What is Molecular Breast Imaging?
The basics of Functional Imaging

- Functional imaging is the detection of breast abnormality based on the **altered characteristic of the tissue**, rather than its altered morphology.

- A radioactive tracer is injected and **concentrates in hyper-metabolic** or cancerous tissues.

- A gamma camera acquires images of the tracer uptake facilitating **visualization of metabolic activity and disease**.

- Functional information is crucial to distinguish between a **viable vs non-viable** mass.

- Functional changes precede anatomical changes (1)
Nuclear Medicine captures Metabolic Activity within the Breast

• Nuclear Medicine tracer uptake in cancer cells is higher than normal tissue. \(^{(2,3)}\)

• When used as adjunct to Mammography, it is possible to get a complete picture, combining functional changes with anatomical changes.\(^{(1)}\)

• Image quality in NM is highly impacted by distance between the body and the detector.

The goal of MBI is to obtain the same image positioning as Mammography, but to capture tissue physiology rather than anatomy.
Nuclear Medicine Breast Imaging has Evolved

From... **LARGE** system with limited ability to detect 15-20mm breast lesions
To.... **SMALL** system with significant ability to detect ~5mm breast lesions

Scintimammography
- Large detectors
- Detectors far from breast
- Photomultiplier Tube; scintillation

Tumor detectability 15 – 20 mm

Breast Specific Gamma Imaging (BSGI) – Single Head
- Small detectors
- Detectors close to breast
- Photomultiplier Tube; scintillation

Sodium Iodide based detectors

Molecular Breast Imaging (MBI) – Dual head.
- Small detectors
- Detectors close to breast
- Direct conversion; no scintillation

Tumor detectability ~5 mm

CZT-based, Direct Conversion Detectors

DOC#1390262, May 2013
Nuclear Medicine Breast Imaging has Evolved

• 99mTc sestamibi cleared by the FDA for Scintimammography Breast Imaging in 1997

• Several large multi center studies undertaken in the late 1990s
  • Taillefer: Sem Nuc Med 29:16; 1999 - 2009 patients; **Sensitivity = 85%; Specificity = 89%**
  • Buscombe: NM communication 2006, 27: 589–594 - Meta-analysis of scintimammography: Multi center results of 3049 pts; **Sensitivity = 85%; specificity = 83%**

• Scintimammography sensitivity highly dependent on lesion size…lesions < 15 mm sensitivity = 55%
Impact of Tumor Size\textsuperscript{(4)}

Survival is considerably improved for women diagnosed with smaller tumors than those with larger tumors.

Breast cancer relative survival by size of cancer
Today’s Situation

Legend: 
Dx = diagnosis; Horm = hormonal therapy; Tax = taxane-containing regimen; Anth = anthracycline-containing regimen; Her2 = Her2 antagonist-containing regimen (lapatinib or trastuzumab; Bev = bevacizumab - containing regimen. All figures represent sum of US + EU5 patients at each stage presenting in 1 year. Numbers are directional and will be subject to further validation through Q4 2011. Sources: IntrinsiQ, IMA Oncology Analyzer MAT Q2 2011; DecisionResources Breast Cancer Pharmacor 2011, DaVinci, various literature sources.

Abridged Model
Patients

Work in Progress
MBI & the current profile of breast imaging

Screening
- Senographe* Essential Mammography
- Somov Automated Breast Ultrasound (ABUS*)

Diagnosis
- Senobright
- Logic* E9 Ultrasound
- Molecular Diagnostic Testing
- MR Guided Biopsy

Staging
- Discovery NM750b Molecular Breast Imaging
- Magnetic Resonance Imaging
- CT Patient Care

Treatment Planning
- Discovery* CT 590 RT & Optima* CT580 RT
- Discovery NM750b Molecular Breast Imaging
- Magnetic Resonance Imaging
- CT Patient Care

Monitoring
- PET VCAR
- Circular Tumor (CTC) Testing
- Discovery NM750b Molecular Breast Imaging
- MR Treatment & Monitoring
- CT Patient Care

Is there something? What is it? How severe is it? What’s next? Is it working?
Wide variety of indications for MBI

**Diagnosis**
- Dense breast diagnosis
- Equivocal exams
- Limited mammogram
- Breast implants
- Monitoring for recurrence
- Indeterminate breast abnormalities and remaining diagnostic concern

**Staging**
- Evaluating the extent of the disease
- Initial staging-detecting multi-centric, multi-focal, or bilateral disease

**Treatment monitoring and planning**
- Assessing response to neo-adjuvant chemotherapy
- Surgical planning for residual disease

Now you can tailor the choice of imaging modality to best fit your patient’s needs
Dense Breast Statistics\(^{(6)}\)

- Women with dense breasts have a 4 to 6 fold increased risk of developing breast cancer.
- 40% of women have dense breast tissue.
- Breast density is one of the strongest predictors of the failure of mammography to detect cancer.
- Mammography misses every other cancer in dense breasts.
- Breast density is a well-established predictor of breast cancer risk.
- Breast density is a greater risk factor than having two first degree relatives with breast cancer.

