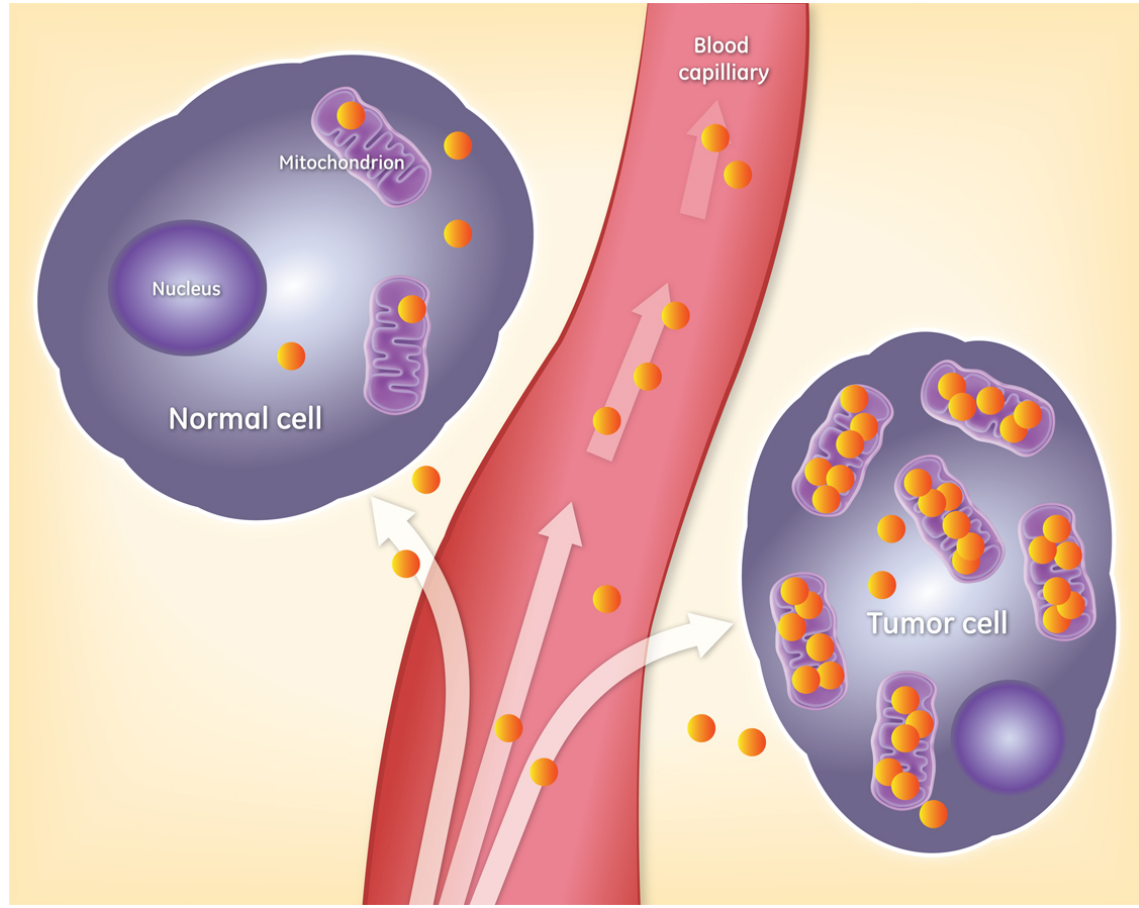
What is Molecular Breast Imaging?

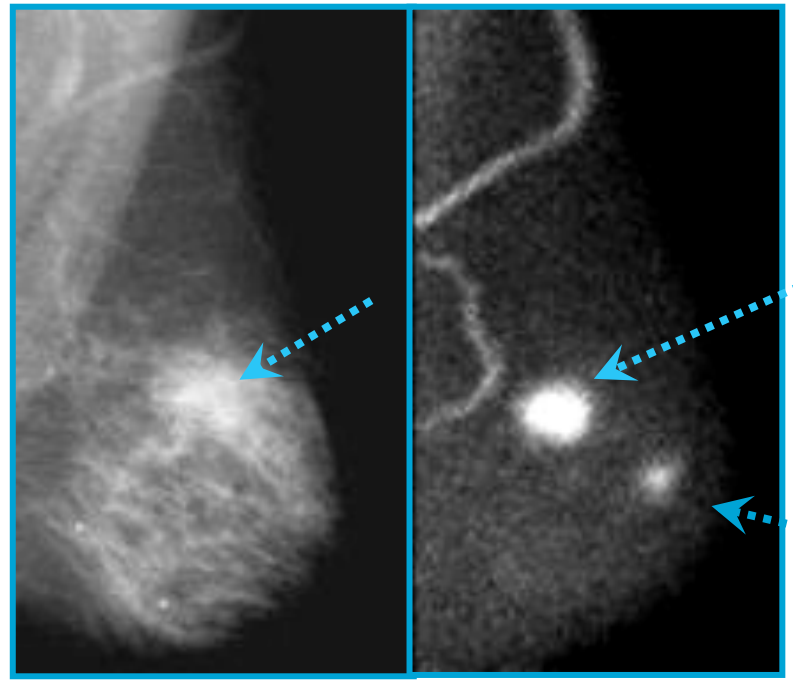
The basics of Functional Imaging

- 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

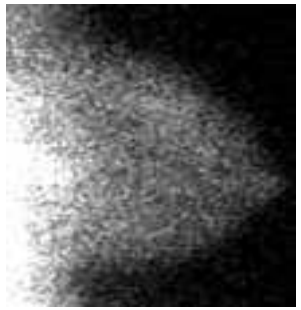


The goal of MBI is to obtain the same image positioning as Mammography, but to capture tissue physiology rather than anatomy.

Image Courtesy of Mayo Clinic Rochester Minnesota
DOC#1390262, May 2013

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

Sodium Iodide based detectors

Breast Specific Gamma Imaging (BSGI) – Single Head

- Small detectors
- Detectors close to breast
- Photomultiplier Tube; scintillation

