with the mini gamma camera within 3 minutes post injection of MiraLuma.

ACKNOWLEDGMENTS

We thank the entire staff at the Riverside Diagnostic and Breast Imaging Center. In particular we acknowledge the valuable assistance of Gail Geer and Vonda Firth who are the mammographers responsible for the Fischer system; Cindy Stevenson and Jenine Chapman who were the nuclear technologists who handled the dose injections and gamma cameras; and Lisa Grounds and Tanya Smith for providing nursing support. We thank Christopher Cuevas, Bill Gunning and Delisa Smith of the Jefferson Lab Fast Electronics Group for their valuable assistance with the electronics. Thanks also go to Gail Franco for the machining of mechanical components of the detector head. We thank Dupont Inc. for donating the needed doses of MiraLuma. Bicron Corporation's Mark Lowdermilk and Daniel Herr and Hamamatsu Photonics' Edward Baro and Earl Hergert are thanked for providing us in a timely fashion with their high quality scintillator arrays and PSPMTs, respectively.

REFERENCES

[1] Fischer Imaging Corporation, Denver Colorado.
 [2] J. Villanueva-Mayer, M.H. Leonard Jr., E. Briscoe, F. Cesani, S.A. Ali, S. Rhoden, M. Hove and D. Cowan,

"Mammoscintigraphy with Technetium-99m-Sestamibi in Suspected Breast Cancer," *J. Nucl. Med.*, vol. 37, no. 6, pp. 926-930, 1996.
 [3] D.B. Kopans, "The positive predictive value of mammography," *Am. J. Roentgenology*, 158, pp. 521-526, 1992.
 [4] I. Khalkhali, I. Mena, L. Diggles, "Review of imaging techniques for the diagnosis of breast cancer: a new role of prone scintimammography using technetium-99m sestamibi," *Eur. J. Nucl. Med.*, vol. 21 no. 4, pp. 357-362, 1994.
 [5] I. Khalkhali, I. Mena, E. Jouanne, L. Diggles, R. Venegas, J. Block, K. Alle, S. Klein, "Prone scintimammography in patients with suspicion of carcinoma of the breast," *J. Am. Coll. Surg.*, vol. 178(5) pp. 491-497, 1994.
 [6] I. Khalkhali, J.A. Cutrone, I.G. Mena, L.E. Diggles, R.J. Venegas, H.I. Vargas, B.L. Jackson, S. Khalkhali, J.F. Moss, S.R. Klein "Scintimammography: the complementary role of Tc-99m sestamibi prone breast imaging for the diagnosis of breast carcinoma," *Radiology*, vol. 196(2) pp. 421-426, 1995.
 [7] J. Tolmos, J.A. Cutrone, B. Wang, H.I. Vargas, M. Stuntz, F.S. Mishkin, L.E. Diggles, R.J. Venegas, S.R. Klein, and I. Khalkhali, "Scintimammographic analysis of nonpalpable breast lesions previously identified by conventional mammography," *J. Nat. Can Inst.* 90, pp. 846-849, 1998.
 [8] F. Scopinaro, R. Pani, G. De Vincentis, A. Soluri, R. Pelleprini, L.M. Porfiri, "High-resolution scintimammography improves the accuracy of technetium-99m methoxyisobutylisonitrile scintimammography: use of a dedicated gamma camera," *Eur. J. Nucl. Med.*, vol. 26, pp. 1279-1299, 1999.
 [9] I. Khalkhali, F.S. Mishkin, L.E. Diggles and S.R. Klein, "Radionuclide-Guided Sterotatic Prebiopsy Localization of Nonpalpable Breast Lesions with Normal Mammograms," *J. Nucl. Med.*, vol. 38, pp. 1019-1022, 1997.
 [10] L. Liberman, J.H. Smolkin, D.D. Dershaw, E.A. Morris, A.F. Abramson, and P.P. Rosen, "Calcification retrieval at stereotactic, 11-gauge, directional, vacuum-assisted breast biopsy," *Radiology*, vol. 208, pp 251-260, 1998.
 [11] Hamamatsu Corporation, Bridgewater, NJ
 [12] Bicron, Newbury, OH.
 [13] Dr. Mark Williams, Dept of Radiology, University of Virginia Medical Center, Charlottesville, VA.
 [14] M.B. Williams, A.R. Goode, V. Galbis-Reig, S. Majewski, A.G. Weisenberger and R.J. Wojcik, "Performance of a PSPMT based detector for scintimammography," *Phys. Med. and Biol.*, 45, pp.781-800, 2000.
 [15] National Instrument's Incorporated, Austin Texas.
 [16] Sparrow Corporation, Starkville, MS.
 [17] Research Systems Incorporated, Boulder, Colorado.