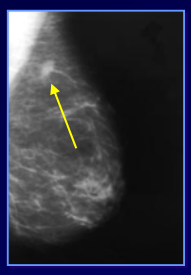
Molecular Breast Imaging

Michael O'Connor, PhD
Department of Radiology
Mayo Clinic
Rochester, MN

This work has been funded in part by the following:
National Institute of Health
Dept. of Defense
Susan G Komen Foundation
Mayo Foundation
Friends for an Earlier Breast Cancer Test

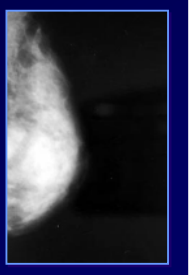
Mammography: The Problem

Breast cancer and tumors appear white on mammogram



Cancer clearly visible in non-dense breast

Sensitivity 80%-90%



Cancer would be occult in dense breast

Sensitivity 40%-70%

Breast Cancer
Comparative Relative Risks

Risk factor	Relative risk
BRCA mutation	20
Lobular carcinoma in situ	8-10
Dense breast parenchyma	4-6
Personal history of breast cancer	3-4
Family history (1° relative)	2.1
Postmenopausal obesity	1.5
Prempro (WHI)	1.26

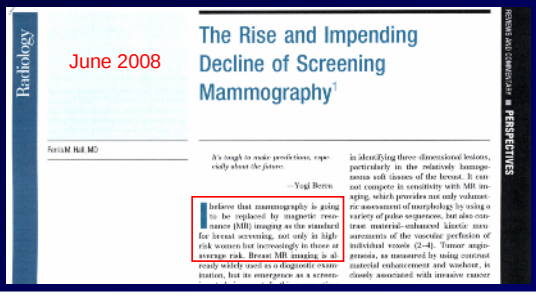
Sensitivity of MMG, US, and MRI in Women at Increased Risk

Author/year	Country	Subjects (no.)	Sensitivity MMG (%)	Sensitivity US (%)	Sensitivity MRI (%)
Kuhl, 2000	Germany	192	33	33	100
Warner, 2004	Canada	236	36	33	77
Kriege, 2004	Netherlands	1,909	40	NA	71
Kuhl, 2005	Germany	529	33	40	91
Leach 2005	U.K.	649	40	NA	77
Sardanelli, 2006	Italy	3571	40	43	81

American Cancer Society

New guidelines issued on March 28th, 2007

Recommend annual MRI screening for women with a high lifetime risk of breast cancer – defined as 20% or more


Radiology

June 2008

The Rise and Impending Decline of Screening Mammography[1]

PERSPECTIVES

MRI: Main Disadvantages

Complexity

- Typical contrast enhanced breast MRI may contain over 1500 images

Cost (Medicare reimbursement rate)

• Analog Mammogram	~$90
• Digital Mammogram	~$140
• Bilateral breast ultrasound	~$200
• Bilateral MRI	> $1,000

Specificity

• (tertiary centers)	~ 90%
• (community centers)	~ 50%

Nuclear Medicine / Molecular Imaging

Scintimammography

- Tc-99m sestamibi approved by the FDA for breast imaging in 1997
- Several large multicenter studies undertaken in late 1990s

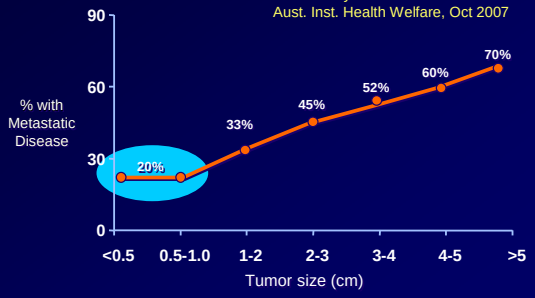
Taillefer: Sem Nucl Med 29:16, 1999
(2009 patients)
Sensitivity = 85%, specificity = 89%

