



Excellence Through Innovation

# Molecular Breast Imaging (MBI) Physics & Performance Testing

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Gamma Medica, Inc., Northridge, CA, USA

## AAPM 2012 Spring Clinical Meeting

Dallas, TX

5 pm Sunday 18 March 2012

Mammography Symposium – SAM  
Advanced Modalities SU-D2

# Disclosures

## Gamma Medica employees:

Brad Patt, PhD – CEO & founder

James Hugg, PhD – CTO, VP-R&D

Bryan Simrak, electronic engineer

Peter Smith, field service engineer

## Mayo Clinic:

Exclusive license of MBI Intellectual Property & know-how to Gamma Medica; contract from Gamma Medica

## Cleveland Clinic:

Contract from Gamma Medica to develop breast lesion phantom

Grant funding from NIH National Cancer Institute (STTR, SBIR Bridge, & R01), Mayo Foundation, Susan G. Komen Foundation

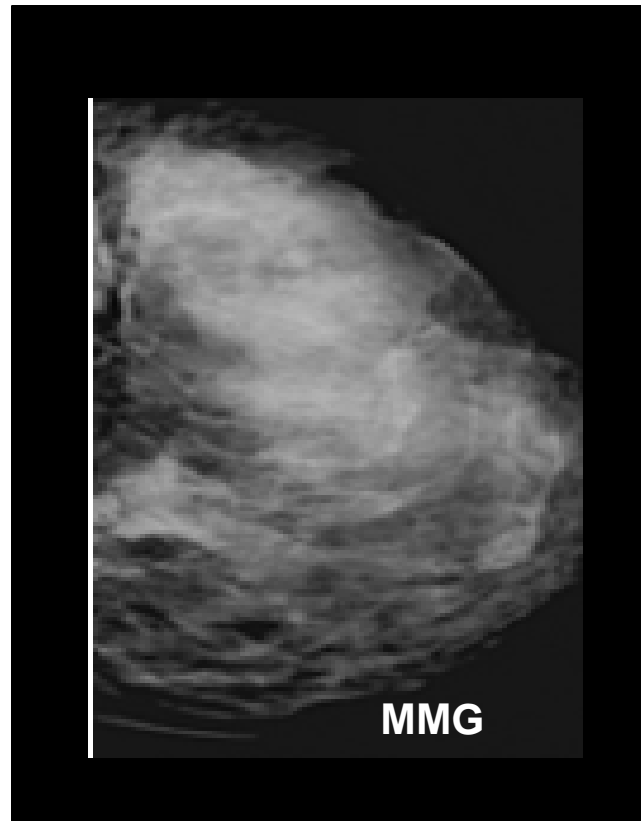
# Learning Objectives

- Understand the physics of MBI, BSGI, and PEM breast imaging.
- Understand how radiation dose can be lowered in MBI, BSGI, and PEM.
- Understand how to characterize the performance of MBI, BSGI, and PEM systems.

# Outline

- Challenge of dense breasts
- Physics of MBI, BSGI, & PEM
- Radiation dose reduction
- Performance of MBI, BSGI, & PEM

# Challenge of Dense Breasts

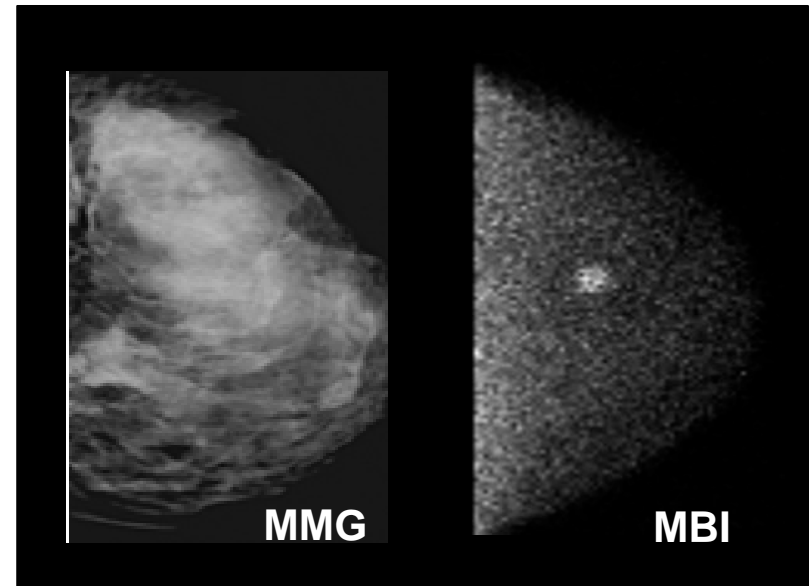


# Dense Breast Tissue

- Breasts are composed of fatty (non-dense) tissue and connective (dense) tissue
  - X-rays do not penetrate dense connective tissue, so cancer is hidden and often can be missed
- How other modalities work in dense breast:
  - Mammography
    - Ineffective in dense breasts – very low sensitivity
    - Cancer is hidden until too late to treat effectively
  - Ultrasound
    - Useful in dense breasts, but results depend on operator's skill
    - Specificity is low
  - Breast MRI
    - Useful in dense breasts, but costs 3x MBI
    - Too many false positives
    - Too many biopsies