Medio-lateral oblique (MLO)

Image courtesy of Dr. Rangarajan. TMH, Mumbai, India.

DOC#1390262, May 2013
Dense Breast Legislation

- California, New York and Virginia have joined Connecticut and Texas in enacting legislation

- Endorsed bills in Pennsylvania, Maine, New Hampshire, New Jersey, South Carolina, Tennessee, Missouri, Kansas and Nebraska

- Efforts underway in Florida, Michigan, Ohio, Oregon and Delaware (7)
Breast Density affects mammography screening procedures

Dense breast tissue can overlap with lesions
Lesions are not always visible with x-ray
Multiple exams are required to confirm diagnosis
For dense breast, MBI technology outperformed mammography in early detection and in finding more cancers\(^8\)

<table>
<thead>
<tr>
<th>Breast Density (BI-RADS Scale)</th>
<th>D1</th>
<th>D2</th>
<th>D3</th>
<th>D4</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity of Mammo (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D1</td>
<td>98%</td>
<td>83%</td>
<td>64%</td>
<td>48%</td>
<td>78%</td>
</tr>
</tbody>
</table>

*MBI is intended as an adjunct to mammography or other breast imaging modalities (it is not intended for primary screening of the population)
Different types of tumors are seen by different modalities \(^{(18)}\)

<table>
<thead>
<tr>
<th></th>
<th>Calcification</th>
<th>Fibrous</th>
<th>Vascular</th>
<th>Metabolic</th>
</tr>
</thead>
<tbody>
<tr>
<td>CESM</td>
<td>+++</td>
<td>+</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td>Digital Breast Tomosynthesis</td>
<td>+</td>
<td>+++</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Mammography</td>
<td>+++</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>MBI</td>
<td>-</td>
<td>-</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>MRI</td>
<td>-</td>
<td>++</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>Ultrasound</td>
<td>+</td>
<td>+++</td>
<td>+</td>
<td>-</td>
</tr>
</tbody>
</table>

**Tumors Detected (In order of effectiveness):**
- Ductal Carcinoma In Situ (DCIS)
- Invasive Ductal Carcinoma (IDC)
- Invasive Ductal Carcinoma (IDC)
- Invasive Lobular Carcinoma (ILC)
- Lobular Carcinoma In Situ (LCIS)
- Lobular Carcinoma In Situ (LCIS)
- Ductal Carcinoma In Situ (DCIS)
- Invasive Ductal Carcinoma (IDC)
- Invasive Lobular Carcinoma (ILC)
- Lobular Carcinoma In Situ (LCIS)
- Ductal Carcinoma In Situ (DCIS)
## Clinical Challenges

<table>
<thead>
<tr>
<th></th>
<th>Mammogram</th>
<th>Ultrasound</th>
<th>MRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not sensitive to radiographically <strong>dense breast</strong> tissue</td>
<td><strong>Low specificity</strong> leading to unnecessary biopsies when used as an adjunct to Mammography(^9)</td>
<td><strong>Expensive</strong> examination</td>
<td></td>
</tr>
<tr>
<td>Uncomfortable for the patient requiring painful breast compression</td>
<td>Inability to distinguish between microcalcifications and malignant tumors(^10)</td>
<td><strong>Low specificity</strong> leading to unnecessary biopsies due to high false positives(^11)</td>
<td></td>
</tr>
<tr>
<td><strong>10% recall rate</strong> on an average with high false positives even after diagnostic mammogram</td>
<td></td>
<td><strong>Difficult examination for obese or claustrophobic women</strong></td>
<td></td>
</tr>
<tr>
<td>Total X-ray radiation dose to breast tissue for diagnostic patients (0.088 – 0.132 rem)</td>
<td></td>
<td><strong>Contraindications</strong> such as allergy to contrast, pacemakers, implants</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Difficulty for patient to remain in prone position through out procedure</strong></td>
</tr>
</tbody>
</table>