Brem: J Nucl Med 43:909, 2002
Sensitivity 35-64% for lesions <1 cm

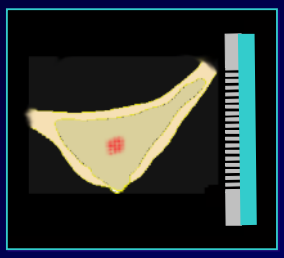
Taillefer: Sem Nucl Med 29:16, 1999
Sensitivity ~55% for masses <1.5 cm

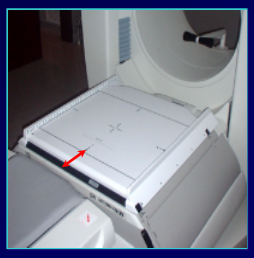
Impact of Tumor Size on Metastatic Disease

<10 mm: 5-year survival = 98%
30 mm : 5-year survival = 70%
Aust. Inst. Health Welfare, Oct 2007



Conventional Scintimammography





Small Field of View Gamma Cameras

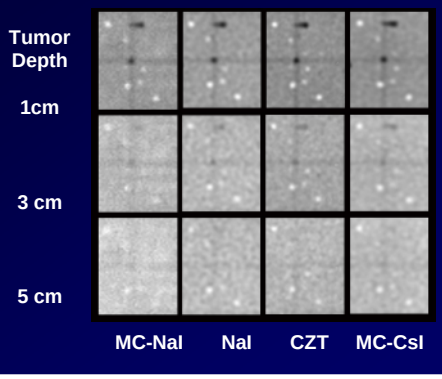
Digirad
Multicrystal
Cesium Iodide
+ Photodiodes

Dilon Inc.
Multicrystal
Sodium Iodide
+ PMTs

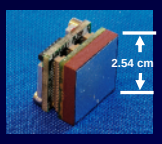
CZT Technology
Cadmium Zinc
Telluride (CZT)
Semiconductor

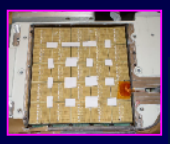
Breast Phantom: Comparison between Systems*

*Hruska CB, et al. Nucl Med Commun, 2005; 26: 441-445

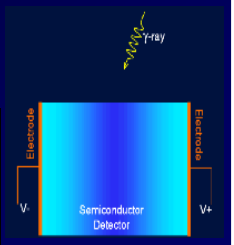


Cadmium Zinc Telluride (CZT) Detector

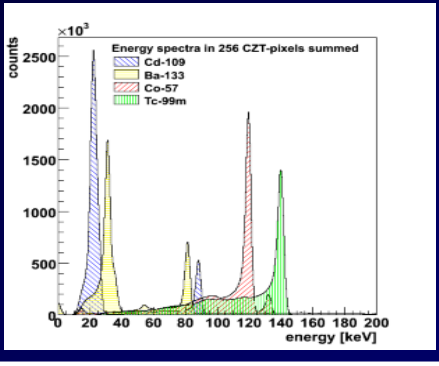




- Excellent Intrinsic Resolution = 1.6 mm
- Excellent Energy Resolution 4.0%
- Can be operated at room temp
- No dead space – ideal for breast imaging
- Expensive – currently limited to small field of view detectors
- First commercial gamma cameras using CZT developed for nuclear cardiology



Energy Resolution - CZT Detector



Molecular Breast Imaging – 2009

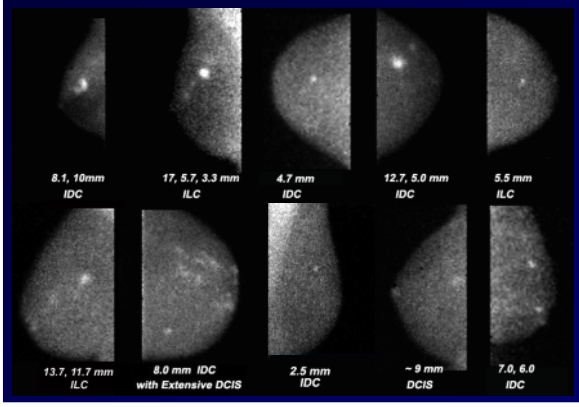
- MBI Prototypes developed at Mayo over last 6 yrs using detectors from Gamma Medica and GE Healthcare
- Cadmium Zinc Telluride (CZT) gamma camera technology
  - Expensive – currently limited to small field of view detectors
- Dual-detector design optimized for breast imaging
- Anticipated cost ~$400 / study