Sodium Iodide based detector

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

Nuclear Medicine Breast Imaging has Evolved

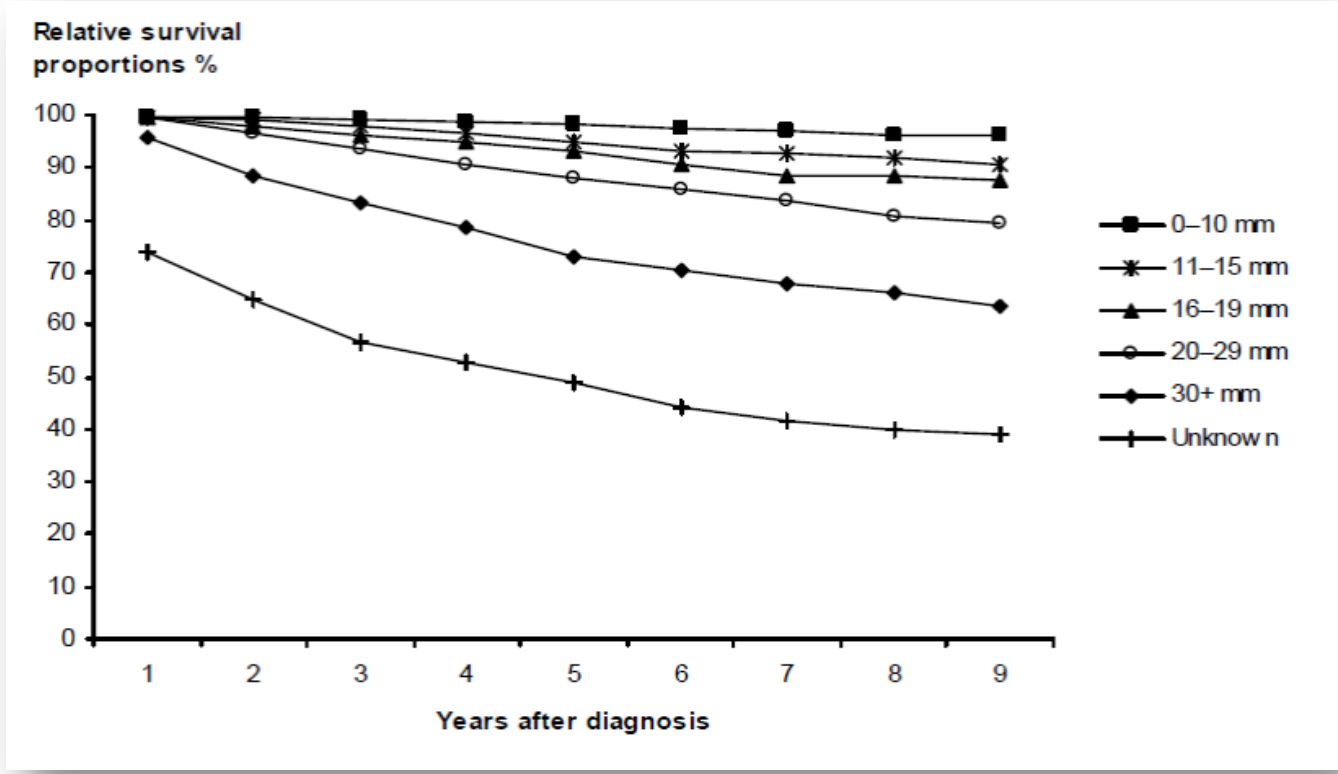
- 99mTc sestamibi cleared by the FDA for Scintimammography Breast Imaging in 1997

- 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%

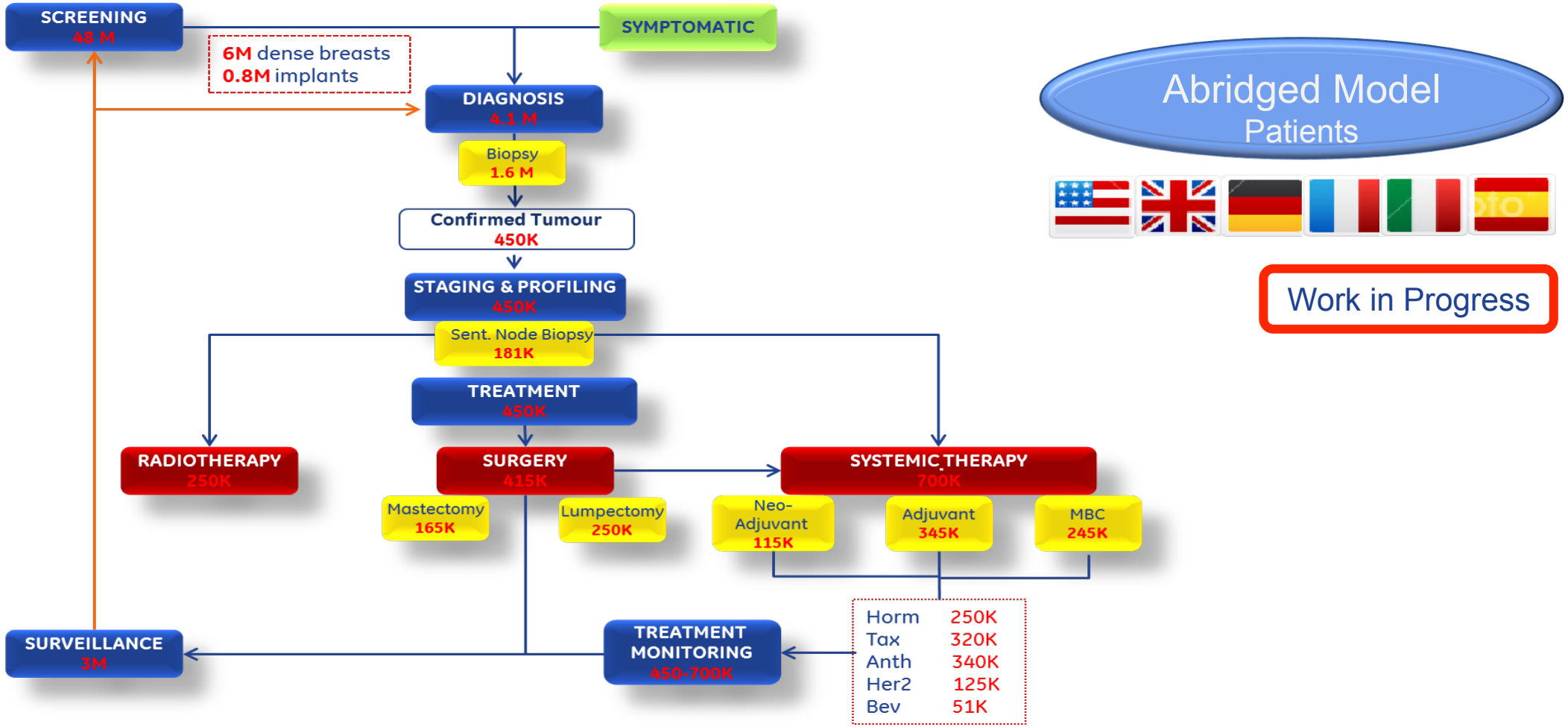
Impact of Tumor Size[4]

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



imagination at work

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; DecsisionResources Breast Cancer Pharmacor 2011, DaVInci, various literature sources

MBI & the current profile of breast imaging

- Senographe* Essential Mammagraphy
- Somov Automated Breast Ultrasound (ABUS*)

Is there something?

- Senobright
- Logic* E9 Ultrasound
- Molecular Diagnostic Testing
- MR Guided Biopsy
- **Discovery NM750b Molecular Breast Imaging**

What is it?