# Dense Breast Tissue – MBI provides a solution

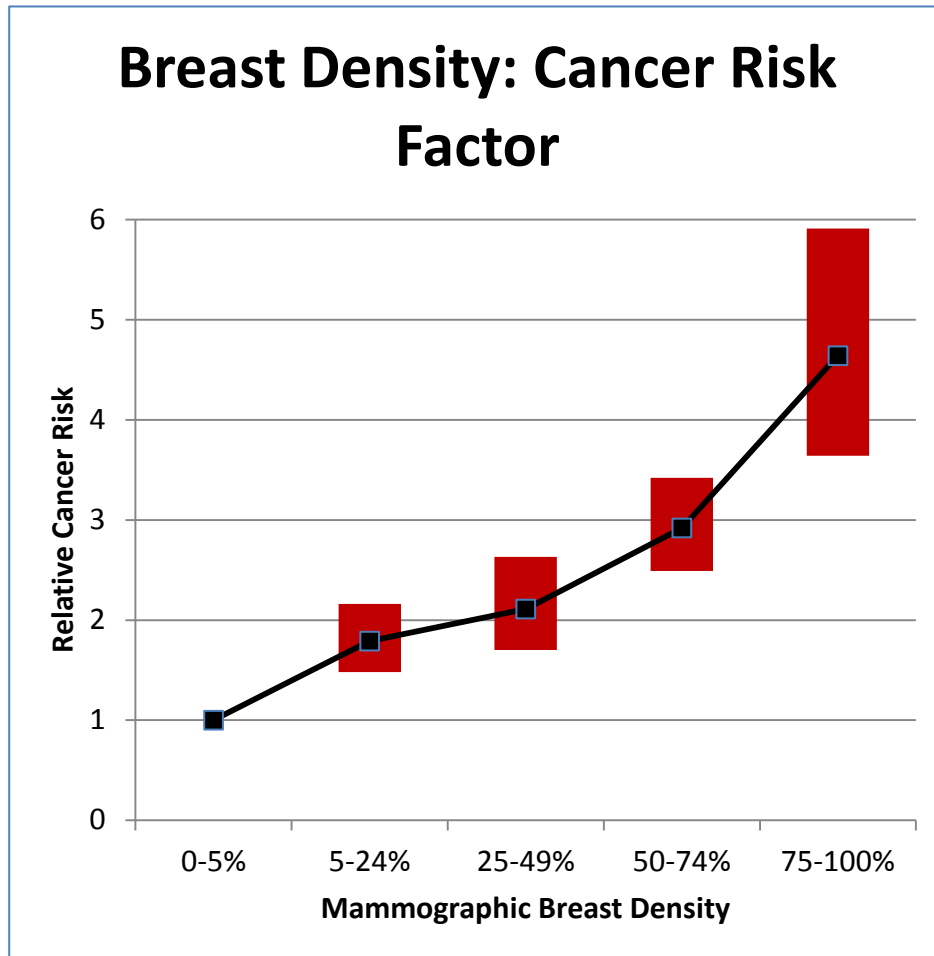
- Cancer is often obscured by dense connective tissue that absorbs many X-rays.
- The sensitivity of screening mammography in dense breasts is below 30%.
- Gamma photons penetrate dense breast tissue with little absorption.



*Courtesy of Mayo Clinic*

Region	> 50% Dense Breast Tissue
Asia	70%
Europe & Americas	40-50%

# Dense Breast Increases Risk for Cancer



A 2002 study in *New England Journal of Medicine* (Boyd) found that:

women with significant dense breast tissue have a 4-6 times greater risk of developing breast cancer

McCormack & Silva, *Cancer Epidemiol Biomarkers Prev* 2006;15:1159-69.

# Breast Density – 3<sup>rd</sup> Highest Relative Risk

<u>Risk factor</u>	<u>Relative risk</u>
BRCAs mutation	20
Lobular carcinoma in situ	8-10
<b>Dense breast parenchyma</b>	<b>4-6</b>
Personal history of breast cancer	3-4
Family history (1 <sup>o</sup> relative)	2.1
Postmenopausal obesity	1.5

“Mammographic density is perhaps the most undervalued and underutilized risk in studies investigating the causes of BC.”

– Boyd, *NEJM*, 2002

# Physics of MBI, BSGI, & PEM



# Scintimammography



## Original protocol

- Inject 20-30 mCi  $^{99m}\text{Tc}$ -sestamibi *i.v.*
- Wait 5 minutes

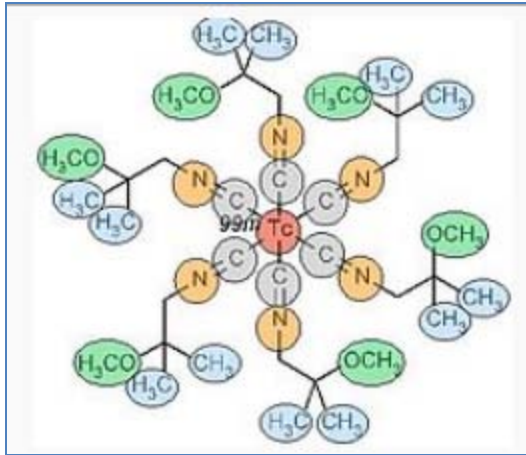
Typical tumor/background uptake ratio: 5-10

## Single-head gamma camera:

- 10 min lateral planar image of suspect breast
- 10 min lateral planar image of contralateral breast
- 10 min anterior planar image of both breasts

MBI evolved from scintimammography (SMM). Only lesions larger than 1 cm could be reliably detected by SMM because of the large distance from the collimator to the breast.