Dual-detector MBI System

How does Molecular Breast Imaging Work?

- Patient receives an IV injection of a radiotracer (Tc-99m sestamibi)
- The tracer preferentially accumulates in cancer cells and is *not* influenced by breast density
- The breast is lightly compressed between the 2 MBI gamma cameras, *only light pain-free compression is necessary*
- Imaging starts ~5 minutes post injection. Acquire CC and MLO views of each breast for 10 minutes / view
- Procedure performed by nuclear medicine technologist trained in mammographic positioning techniques

Can MBI find small breast tumors?



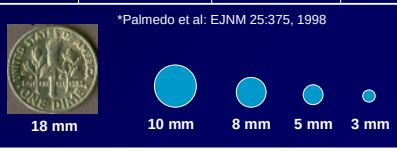
Molecular Breast Imaging: Use of a Dual-Head Dedicated Gamma Camera for Detection of Small Breast Tumors

AJR 2008; Vol 191, 1808-1815

Carrie B. Hruska, Ph.D.[1], Stephen W. Phillips, M.D.[1], Dana H. Whaley, M.D.[1], Deborah J. Rhodes, M.D.[2], Michael K. O'Connor, Ph.D.[1]

Technology	Tumors 5-10 mm in size	Tumors < 5 mm in size	All Tumors (128 in 88 patients)
Standard γ-Camera*	55%	No data	
Single-head MBI	76%	44%	82%
Dual-head MBI	87%	67%	90%

*Palmedo et al: EJNM 25:375, 1998



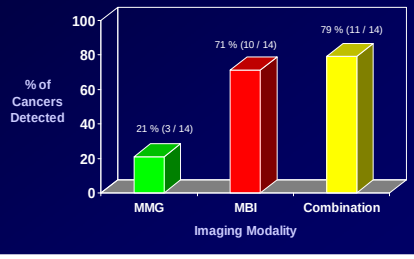
Comparison of Screening MBI and Mammography

- ~1000 patient screening study
- Funded by Susan G Komen Foundation
- Compare MBI and mammography in patients with dense breasts at high risk of breast cancer
  - Prior history of breast cancer
  - Family history in one FDR or two SDR
  - Gail lifetime risk > 20%
  - Prior atypia or LCIS

Question – is MBI a viable screening adjunct to mammography in patients with dense breasts?

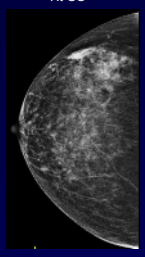
Results

- In 958 patients studied, a total of 14 cancers in 12 patients were diagnosed.
  - 8 cancers detected by MBI alone
  - 1 cancer detected by mammography alone
  - 2 cancers detected by both MBI and mammography

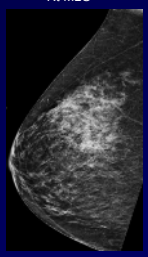


Screening Patient Examples (1)

Rt CC



Rt MLO



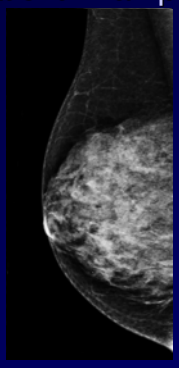
Digital Screening Mammography (Negative)
Molecular Breast Imaging (Positive)

17 mm IDC with DCIS extension

Screening Patient Examples (2)

Digital Screening Mammography (Negative)

