Low-Dose Molecular Breast Imaging for Women with Radiographically Dense Breast Tissue

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Purpose

1 - Purpose

Molecular Breast Imaging (MBI) uses a new semiconductor (CZT) imaging detector in a dual-head configuration to optimize detection of small (<1.0 cm) lesions in early stage breast cancer.

The technique involves the intravenous administration of the radiopharmaceutical 99mTc-sestamibi (MIBI), which is the contrast agent of choice in more than 15 M nuclear cardiology studies annually worldwide. The combination of enhanced permeability and retention in neovasculature with mitochondrial metabolism produce uptake of MIBI in breast cancer lesions that is generally greater than 10:1 compared with background tissue uptake.

Because MBI detects cancers in women with radiographically dense breasts, this new modality has been proposed for use in screening of this population that is underserved by conventional mammography (MMG) due to poor sensitivity.

Screening MBI requires an analysis of the risk/benefit associated with the study. In comparison with screening MMG, the radiation dose from MBI is systemic, whereas in MMG the dose is concentrated within the breast tissue. The wholebody radiation dose from MBI is well documented due to nearly 20 years of nuclear cardiology with MIBI. The proposed screening application places demands upon the MBI modality to reduce the radioactivity necessary to detect small lesions in asymptomatic women. Our analysis, based on the NRC BEIR VII risk tables, concluded that a factor of ~6 reduction in radioactivity is necessary in order for MBI screening benefit/risk ratio to match that of MMG. From the standard 25 mCi injection, one must reduce the MBI injected activity to 3.5 mCi.
Methods and Materials

2. Materials and Methods

Molecular Breast Imaging

MBI is the non-invasive and quantitative imaging of cellular and molecular processes of normal and malignant breast tissue - with the use of an injectable contrast agent - to aid in detection, diagnosis, and treatment assessment.

CZT-based MBI Scanner

Semiconductor CZT

The 140 keV gamma-ray emissions from 99mTc are detected and localized by semiconductor CZT modules (Figure 1). The modules are arranged into two large (15.2 cm x 20.3 cm) plates each with a pixel array of 96x128 (at a 1.59 mm pitch). CZT has high energy resolution (<4.5% ~ 140 keV) for scatter rejection and dual-isotope applications. Our previous work [Pa 97] concluded that pixel pitch for parallel hole collimation is optimized at 1.5 mm.

Registered-hole, tungsten collimator

Figure 2 shows a photograph of the first near-field, registered tungsten collimator, now in use at the Mayo Clinic. Each of the 12,288 holes is registered (or aligned) with a CZT pixel. Sensitivity is improved by covering the pixel edges and shortening hole depth for near-field (<3.0 cm) optimized imaging.

Gamma Medica's LumaGEM™

Figure 5 is a photograph of the dual-head LumaGEM™ (Gamma Medica, Northridge, CA) MBI scanner. It is capable of obtaining crano-caudal (CC) and medio-lateral oblique (MLO) views of a seated female patient by moving the pair of detectors to the correct vertical height (using vertical tower motion) and the correct orientation (CC or MLO) using the circular track shown in Figure 3. Four views of 10 minutes are acquired; compression is light and comfortable (15 lbs compared with 45 lbs for MMG).

BEIR VII Risk Calculations

Excess Absolute Risk (EAR), Lifetime Attributable Risk (LAR)
The BEIR VII report [NRC 06, Chapter 12] prefers the EAR model for estimation of induced breast cancer risk [Law 01]. This model was used to compare cancer incidence and mortality for positron emission tomography (PEM) as well as the 99mTc-MIBI single-photon nuclear technique. Lifetime attributable risks (LAR) are estimated by summing EAR estimates for each year of life after exposure [OC 10a].

The LAR estimates were adjusted for the fraction of a population of 100,000 females expected to survive to various ages between 0-80. EAR was calculated from Equation 12-2 of the BEIR report; LAR was constructed by summing EAR at each age, with weighting for survival. PEM and MBI dose estimates were taken from published sources [Ha 02]. An average level of background radiation in the U.S. is estimated at 3.1 mSv [NCRP 09]. Estimates of lifetime attributable risk of cancer incidence and cancer mortality were calculated for PEM, MBI, Digital Mammography, Screen-Film Mammography, and Background (without medical tests).
Fig. 0: Figure 1. The 2.54 cm x 2.54 cm (1” x 1”) CZT imaging module has an array of 16 x 16 pixels (1.59 mm pitch). The CZT is 5 mm in thickness.