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

How severe is it?

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

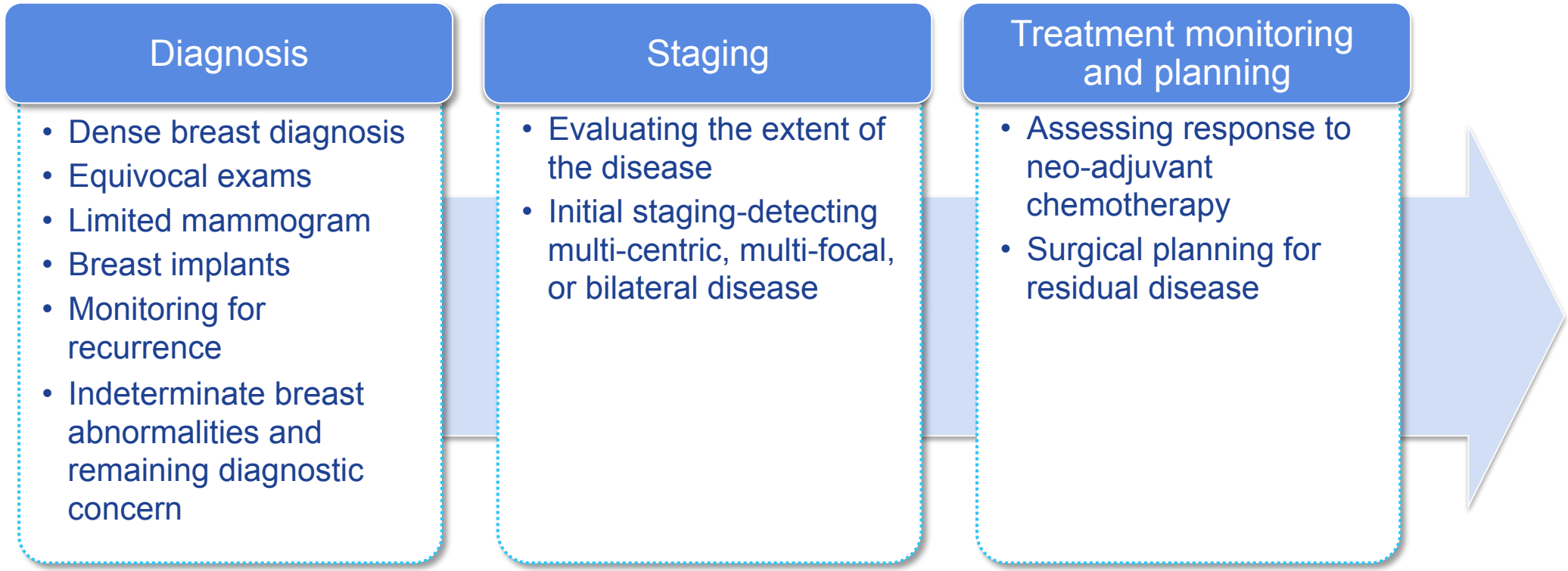
What's next?

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

Is it working?

DOC#1390262, May 2013

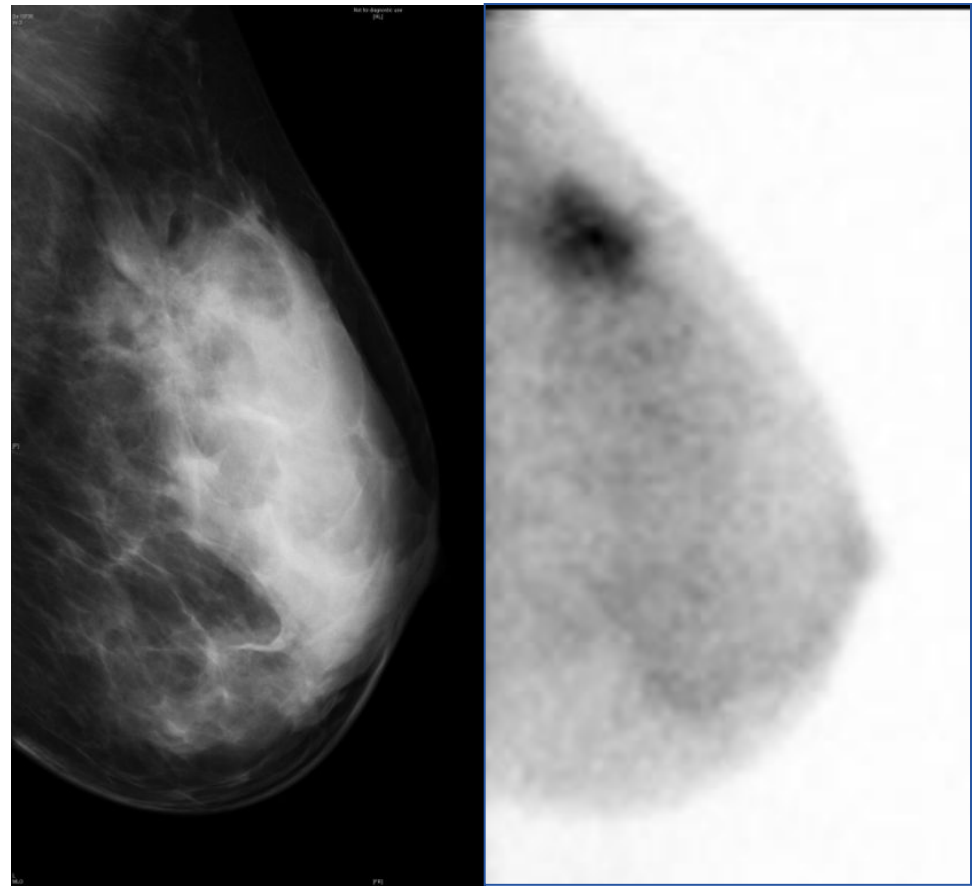
Wide variety of indications for MBI[5]



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.