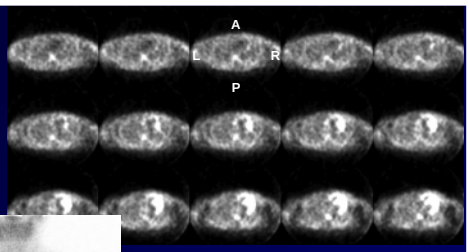
Molecular Breast Imaging (Positive)

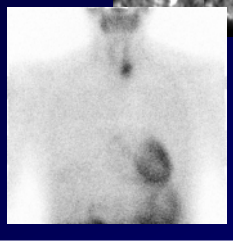


Rt MLO

9 mm Ductal Carcinoma In Situ

MBI vs. SPECT



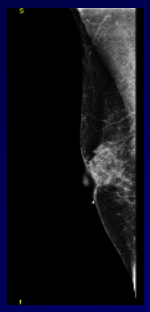


Parathyroid scan with Tc-99m sestamibi performed 4 weeks prior to MBI study in Screening Patient Example #3

Screening Patient Examples (3)

Digital Screening Mammography (Negative)

Molecular Breast Imaging (Positive)

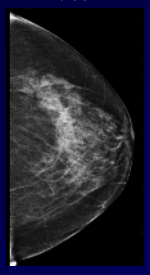


Rt MLO

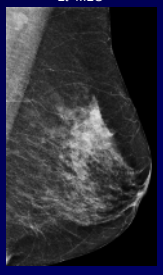
9 mm Invasive Ductal Carcinoma

Screening Patient Examples (4)

Lt CC



Lt MLO



Digital Screening Mammography (Negative)
Molecular Breast Imaging (Positive)

7 mm Tubulolobular Carcinoma

Results in 958 Patients with 12-month Follow-up

Sensitivity: All cancers detected by any means in the 12-month period since the MBI study.

10 / 14 cancers detected by MBI
(sensitivity = 71%)

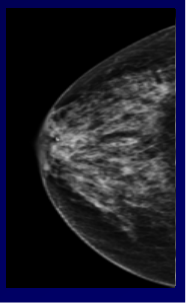
3 / 14 cancers detected by mammography
(sensitivity = 21%)

Specificity: Patients with a negative follow-up mammogram at 1 year and no clinical symptoms at 12-months were assumed to be disease free

Specificity - MBI	93%	Recall Rate – 7.5 %
Specificity - mammography	90%	Recall Rate – 9.2 %

Molecular Breast Imaging in Patients undergoing Myocardial Perfusion Imaging

- MBIs performed in women presented for myocardial perfusion studies, no additional dose needed
- Of 158 patients
  - 3 cancers detected, 1 only detected by MBI
  - 1 patient with uptake in papilloma and atypia
  - 154 patients with negative findings
- Negative screening mammogram
- Myocardial perfusion scan and MBI 1 week later
- Follow-up Dx mmg/US positive, 8 mm IDC/DCIS
- Breast MRI correlated with MBI