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**Fig. 0:** Figure 2. The concept of the "registered" collimator is shown. Each pixel (gold contact at the top of the CZT detector) is aligned with a collimator hole. This effectively removes the intrinsic resolution from the system spatial resolution.

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Fig. 0: Figure 3. The near-field, registered tungsten collimator shown on a single CZT detector head (15.2 cm x 20.3 cm field-of-view). A protective cover and sterile padding are routinely used for clinical imaging (not shown).

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Fig. 0: Figure 4. The collimator is optimized to a distance of one-half of the average breast thickness - i.e., a distance of 3.0 cm. This optimization is detailed by Weinmann [We 09], and results in a peak count efficiency for the registered collimator at slightly less than 1.5 mm pixel pitch. Detectors with larger pixels will have lower efficiencies, as shown in Figure 4. The higher the detection efficiency, the lower the dose required (or, equivalently, the lower the acquisition time per view).

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**Fig. 0:** Figure 5. The LumaGEM scanner (Gamma Medica, Northridge, California, USA) shown in the craniocaudal imaging position. Medio-lateral oblique (MLO) views are obtained by moving the two heads along the arc to an orthogonal position.

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<table>
<thead>
<tr>
<th>Modality</th>
<th>Radiation</th>
<th>Dose / year</th>
<th>Risk*: Attributable Deaths / 100,000</th>
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<td>540</td>
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<td>&gt;8** mCi $^{99}$mTc-MIBI</td>
<td>~2.4 mSv</td>
<td>140</td>
<td>~2200**</td>
<td>~16:1</td>
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<td>GammaMedica LumaGEM™</td>
<td>2-4 mCi $^{99}$mTc-MIBI</td>
<td>~0.6-1.2 mSv</td>
<td>36-72</td>
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**Fig. 0**: Figure 6. Comparison of the benefit/risk ratios of breast-screening modalities that have radiation dose associated with the studies.

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**Fig. 0:** Figure 7. Top row shows cranio-caudal mammogram (left) and MBI with 7 mm lesion at right. Bottom row shows medio-lateral mammogram (left) with the associated MBI view (right). MBI is clearly positive; mammography was read as negative in both views. Courtesy of Dr. Michael O’Connor, Mayo Clinic.

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Results

Comparison of Benefit/Risk

Addressing the concerns

An important paper was published in 2010 by Hendrick in which wholebody radiation dose concerns were voiced about BSGI and other nuclear medicine scans breast scans such as PEM [He 10].

O'Connor's paper [Oc 10a] helped to put these concerns in perspective by calculating benefit/risk ratios of the various screening modalities based on the BEIR VII formalism described in Section 3. With the pixel size optimized at 1.6 mm, the detection efficiency is 3.6 times greater than that which was obtained with the standard high sens hex-hole collimator. Further dose reductions can be realized with the dual-head system through software that combines the conjugate views and uses resolution recovery and denoising [Oc 10b]. Sidebar Figure 1 (Figure 6) shows that LumaGEM with low-dose collimation and software can achieve nearly the same level of wholebody dose equivalent as a full four view mammography study.
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Conclusion

MBI Example: 7 mm Lesion

An ongoing screening study at Mayo Clinic with MBI in a cohort of patients with radiographically dense breast has reported promising results of a factor of three improvement in detection sensitivity over mammography in this population [Rh 10]. In Sidebar Figure 1 (Figure 7) we can see an example, courtesy of Dr. Michael O'Connor of the Mayo Clinic, of a 7 mm tubulolobular carcinoma confirmed on biopsy that was called negative on the mammogram. This example demonstrates the potential of MBI to be an effective alternative to mammography in these cases.

Takeaway Message:

Molecular Breast Imaging the LumaGEM can be done with sufficiently low wholebody radiation dose to be a viable screening tool for women with dense breast tissue.

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