# $^{99m}\text{Tc}$ -Sestamibi (MIBI) (Cardiolite, Miraluma)



Wikipedia

**Half-life = 6 hours**  
**140 keV gamma emission**

FDA clearance for breast 1997  
(20-30 mCi, 740-1110 MBq *i.v.*)

Indicated for:

- planar imaging as a second line diagnostic drug after mammography to assist in the evaluation of breast lesions in patients with an abnormal mammogram or a palpable breast mass

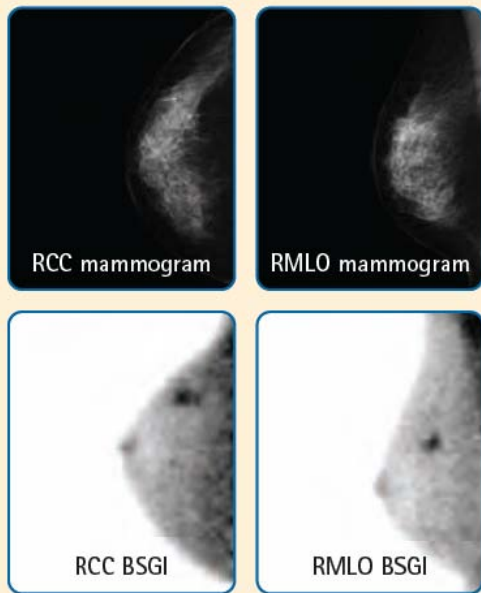
Not indicated for:

- breast cancer screening,
- to confirm the presence or absence of malignancy, and
- not an alternative to biopsy

Generic since Sept 2008

MIBI is 2-methoxy isobutyl isonitrile

# Breast-Specific Gamma Imaging (BSGI)



- Single detector head
- NaI pixels (3.2 mm pitch , 6 mm thick)
- PS-PMT photodetectors
- 12% FWHM @140 keV

Dilon 6800, 15 cm x 20 cm

1<sup>st</sup> sale – 2005  
~140 installations

15-30 mCi <sup>99m</sup>Tc-sestamibi

# Breast-Specific Gamma Imaging (BSGI)



Dilon Acella, 20 cm x 25 cm  
(uses DigiRad detector)



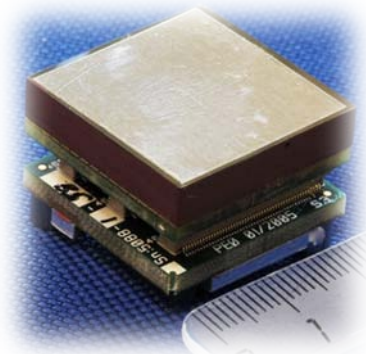
DigiRad Ergo with BSGI attachment, 31 cm x 40 cm

- Single detector head
- CsI pixels (3 mm pitch, 6 mm thick)
- Si photodiodes

1<sup>st</sup> offer – 2011  
? installations

# Molecular Breast Imaging (MBI)

- 8\* mCi  $^{99m}\text{Tc}$ -sestamibi *i.v.*
- mild stabilization (~1/3 MMG force)
- scan within 5 minutes
- 4 views: LCC, LMLO, RCC, RMLO
- 5-10 min/view



Gamma ray detector CZT module



  
lumaGEM®

\* 8 mCi is current Mayo Clinic protocol; 2-4 mCi goal (2013)

# Molecular Breast Imaging (MBI) Protocol

- The patient is injected with Tc-99m Sestamibi
- The injection is in the contra-lateral arm
- If there are suspicious areas in both breasts an injection in the foot is preferred
- The patient is imaged about 5 minutes after injection
- **8 mCi – 5 minutes/view**
- 4 mCi – 10 minutes/view



## Easily able to do both CC and MLO views

- LumaGEM™ uses light compression (15 lbs of force as compared to 40-45 lbs used in mammography)
- Breast tissue simply needs to be immobilized / stabilized