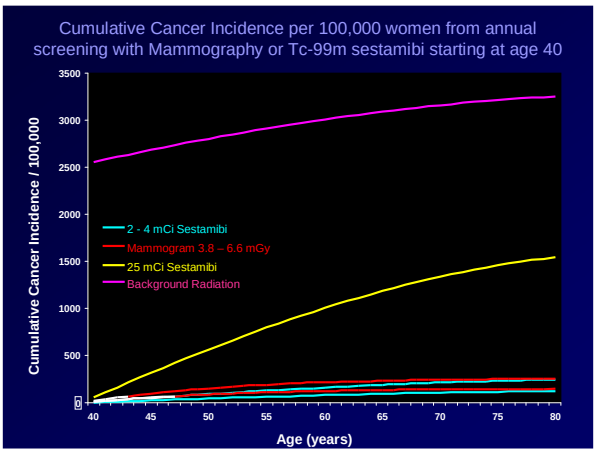


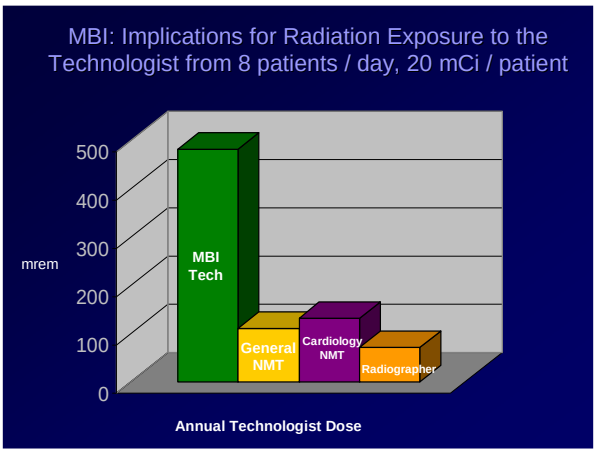
MBI - Potential Screening Application

- MBI has 2-3 times sensitivity of mammography in the high-risk and dense breast populations
- MBI appears to have comparable sensitivity (80%) to that reported for MRI in women at increased risk of breast cancer
- American Cancer Society guidelines recommend annual MRI if lifetime risk exceeds 20%: would impact up to 1.5 million women annually in the U.S.
- Cost of MBI estimated at ~1/5th cost of Breast MBI
- Currently no clinical systems available
  - First clinical systems in late 2009 ?

MBI - Limitations and Disadvantages

- False positive findings in some cases of fibroadenomas, papillomas, fat necrosis.
- Uptake of Sestamibi is influenced by hormonal changes
- MBI - high radiation dose relative to mammography

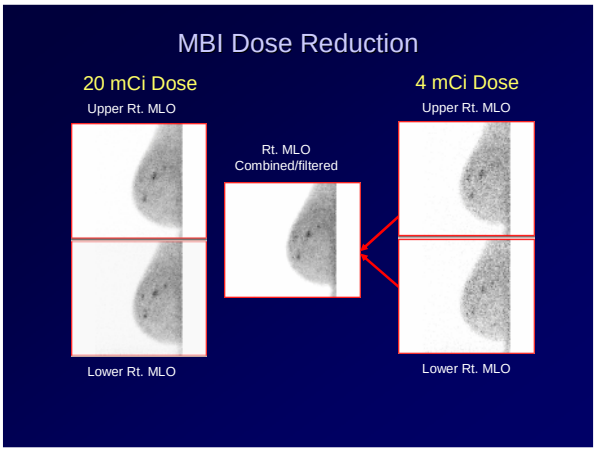




MBI – Radiation Dose

Radiation risk to patients / technologists

- MBI with 20 mCi Tc-99m sestamibi = 6.5 mSv
- Mammogram is < 1.0 mSv
- Dose reduction techniques have been developed to reduce administered dose of Tc-99m sestamibi to 2-4 mCi
  - collimator optimization
  - energy window optimization
  - noise reduction algorithms
  - composite image from opposing detectors



MBI - Future Directions

- Clinical applications
  - Screening in high-risk women
  - Pre-operative staging to exclude multifocal/contralateral cancers
  - Neo-adjuvant chemotherapy evaluation
- Alternative radiotracers
  - Improved detection of lesions < 5 mm
  - Improved detection of DCIS and atypia

Molecular Breast Imaging

Future Developments – New Radiopharmaceuticals

- Tc-99m Sestamibi
- Tc-99m Bombesin
- Tc-99m αV-β3 Integrin
- Tc-99m Annexin V
- Tc-99m Glucarate
- Tc-99m EC-glucosamine
- Tc-99m (V)-DMSA
- Tc-99m Vitamin B12
- I-123 Iodo-estradiol
- I-123 Methoxy-vinylestradiol
- I-123 Dimethyl-Tamoxifen
- I-123 Iodo-methoxybenzamide