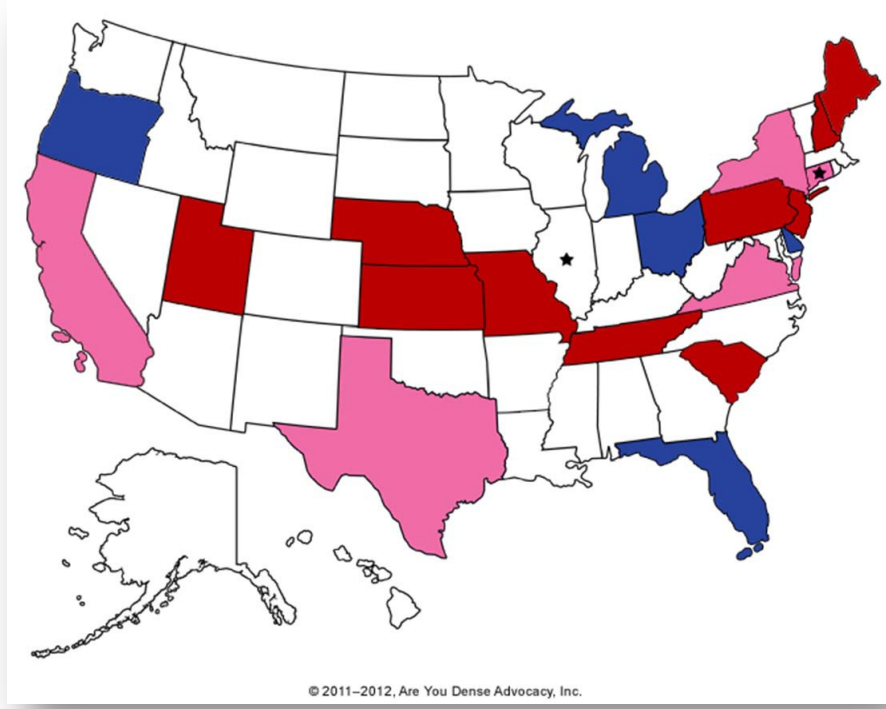


Medio-lateral oblique (MLO)

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]



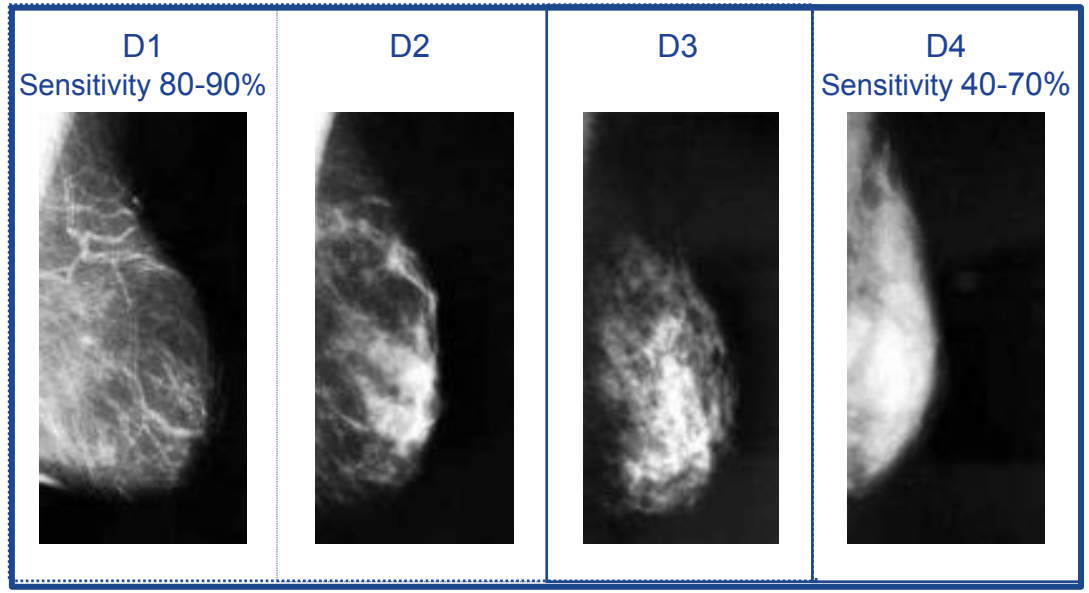
Breast Density affects mammography screening procedures

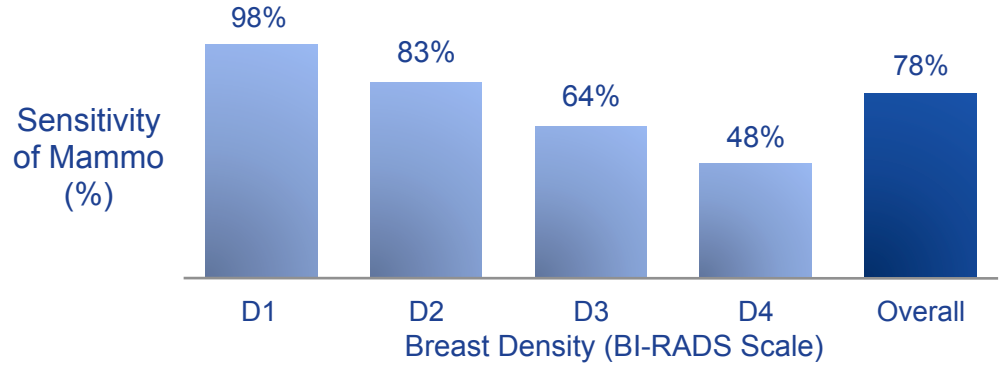
Dense breast tissue can overlap with lesions

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)





imagination at work

*MBI is intended as an adjunct to mammography or other breast imaging modalities (it is not intended for primary screening of the popu

Images: Technique and Performance of Cancer Diagnosis Using a CZT Semiconductor Gamma Camera for Molecular Breast Imaging, I. M. Blevis$_1$, O. Zak$_1$, M. K. O'Connor2, C. Hruska2, D. Rhodes$_2$, S. Phillips$_{2\,1}$ General Electric Healthcare, Haifa, Israel 2Mayo Clinic, Rochester, MN, USA

Different types of tumors are seen by different modalities[18]

	Calcification	Fibrous	Vascular	Metabolic
				
CESM	+++	++	++	-
Digital Breast Tomosynthesis	++	+++	-	-
Mammography	+++	++	-	-
MBI	-	-	+++	+++
MRI	-	++	+++	++
Ultrasound	+	+++	+	-
Tumors Detected (In order of effectiveness)	Ductal Carcinoma In Situ (DCIS) Invasive Ductal Carcinoma (IDC)	Ductal Carcinoma In Situ (DCIS) Invasive Ductal Carcinoma (IDC) Invasive Lobular Carcinoma (ILC) Lobular Carcinoma In Situ (LCIS)	Invasive Ductal Carcinoma (IDC) Invasive Lobular Carcinoma (ILC) 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