# 2 Commercial MBI Systems



Gamma Medica  
LumaGEM  
1<sup>st</sup> sale – 2009  
20 installations

Both are  
FDA 510(k)  
cleared

Both are dual  
head & use  
CZT detectors

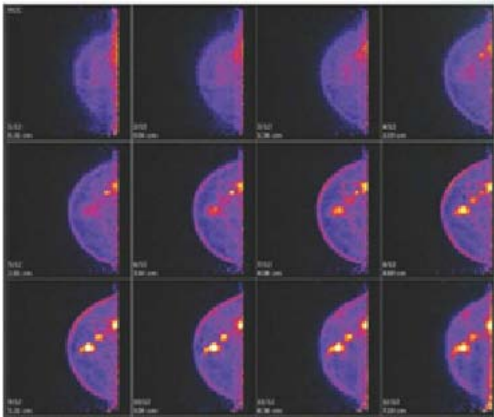


GE Healthcare Discovery  
NM750b  
1<sup>st</sup> sale – 2012  
4 installations

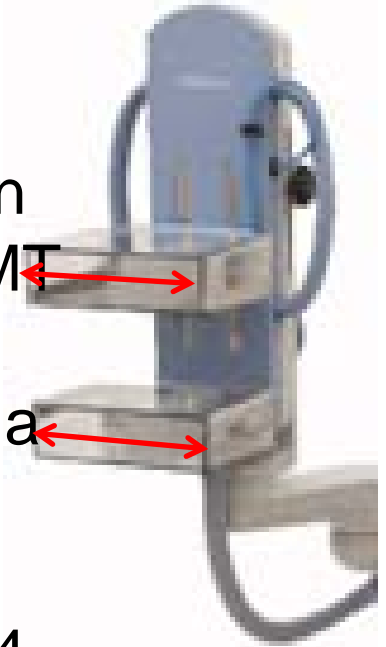
# Positron Emission Mammography (PFM)



Naviscan PEM  
16 cm x 24 cm  
1<sup>st</sup> Sale – 2005  
50 installations



- $^{18}\text{F}$ -FDG (2 hour half-life) and coincidence detection using small scintillator/PMT detectors that physically scan side-to-side to form a limited-angle PET scan.



- Patient preparation: 12-24 hour fast, 1-2 hour quiet uptake delay after injection of 10 mCi  $^{18}\text{F}$ -FDG.

14% FWHM @ 511 keV

# MBI, BSGI, & PEM Instruments

Gamma Medica  
LumaGEM MBI



GEHC  
MBI



Dilon, Digirad  
Single Head BSGI



Naviscan  
PEM



## MBI, BSGI, & PEM

- Significantly improves specificity versus other secondary screening modalities (similar sensitivity to MRI)
- Cost of both capital equipment to providers and scan to payers is approx. one-third of MRI

Q1: What is the radiopharmaceutical (and its half-life) most commonly used for MBI or BSGI?

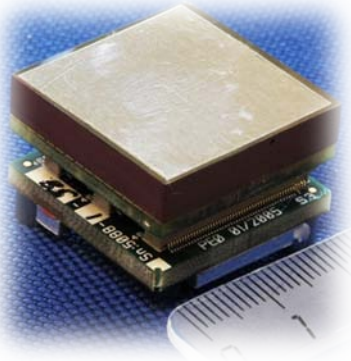
- 0% a)  $^{18}\text{F}$ -FDG (2 hr)
- 0% b)  $^{123}\text{I}$ -MIBG (13 hr)
- 0% c)  $^{99\text{m}}\text{Tc}$ -Tetrofosmin (4 hr)
- 0% d)  $^{99\text{m}}\text{Tc}$ -Sestamibi (13 hr)
- 0% e)  $^{99\text{m}}\text{Tc}$ -Sestamibi (6 hr)

Q1: What is the radiopharmaceutical (and its half-life) most commonly used for MBI or BSGI?

- a)  $^{18}\text{F}$ -FDG (2 hr)
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- c)  $^{99\text{m}}\text{Tc}$ -Tetrofosmin (4 hr)
- d)  $^{99\text{m}}\text{Tc}$ -Sestamibi (13 hr)
- e)  $^{99\text{m}}\text{Tc}$ -Sestamibi (6 hr)

Reference: SJ Goldsmith, et al, SNM Practice Guideline for Breast Scintigraphy with Breast-Specific  $\gamma$ -Cameras 1.0, *J Nuc Med Tech* 2010: 38; 219-224.

# Key Technology: solid state gamma sensor (CZT) with custom ASICs

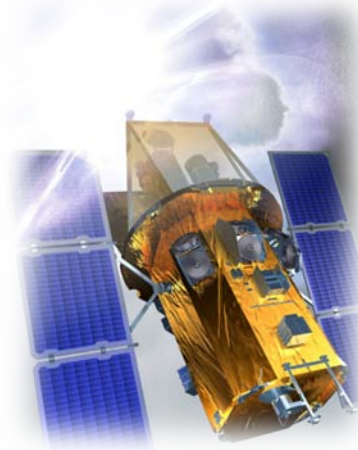


Gamma ray detector CZT module used in **LumaGEM**



ASIC technology developed from space and high-energy physics applications.

