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Advantages of a Dual-Head CZT System for Molecular Breast Imaging

Douglas J. Wagenaar, Gina Caravaglia, Michael O'Connor†, Carrie Hruska†, Bradley E. Patt

Northridge, CA, USA and Oslo, Norway; †Mayo Clinic, Rochester, MN
http://gm-ideas.com

ABSTRACT

Single photon nuclear imaging of the whole body and the myocardium is now exclusively by dual-headed systems. The only rationale for the use of dual heads is a doubling of counts acquired or a halving of imaging time. Preliminary clinical results with a dual-head breast scanner demonstrate that several advantages far beyond a simple doubling of counts can be exploited. Most importantly, the fall-off of spatial resolution with distance allows low-contrast lesions located opposite a single detector to be lost in noise, whereas a second detector will find this lost lesion due to its proximity. Several cases of increased sensitivity are presented to accentuate this elegant finding. Secondly, two opposing views offers two samplings of spatial resolution and thereby a method to localize the lesion in depth as well as to estimate the blur-free lesion size (partial volume correction) through resolution recovery. Depth localization and lesion size allows attenuation correction and quantitation of tracer uptake to be computed. Thus a simple opposing view hardware design can provide quantitative evaluation of hot lesions in the breast for any of the variety of new radiopharmaceuticals that are under development for molecular imaging of breast cancer. This "Molecular Breast Imaging" tool's performance is further enhanced through the use of semiconductor CZT in the LumaGem™ (GMI), which has superior energy resolution performance resulting in scatter rejection and uniform-appearing images from chest wall to nipple. Clinical examples of CZT's superior scatter rejection are shown. Finally, the data acquisition method is upright, mammography-type to provide patient familiarity and comfort since the compression is mild compared with that of x-ray. Examples are shown of cranio-caudal and medio-lateral views that are rendered in a format that is easily compared with their corresponding digital mammography images.

INTRODUCTION

The evolution of gamma camera technology has resulted in the introduction of a Cadmium Zinc Telluride (CZT)-based Molecular Breast Imager. It has long been known that functional imaging has brought a new light to breast cancer interpretation, however identifying occult breast lesions that are small and located deep within the breast tissue was difficult with conventional gamma cameras. Dedicated breast units demonstrate better results; however image contrast and resolution are not at their peak. The new CZT detectors are compact units that offer superior energy resolution and spatial resolution with minimal dead space, allowing the closest access to the chest wall. Researchers at the Mayo Clinic and Gamma Medica have designed a dual-headed CZT camera that improves lesion detection sensitivity. Two studies are currently being conducted at the Mayo Clinic using the dual-headed CZT camera. The first study analysis the sensitivity of the dual-headed CZT camera in lesions less than 20mm.The second study investigates the capabilities of the dual-headed CZT camera as a screening modality for women with radiographically dense breasts (which turns out to be a significant breast cancer risk factor) . Preliminary results indicate that the lesion detection sensitivity of the CZT dual-headed camera for lesions less than 10 mm in size is >85%. Use of Molecular Breast Imaging for screening of women with dense breast tissue may be an efficacious first use for this promising modality (see Appendix).

MATERIALS AND METHODS: CZT

Conventional scintimammography has an overall sensitivity of 80% -85%; however these values drop significantly in lesions less 15mm. Sensitivity is approximately 55% for masses <15 mm and 35-64% for lesions <1 cm [Taillefer, 1999; Howarth 1999; Lumachi 2001; Brem 2002]. The visualization of lesions less than 10mm is important because the chance of metastatic disease is relatively constant below this size. Metastatic disease will be present in about 20% of primaries found between 0-5 mm and 5-10 mm, dramatically increasing once the primary is >10 mm. Thus early cancer detection significantly lessens the mortality and morbidity of the disease. The conventional gamma camera's lack of sensitivity is due to its bulky design allowing poor access to the breast and hence poor spatial resolution. Another important limitation in lesion detection of conventional gamma cameras is the use of NaI, which has an energy resolution for 140 keV of 9-10%. Superior rejection of scattered radiation can be expected through the use of detector material with improved energy resolution.

The first-generation dedicated breast cameras developed by Gamma Medica Ideas have significantly improved breasting imaging (Patt 1998; Itti 2003). They produced better images by introducing pixellated sodium iodide crystals and allowing closer access to the breast and the chest wall. Spatial resolution was dramatically improved by the combination of intrinsic resolution contribution and the allowed close-proximity. Furthermore, sensitivity for detecting occult breast lesions in a high risk screening population was shown to increase (Coover, 2004). The smallest lesion detected was 5mm.