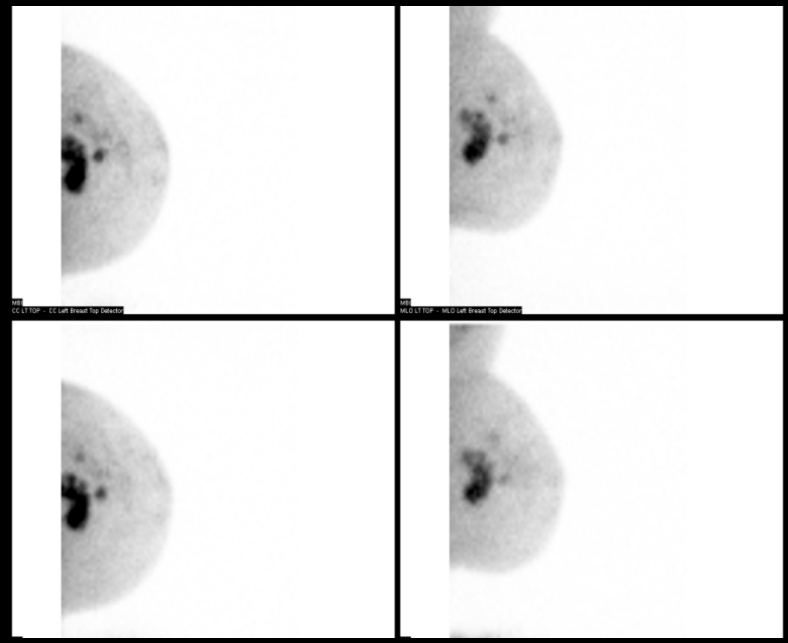
Mammogram	Ultrasound	MRI
Not sensitive to radiographically **dense breast** tissue	**Low specificity** leading to unnecessary biopsies when used as an adjunct to Mammography[9]	**Expensive** examination
Uncomfortable for the patient requiring painful breast compression	Inability to distinguish between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

MBI used as an adjunct to Mammography and Ultrasound provides an additional tool for making a stronger diagnosis

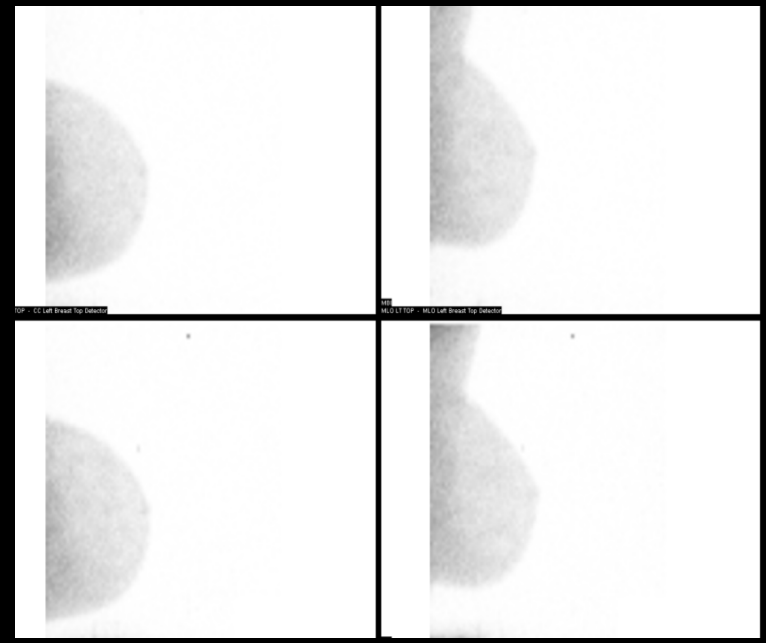
Treatment Monitoring (Neo Adjuvant Therapy)

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.

Baseline
Nov ‘10



Follow up
7 months
later

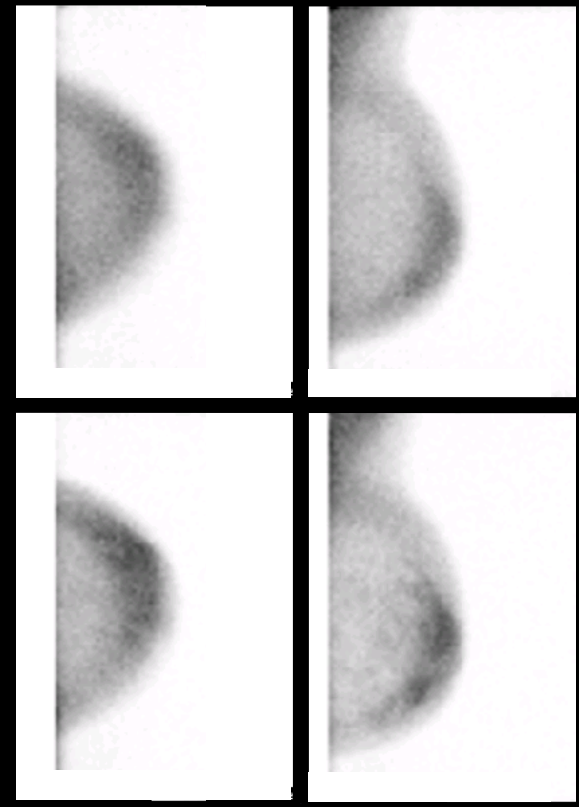


Images courtesy of Prof. Even-Sapir, Tel Aviv Sourasky Medical Centre, Israel

Molecular Breast Imaging & Implants

Right Breast

CC MLO



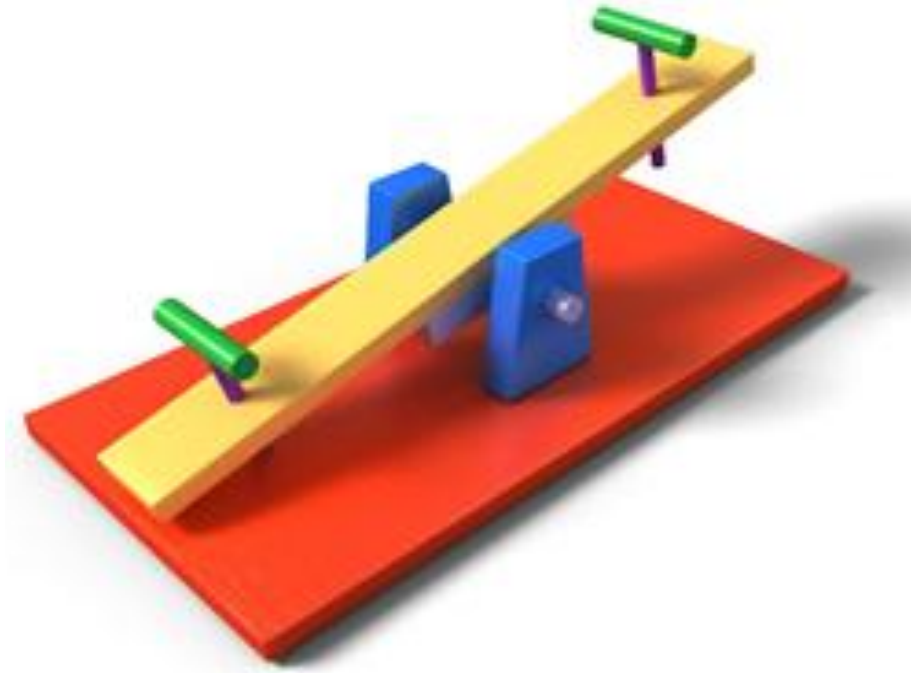
Left Breast

CC MLO

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[12-17]

	Injected Activity	Effective Dose
Screening & Diagnostic Mammography	n/a	0.88-1.32 mSv
MBI/BSGI (Sestamibi)	20 mCi	6.7 mSv
Cardiac Perfusion Test	35 mCi	11.7 mSv
CT chest	n/a	7.8 mSv
Coronary CT (women)	n/a	10.2 mSv
PET (F-18 FDG)	10 mCi	11.1 mSv
CT abdomen & pelvis	n/a	14.7 mSv
PET/CT	10 mCi	23.0 mSv

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.