Below: NASA SWIFT satellite



Sept 7 2010



Den siste ferden med en romferge går i februar neste år. Om bord er norske instrumenter. FOTO: DON EMMERT/AFP

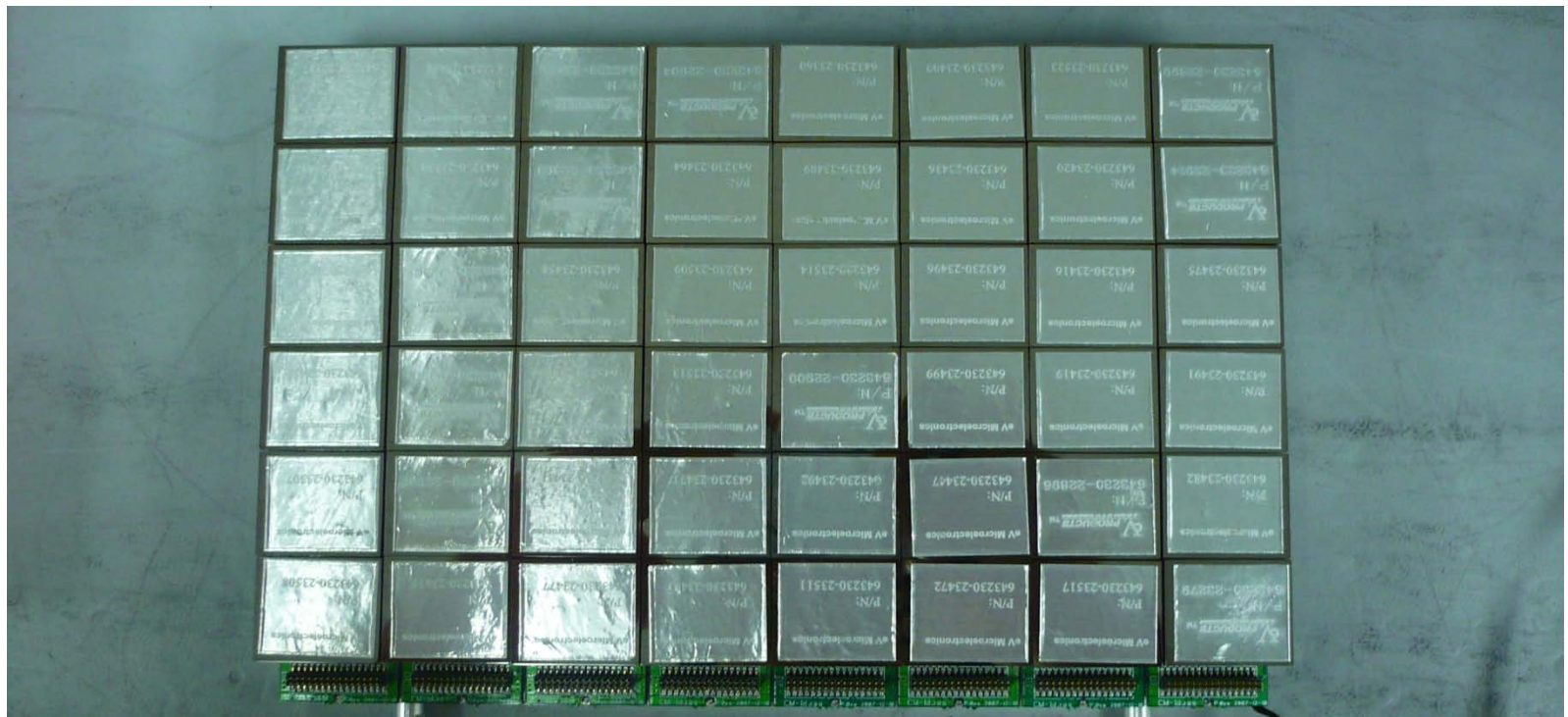
## Norsk instrument på romfergen

■ Om bord i den siste romfergen vil det sitte et instrument med en norsk komponent. Fra romstasjonen skal det jaktes på antimaterie og mørk materie, skriver Norsk Romsenter.

Instrumentet heter AMS-02 (Alpha Magnetic Spectrometer) og er en av de mest komplekse vitenskapelige instrumentene som noen gang er bygget. Selskapet Gamma Medica-Ideas på Fornebu har levert en komponent til den største detektoren på AMS-02. Komponentene er en integrert krets som er koblet til sensoren på detektoren. Den registrerer signalene fra partiklene som går gjennom detektoren og kobler dem videre til et datasystem om bord i AMS.

# New Crystal and Solid State Technology

- Cadmium-Zinc-Telluride ( $\text{Cd}_{0.9}\text{Zn}_{0.1}\text{Te}$ ) Crystals (CZT)
- Detector has 8 by 6 module configuration
- Each crystal unit is 1" X 1"
- Field of View is 16 cm X 20 cm (wide FOV available: 16 cm x 24 cm)



# Cadmium Zinc Telluride (CZT)

Three major commercial sources of CZT

- Endicott Interconnect (former eV Products) [Pennsylvania]
- GE Healthcare (former Orbotec / Imarad) [Israel]
- Redlen [British Columbia, Canada]

Two dominant detector module configurations:

Both - 5 mm thick,  $16 \times 16 = 256$  pixels/module

- Gamma Medica (optimized for breast):
  - 2.5 cm x 2.5 cm, 1.6 mm pixel pitch, 4.7% FWHM @140 keV
- GE Healthcare (optimized for heart):
  - 4 cm x 4 cm, 2.5 mm pixel pitch, 6% FWHM @140 keV

Q2: Compare BSGI and MBI: how many detector heads are used and what type of detectors?