MBI used as an adjunct to Mammography and Ultrasound provides an additional tool for making a stronger diagnosis
50 yo patient with dense breasts, biopsy proven IDC grade III and metastases in axillary lymph nodes. Following neo-adjuvant treatment, tumor was reduced in size on ultrasound. MBI images showed no enhancement, indicating on successful treatment. Post Neo Adjuvant: Lt lumpectomy, Axilla dissection: Fibrosis, scarring and sclerosing adenosis. No residual tumor seen.
Molecular Breast Imaging & Implants

Images courtesy of Prof. Even-Sapir, Tel Aviv Sourasky Medical Centre, Israel
Few Facts on Nuclear Medicine Dose and MBI

• The intravenous injection of a radiotracer in Nuclear Medicine is a different type of radiation risk than mammography. It’s whole body radiation versus breast only radiation.

• Image quality depends on the image statistics. High image statistic can be achieved by:
  • Injecting higher dose …or…
  • Increasing the acquisition time …or…
  • Improving the detection efficiency

• New technologies are in place to improve the detector efficiency by getting the detector closer to the breast, increasing the system sensitivity ultimately resulting in the potential for lower injected dose.
## Radiation dose from common diagnostic imaging procedures

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Injected Activity</th>
<th>Effective Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screening &amp; Diagnostic Mammography</td>
<td>n/a</td>
<td>0.88-1.32 mSv</td>
</tr>
<tr>
<td>MBI/BSGI (Sestamibi)</td>
<td>20 mCi</td>
<td>6.7 mSv</td>
</tr>
<tr>
<td>Cardiac Perfusion Test</td>
<td>35 mCi</td>
<td>11.7 mSv</td>
</tr>
<tr>
<td>CT chest</td>
<td>n/a</td>
<td>7.8 mSv</td>
</tr>
<tr>
<td>Coronary CT (women)</td>
<td>n/a</td>
<td>10.2 mSv</td>
</tr>
<tr>
<td>PET (F-18 FDG)</td>
<td>10 mCi</td>
<td>11.1 mSv</td>
</tr>
<tr>
<td>CT abdomen &amp; pelvis</td>
<td>n/a</td>
<td>14.7 mSv</td>
</tr>
<tr>
<td>PET/CT</td>
<td>10 mCi</td>
<td>23.0 mSv</td>
</tr>
</tbody>
</table>
Is a Lower Dose Possible with MBI?

Extensive work at has been done to lower the current dose.

The following case studies from Tel Aviv Medical Center have been provided to show low dose MBI images.

These images are simulated by using time limited data obtained from the original full data set at nominal injected dose.
Case #1
Increased Sensitivity may allow reduced dose in future use

20 mCi Full data

2 tumor masses of invasive lobular carcinoma, with multifocal LCIS component.

2 lymph nodes show met. carcinoma
Case #1

8 mCi Equivalent

Images courtesy of Prof. Even-Sapir, Tel Aviv Sourasky Medical Centre, Israel

*Low dose images were simulated by using time limited data obtained from the full data set at nominal injected dose
Case #1

4 mCi Equivalent

*Low dose images were simulated by using time limited data obtained from the full data set at nominal injected dose.
Case #2
Increased Sensitivity may allow reduced dose in future use

20 mCi Full data

Images courtesy of Prof. Even-Sapir, Tel Aviv Sourasky Medical Centre, Israel
Case #2

8 mCi Equivalent

Images courtesy of Prof. Even-Sapir, Tel Aviv Sourasky Medical Centre, Israel

*Low dose images were simulated by using time limited data obtained from the full data set at nominal injected dose
Case #2

4 mCi Equivalent

*Low dose images were simulated by using time limited data obtained from the full data set at nominal injected dose.

Images courtesy of Prof. Even-Sapir, Tel Aviv Sourasky Medical Centre, Israel.
Sources

5. SNM Guideline for Breast Scintigraphy with Breast-Specific Gamma Cameras, Version 1.0 Published June 4, 2010
8. Deborah J. Rhodes, Carrie B. Hruska, Stephan W. Phillips, Dana H. Whaley, and Michael K.O’connor, Dedicated Dual-Head Gamma Imaging for Breast Cancer Screening in Women with Mammographically Dense Breasts, Radiology 100625; Published online November 2, 2010, doi 10.1148/radiol.10100625 *study was performed using detector prototype of Discovery NM 750b
9. ACRIN 666 trial reported “A substantial increase in the number of benign biopsies due to the addition of ultrasound compared to mammography alone”
10. Abstract BSGI vs Ultrasound: Jean M.Weigert RSNA 2008
Thank You