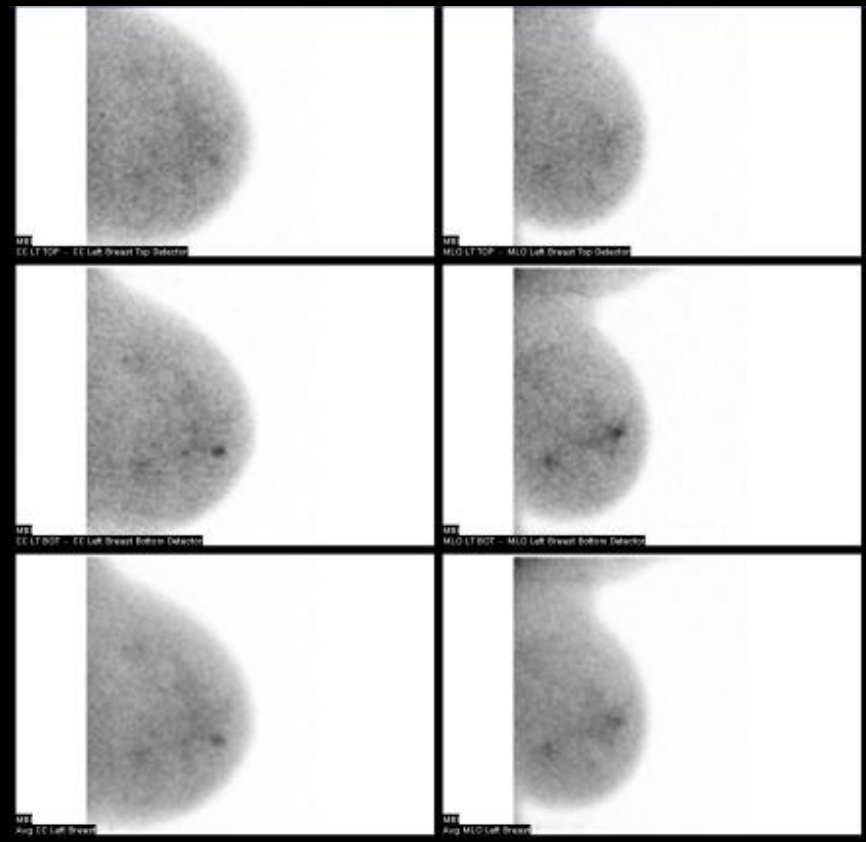
Case #1

Increased Sensitivity may allow reduced dose in future use

20 mCi Full data

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

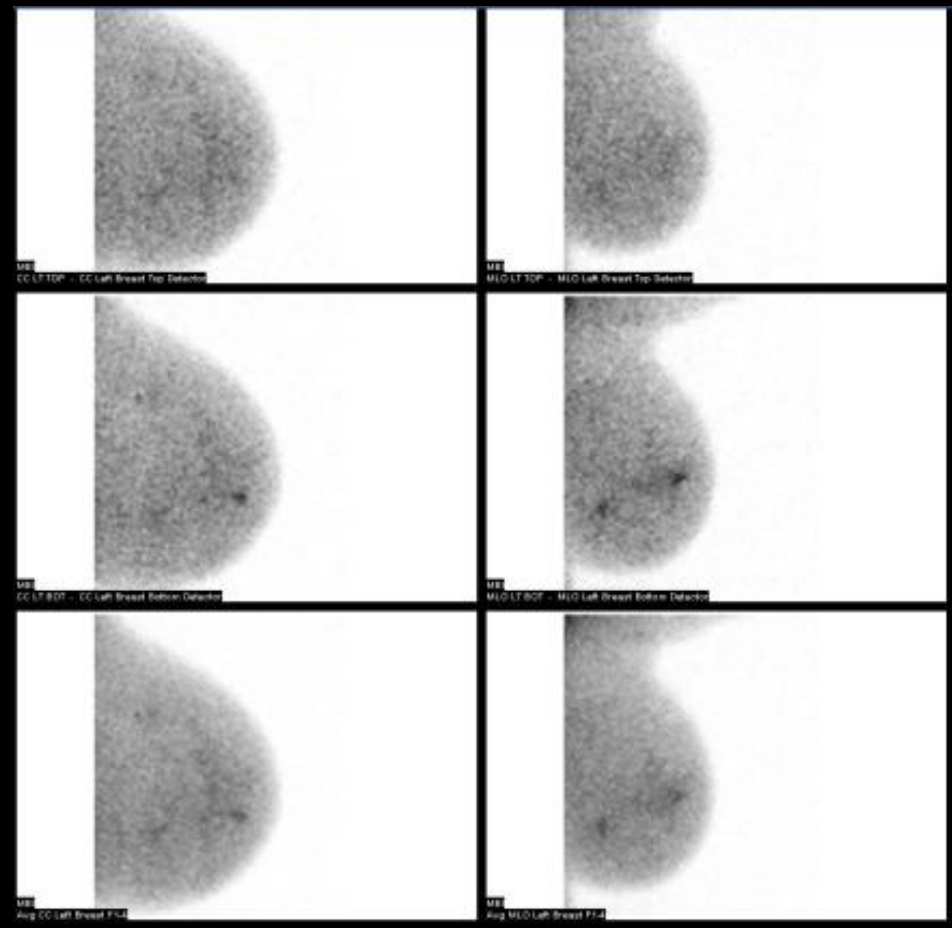
2 lymph nodes show met. carcinoma



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

Case #1