0% a) BSGI: 2 CZT; MBI: 1 scintillator

0% b) BSGI: 1 CZT; MBI: 2 scintillator

0% c) BSGI: 1 scintillator; MBI 2 CZT

0% d) BSGI: 2 scintillator; MBI 1 CZT

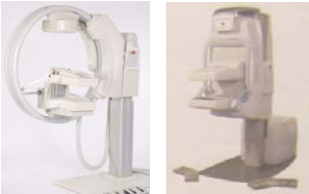




0% e) BSGI: 1 scintillator; MBI 2 scintillator

Q2: Compare BSGI and MBI: how many detector heads are used and what type of detectors?

- a) BSGI: 2 CZT; MBI: 1 scintillator
- b) BSGI: 1 CZT; MBI: 2 scintillator
- c) BSGI: 1 scintillator; MBI 2 CZT**
- d) BSGI: 2 scintillator; MBI 1 CZT
- e) BSGI: 1 scintillator; MBI 2 scintillator


Reference: M O'Connor, et al, Molecular Breast Imaging, *Expert Reviews Anticancer Ther* 2009; 9: 1073-80.

# Comparison of Breast Imaging Modalities

	MBI	Digital Mammography	Tomosynthesis	MRI	Ultrasound
					
<b>Probe</b>	Gamma emission	X-ray transmission	X-ray transmission	RF excitation / emission	Sound-wave transmission
<b>Imaging Type</b>	Molecular	Anatomic	3D Anatomic	3D Anatomic / Physiologic	Anatomic
<b>Clinical Indications</b>	Secondary Dx / dense-breast screening	Screening	Secondary Dx / dense-breast screening (TBD)	Secondary Dx	Secondary Dx
<b>Sensitivity</b>	80-95%	30% Dense breast	60%? Dense breast (TBD)	80-91%	50% dense breast with Mammography
<b>Specificity</b>	76-94%	70-80%	80-90% (TBD)	20-90%	50-60%
<b>Reimbursement</b>	\$300-\$600	\$85-\$140	\$85-\$140 (TBD)	\$535-\$1,200	\$90-\$150
<b>Whole-Body Radiation Dose</b>	1.2 mSv	0.5 mSv	1.0 mSv	0	0
<b>Patient Tolerance</b>	~100% (mild immobilization)	~80% (painful compression)	~80% (painful compression)	~60% (prone)	~100%
<b>Interpretation Difficulty</b>	Easy hot spot images	More difficult	More difficult	Most difficult & most images	More difficult - operator dependent
<b>Exam Time</b>	40 minutes or *20 minutes	15 to 20 minutes	15 to 20 minutes	60 to 90 minutes	45 to 60 minutes
<b>Advantages</b>	Highest sensitivity and specificity; Low dose; Mild immobilization	Lowest cost; Low dose; High accessibility	Better dense-breast sensitivity than mammography	High sensitivity; No radiation	Low cost; No radiation; High accessibility
<b>Disadvantages</b>	*Currently: long exam	Low dense breast sensitivity; Painful compression	Double MMG dose; Painful compression	Lower specificity; False positives; Difficult to read; Low patient tolerance; Many contraindications; Highest cost; Slow	Low sensitivity; Low specificity; False positives; Operator dependent; Slow

\* Improvements in progress will result in 20 minute exam and dense-breast screening PMA (c. 2013).

# Comparison of Molecular Imaging Products

	Gamma Medica	GE Healthcare	Dilon	Naviscan
				
<b>Modality</b>	MBI	MBI	Breast Specific Gamma Imaging	Positron Emission Mammography (PEM)
<b>Detector Configuration</b>	2 heads only	1 or 2 heads	1 head only	2 heads only
<b>Detectors</b>	CZT	CZT	Nal+PS-PMTs (6800) or CsI+APDs (Acella)	LSO/LYSO + PS-PMTs
<b>Energy Resolution</b>	4.7% FWHM @140 keV	6.0% FWHM @140 keV	12.0% FWHM @140 keV	14.0% FWHM @ 511keV
<b>Pixel Pitch (Intrinsic Resolution)</b>	1.6 mm	2.5 mm	3.2 mm	2.0 mm
<b># Pixels / System</b>	24,576	12,288 or 6,144 (single)	3,072 (6800) or 5,248 (Acella)	4,056
<b>Collimator</b>	Registered tungsten low-dose	Registered lead	LEGP lead	Coincidence for PET
<b>Geometric Efficiency (System Sensitivity)</b>	1,600 cps/MBq	550 (single) or 1,100 cps/MBq	400 cps/MBq (single head)	unpublished
<b>Clinical Dose</b>	*4 mCi 99mTc-Sestamibi	8 mCi 99mTc-Sestamibi	15 mCi 99mTc-Sestamibi	10 mCi 18F-FDG
<b>Whole-Body Dose</b>	*1.2 mSv	2.4 mSv	4.5 mSv	7 mSv
<b>Biopsy Guidance</b>	Yes: mid-2012	Under development	Yes	Yes
<b>Useful Field of View</b>	15.4 x 20.5 cm <sup>2</sup> or 15.4 x 24.0 cm <sup>2</sup>	15.7 x 23.6 cm <sup>2</sup>	15.0 x 20.0 cm <sup>2</sup> or 20.0 x 25.0 cm <sup>2</sup>	16.3 x 24.0 cm <sup>2</sup>
<b>Integral Uniformity</b>	1.1%	1.2%	10%	unpublished

\* Improvements in progress will result in 2 mCi (0.6 mSv) in early 2013.