The use of semiconductor CZT for nuclear breast imaging was first proposed by Singh (1998). Progress in the development of this technology led to further use of CZT for breast imaging by Tornai (2002) and Eisen (2002). The Tornai group included GMI scientists Parnham and Patt (co-authors on the present work), and the technology of the 2002 report is retained by GMI in the prototype used to produce the results for this poster. The close proximity afforded by the use of solid-state detectors means the intrinsic resolution of the detector will have a greater influence on the observed "extrinsic" resolution. For this reason, it was desirable to reduce the pixel pitch of the CZT camera from 2.5 mm to 1.6 mm (Tornai 2005). Figure 1 shows the two generations of CZT modules developed by GMI. Figure 2 shows a 5 module x 5 module CZT detector and associated circuitry. Figure 3 shows the improvement in energy resolution and photopeak fraction for 1.6 mm pixel CZT compared with two pixellated NaI detectors. The energy resolution advantages of CZT have been reported [Cutler, 2005], and for a simulated 7 mm lesion in as a function of breast thickness CZT outperforms NaI in an observer study (see Figure 4).

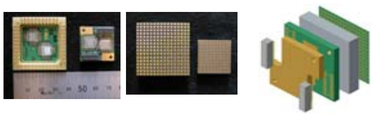

Figure 1. The ASIC electronics for the 16x16 pixel detectors are shown at the left for both the 2.5 mm and the 1.6 mm CZT modules. In the center, the corresponding pixel patterns for the two modules are shown. At the right, the module assembly is depicted, from the electronics to the cathode plate.

Figure 2. A 5 module x 5 module CZT detector and associated electronics. The detector is shown with the collimator removed. Each module is 2.54 cm x 2.54 cm.

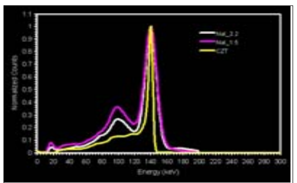

Figure 3. 140 keV spectra for CZT and two pixellated NaI cameras

CZT	NaI 1.5 (Pink)	NaI 2.2 (White)
6.5 keV (4.6%)	16.8 keV (12%)	18.5 keV (13.2%)

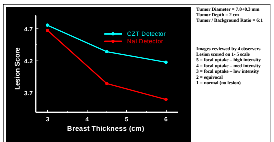

Figure 4. Conspicuity of a 7 mm lesion as judged by 4 observers with CZT (upper curve) and NaI (lower). Contrast is enhanced in CZT by the combination of the rejection of scatter and the high intrinsic spatial resolution.

CLINICAL TRIALS AT MAYO CLINIC

Clinical molecular breast imaging studies with CZT have been ongoing since 2004 with a 100 patient study of women with BI-RADS 4 or 5 (high likelihood of cancer diagnosis) on mammography and < 20 mm lesion size, to show the improvement in lesion detectability over scintimammography due to detector material and access to breast tissues. Mild compression is applied, and a mammography-like gantry allows the acquisition of cranio-caudal and medio-lateral views. Compression stabilizes the breast against motion, spreads the tissues to fill more of the field-of-view and reduce overlapping structures, and reduces thickness and hence scatter. Figure 5 shows a typical lesion detected with Tc-99m sestamibi in the CZT (LuamGem™) study at Mayo Clinic. The detector head in this study has a 20.3 cm x 15.2 cm field-of-view and utilizes a general purpose parallel hole collimator (270 cpm/μCi).

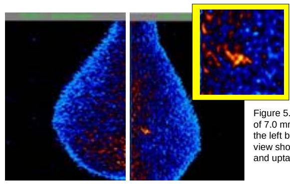

Figure 5. Medio-lateral view of 7.0 mm cancerous lesion in the left breast. Cranio-caudal view showed similar shape and uptake appearance.

Figures 5 and 6 demonstrate the imaging capability of CZT detector technology in detecting small breast lesions. Figure 5 demonstrates visualized structure that appears to mimic the spiculations associated with breast cancer; Figure 6 demonstrates the ability to visualize a pathology-proven 3.7 mm lesion.

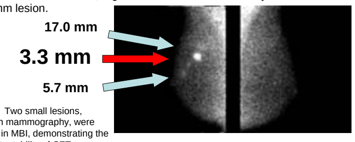

Figure 6. Two small lesions, unseen in mammography, were detected in MBI, demonstrating the lesion detectability of CZT camera.

DUAL-HEAD MBI

The overall detectability of breast lesions was shown to improve through the use of dual-heads (McElroy, 2002; Kieper, 2002). Figure 7 demonstrates with a breast-like phantom and realistic lesion and background radioactivity levels how small lesions can be missed due to their distance from the camera surface. The simple premise of dual-headed molecular breast imaging is that lesions can be no farther than ½ the thickness of the breast from a detector. A dual-head CZT prototype based on CZT detectors from the LumaGEM™ (Gamma Medica-Ideas, Inc.) has been assembled at the Mayo Clinic. Figure 8 is a photograph of this device. Again, both mammographic views can be obtained with this prototype, and compression is 1/3 the pressure as that of mammography.