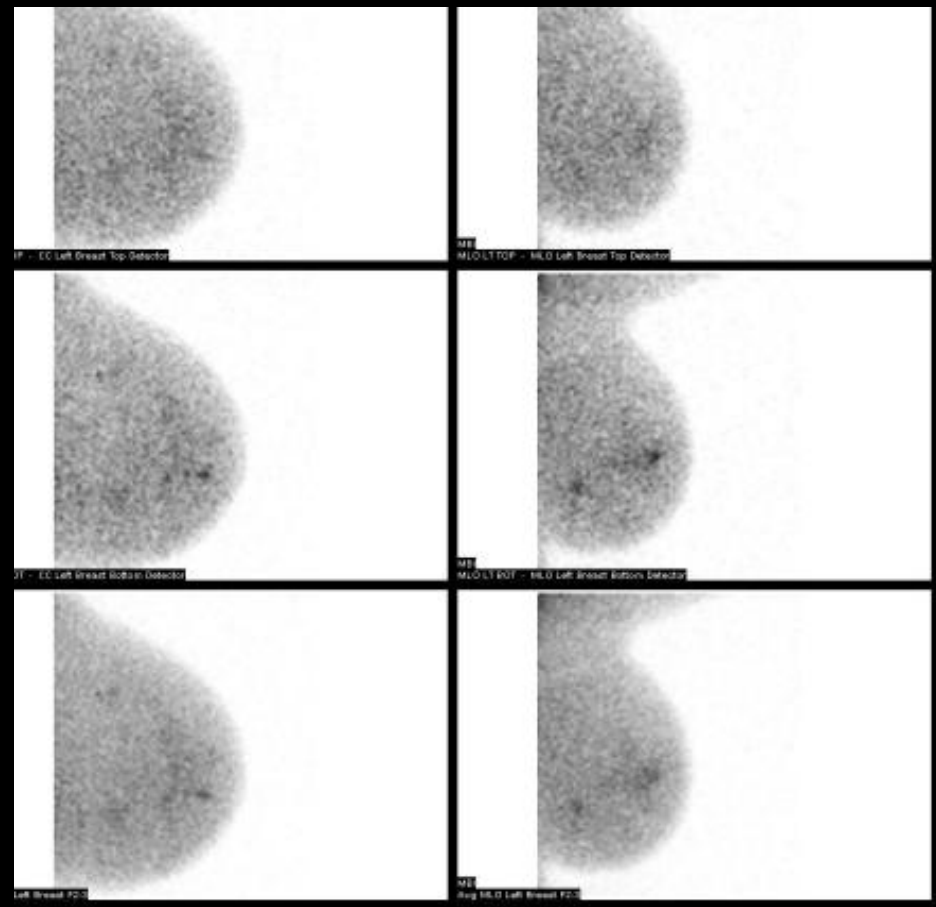
8 mCi Equivalent



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

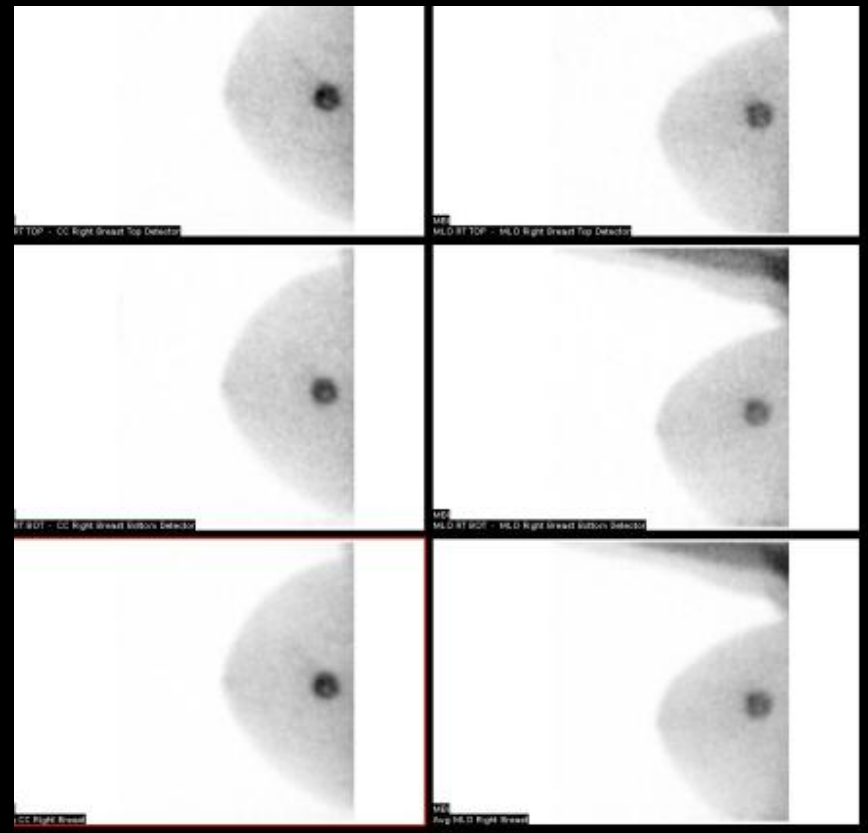


Images courtesy of Prof. Even-Sapir, Tel Aviv Sourasky Medical Centre, Israel
*Low dose images were simulated by using time limited data obtained from the full data set at nominal injected dose