## Published Clinical Studies: Sassari, Italy 1635 patients



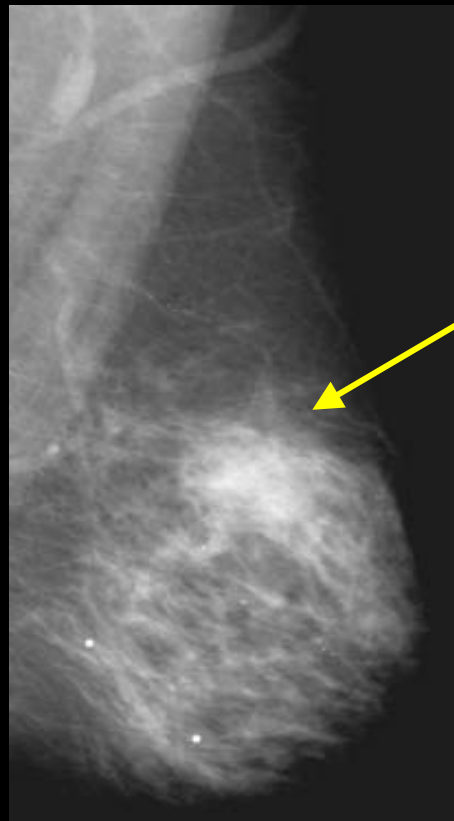
Author	Study	Pt. #	Sensitivity (%)	Specificity (%)	Reference
Spanu	Compare w/SPECT, <sup>99m</sup> Tc-tetrofosmin (TF)	29	93	100	EANM 2006 P211
Spanu	BrCa detection, TF	85	90.3-100%	91.7	Int J Onc 31: 369-377 (2007)
Spanu	BrCa detection, TF	129	92.5-100%	88.2	EANM 2007 P198
Spanu	Neoadjuvant, TF	32			EANM 2007 P201
Spanu	Neoadjuvant, TF	38			SNM 2008 1445
Spanu	BrCa detection, TF	242	95.4%		SNM 2008 1447
Spanu	BrCa detection, TF	145	97.2%	86.4	Clin Nuc Med 33(11) (2008):739-742
Spanu	Compare w/mammo, TF	232	93.2 (90.1 mammo) 87.5 (47.5 mammo) 89.6 (37.9 mammo)	88.2 (52.9 mammo)	QJ Nuc Med 53(2) (2009): 133-143
Spanu	BrCa detection, TF	321	88.9-100	86.4	SNM 2009 1696
Spanu	Compare w/mammo, TF Concl: 30% can avoid Bx	353	87.5-	88.6	SNM 2010 1623
Spanu	Compare w/DCE MRI, TF Concl: MRI overstages	29	96.5 (96.5 MRI)		SNM 2010 1205

# Published Clinical Studies: Mayo Clinic 2747 patients



Author	Study	Pt. #	Sensitivity (%)	Specificity (%)	Reference
Rhodes	BrCa detection	40	92		Mayo Clin Proc 80(1) (2005): 24-30
O'Connor	MBI for small tumor detection	100	85% (overall)		Int J Onc 31: 369-377 (2007)
O'Connor	MBI as adjunct to mammo	800	85.7 (28.6 mammo)	93.9 (91.2 mammo)	SNM 2008 Abst 159
Hruska	BrCa detection in high-risk	650	85%		Amer J Surg 196(4) (2008) 470-476
Hruska	Compare dual camera versus single; BI-RADS 4 or 5	150	90(80 single) all 82(68 single) <10 mm		Amer J Roent 191 (2008) 1805-1815
Rhodes	Compare w/mammo, Screening of dense breasts	1007	50(25 mammo) DCIS 100(29 mammo) Invasive 82(27 mammo) All Ca 91 All Ca MBI/Mammo	93 (91 mammo)	Radiol 258 (2011): 106-118.

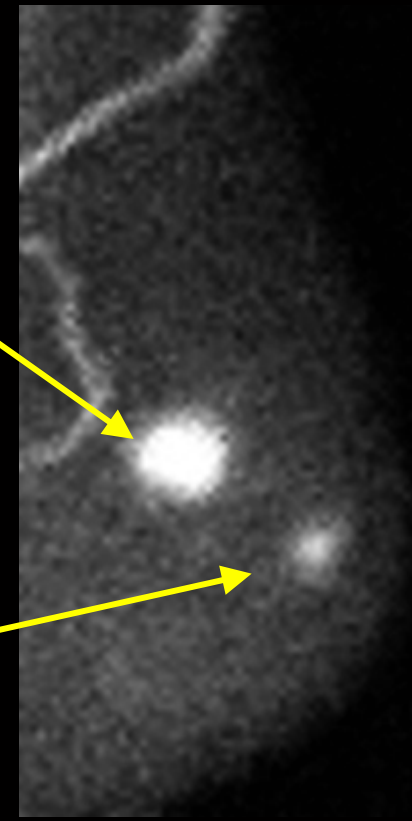
# Molecular Breast Imaging (MBI) *Secondary Diagnosis*