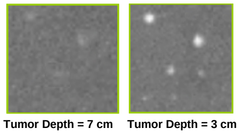

Figure 7. The principle behind the improvement in small lesion detectability with dual heads is shown here. Smallest lesions must be close to the detector to be visible.

Figure 8. The dual-head CZT prototype in use at the Mayo Clinic.

Figure 9. The advantage of dual-head MBI is demonstrate in these images, where the 6.0 mm lesion in the left breast is only well seen in the images from the upper detector.

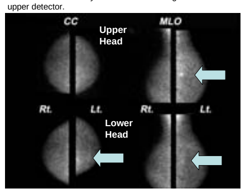

Figure 9 clearly demonstrates the advantage of the dual-head system in improving the detection of lesions that are located in the upper inner quadrant of the breast. In the CC view from the lower detector, there appears to be a suspicious brightness near the chest wall, ¼ from the bottom of the image. The lower detector MLO view, shows only a faint hint of a lesion. However the upper detector, which is close to the upper inner quadrant of the breast clearly shows the small 6 mm lesion close to the chest wall.

This lesion was found to be a 6 mm invasive ductal carcinoma at surgery. This is an example of the encouraging results that have led to a new 2000-patient screening study comparing MBI to mammography in women at high risk of breast cancer with dense-breast tissue. Preliminary results in the first 155 patients from this screening study, have found a total of 4 tumors as well as one case of atypical ductal hyperplasia in 155 subjects. Only one of these was detected on conventional mammogram.

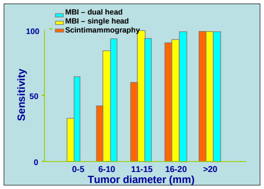

Figure 10. Detection sensitivity of small lesions (6-10 mm) is at or above 90% for the dual-head CZT prototype.

SUMMARY

The preliminary detection sensitivity values are plotted in Figure 10 as a function of lesion size. This figure shows the progression of technology: scintimammography could not reliably detect lesions less than 15 mm; single-head CZT could reliably detect lesions down to 6 mm. The dual-head CZT based on the LumaGem™ shows high sensitivity for the detection of lesions < 6 mm. Both single and dual head systems (more so for the dual head) promise to be able to detect lesions in the important early growth stage at which the disease is most treatable. This technical capability opens the door to the study of other breast imaging radiopharmaceuticals that are under investigation (see Appendix). Future work involves additional processing of the data; combining the two views to form a single view, evaluating the depth of the lesion based upon measured signals from the two heads, correcting for attenuation, and recovery of resolution.

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APPENDIX

The results of this poster demonstrate high lesion detectability for sizes less than 10 mm for Tc-99m MIBI. Other biological processes can and will be imaged in the future of Molecular Breast Imaging.

TYPE	Trade Name	Name	Nuclide	Author	Institution	Process Targeted
Antibody						
		HIS_6-$(Z_{HER2:4})_2$	^{99m}Tc; ^{125}I	Orlova (2006)	Uppsala, Sweden	HER2 receptor
	CEAScan	Anti-CEA	^{99m}Tc	Lind (1991)		
	Oncoscint		^{111}In			
		Anti-EGFR				
Peptide						
	NeoSPECT	depreotide	^{99m}Tc	Many	GE-Amersham	Neuroendocrine
	OctreoScan	octreotide	^{111}In	Many	Mallinckrodt	Neuroendocrine
	Bombesin	Gastrin Rlsng	^{177}Lu	Hoffmank (2005)	Univ Missouri	
	Bombesin	Gastrin Rlsng	^{99m}Tc	Soluri (2003); Scopinaro (2002)		Gastrin
Chemotherapy						
		Tamoxifen	^{123}I	Van De Wiele		Monitor therapy
Hormone						
		Estradiol	^{123}I			Hormone receptor
Lipophilic/Cationic						Mitochon metab
	Miraluma[1]	Sestamibi	^{99m}Tc	Many	Bristol-Myers Squibb	
	Myoview	Tetrofosmin	^{99m}Tc	Spanu (2002)	GE-Amersham	
Protein						
	Apomate	Annexin-V	^{99m}Tc	Many	Theseus	Apoptosis
Factor						
	Vit B-9	Folate		Mueller (2005)	P Scherrer Institute	
	Vit B-12	Folic Acid				
Metab./Perfusion						Glucose met.
		Thio-glucose	^{99m}Tc		Ohio St Medical	
		EC-DG	^{99m}Tc		Cell Point	
		Glucarate	^{99m}Tc	Liu (2004)		Injury/Infarct
	Ceretec	Exametazine	^{99m}Tc	Wilczek (2004)	GE-Amersham	Perfusion
CLINICAL NM						
		MDP	^{99m}Tc			
	Tl-chloride	Thallium	^{201}Tl	Sehweil (1989)		ATPase pump
		(V) DMSA	^{99m}Tc	Papantoniou (2005)		

[1] Miraluma was removed from the market for breast cancer imaging by Bristol-Myers Squibb in 2005.