Case #2

Increased Sensitivity may allow reduced dose in future use

20 mCi Full data

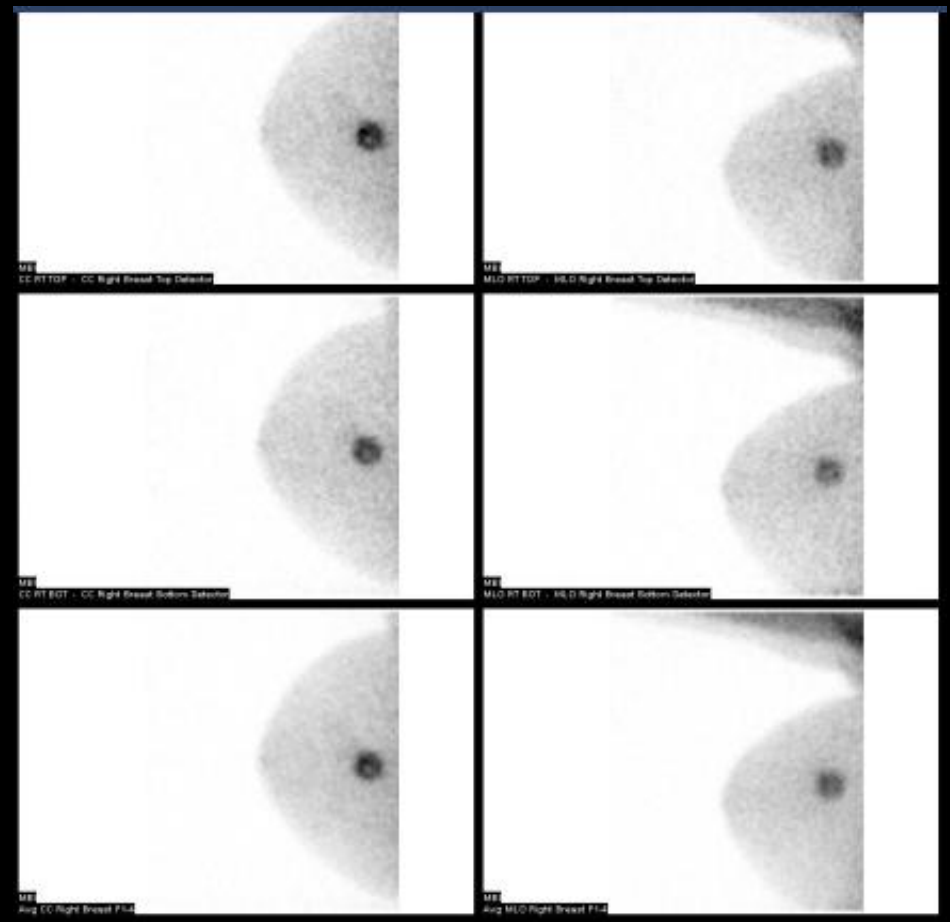


Images courtesy of Prof. Even-Sapir, Tel Aviv Sourasky Medical Centre, Israel

Case #2

A

8 mCi Equivalent

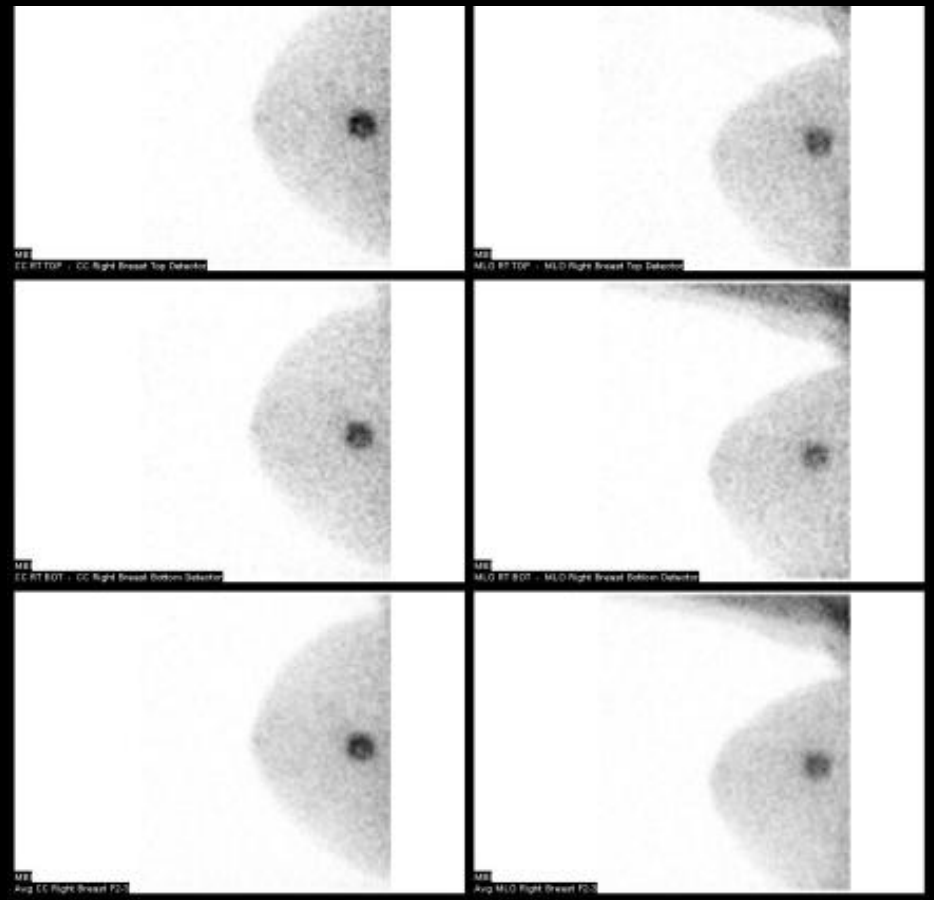


Images courtesy of Prof. Even-Sapir, Tel Aviv Sourasky Medical Centre, Israel
*Low dose images were simulated by using time limited data obtained from the full data set at nominal injected dose

Case #2

A

4 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

Sources

1. A meta-analysis of scintimammography: an evidence-based approach to its clinical utility, Rahain Hussaina and John R. Buscombeb, Nuclear Medicine Communications 2006, Vol 27 No 7
2. Maublant JC, Zhang Z, Rapp M, Ollier M, Michelot J, Veyre A. In vitro uptake of technetium-99m-teboroxime in carcinoma cell lines and normal cells: comparison with technetium-99m-sestamibi and thallium-201. J Nucl Med. 1993 ;34:1949-52.
3. Carvalho PA, Chiu ML, Kronauge JF, Kawamura M, Jones AG, Holman BL, Piwnica-Worms D. Subcellular distribution and analysis of technetium-99m-MIBI in isolated perfused rat hearts. JNucl Med. 1992; 33:1516-22
4. AIHW & NBCC (National Breast Cancer Centre) 2007. Breast cancer survival by size and nodal status. Cancer series no. 39 Cat. no. CAN34. Canberra: AIHW)
5. SNM Guideline for Breast Scintigraphy with Breast-Specific Gamma Cameras, Version 1.0 Published June 4, 2010
6. 1 http://jnci.oxfordjournals.org/content/92/6/443.full; *JNCI J Natl Cancer Inst (2000) 92 (6): 443. doi: 10.1093/jnci/92.6.443*
7. Source: © 2011-2012, Are You Dense Advocacy, Inc. http://www.areyoudenseadvocacy.org
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
11. Metanalysis - United Biosource Corporation, Literature Review on the Accuracy of Breast Cancer Screening Modalities, 2009
12. Mammography Dosimetry: American College of Radiology, www.acr.org.
13. Sestamibi dosimetry for BSGI: International Commission on Radiologic Protection.
14. Radiation Dose to Patients from Radiopharmaceuticals New York NY: Permamon Press; 1988 ICRP Publication 53 Cardiolite Drug Data Sheet Bristol Myers Squibb May 2003
15. FDG PET/CT 10 mCi 23.0 mSv Radiopharmaceuticals. York, 1988. 53. Sheet. Squibb. 2003.
16. Dosimetry for PEM Dosimetry - F-18-Fluorodeoxyglucose, NUREG/CR-6345, page 9, September 18, 1992.. J.E. Kalinyak, MD, PhD. "Comparison of Radiopharmaceuticals Used in Positron Emission Mammography (PEM) and Breast Specific Gamma Imaging (BSGI). White paper. Naviscan PET Systems, Inc., March 2007.
17. CT of chest abdomen and pelvis: Bushberg et al. The essential physics of Medical Imaging. 2nd ed. Philadelphia PA. Lippincott Williams and Wilkens; 2002 795-812. Coronary CT: Ropers et al. Usefulness of multidetector row spiral CT for the noninvasive detection of coronary artery stenosis. PET/CT: Annals of the International Commission on Radiation Protection.
18. Sanu et all "The Role of Planar Scintimammography With High-Resolution Dedicated Breast Camera in the Diagnosis of Primary Breast Cancer" , (*Clin Nucl Med* 2008;33: 739–742)

Thank You