**Mammogram**

20 mm cancer  
seen on MMG &  
MBI

Additional 10 mm  
cancer seen only  
on MBI

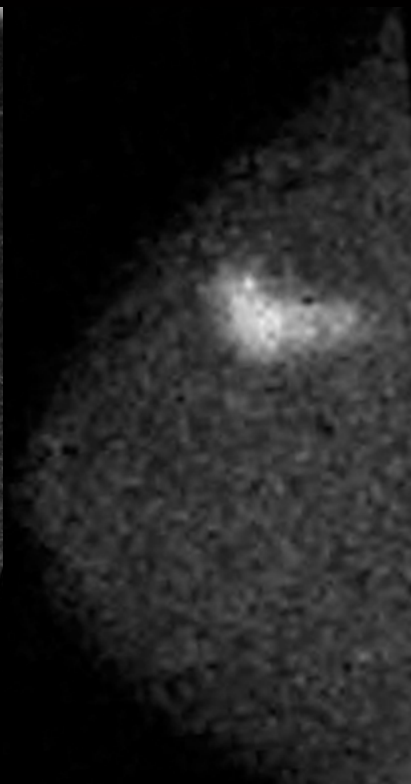
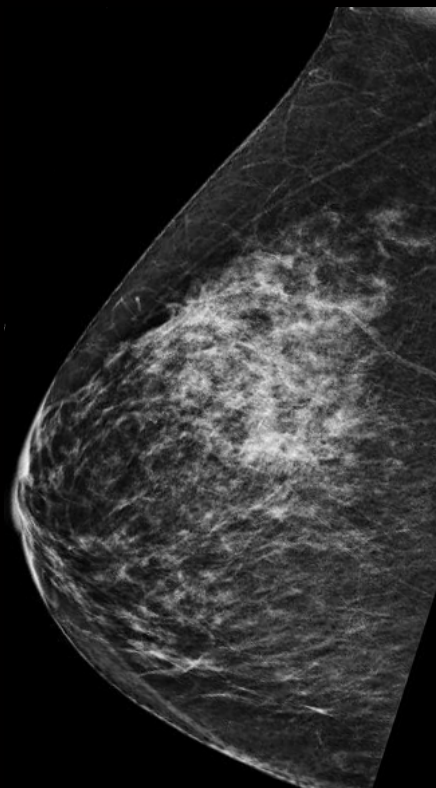
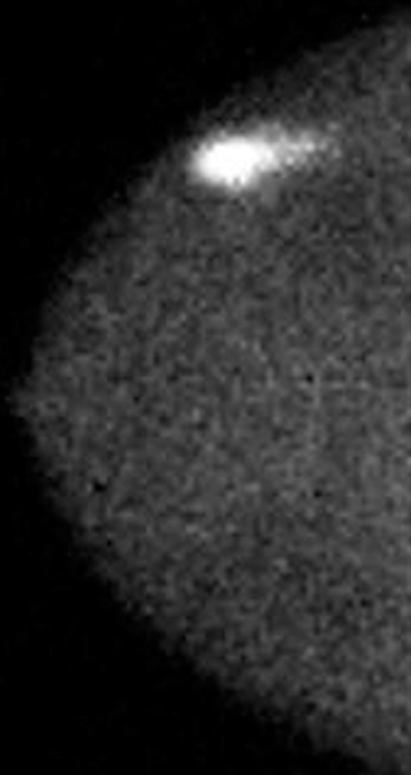
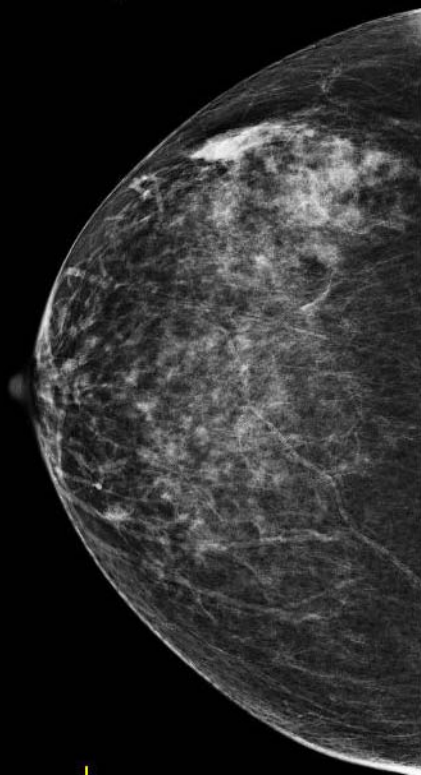


**Molecular Breast Imaging**

# Patient Example: IDC with DCIS extension

Rt CC

Rt MLO



Digital Screening Mammography (Negative)

Molecular Breast Imaging (Positive)

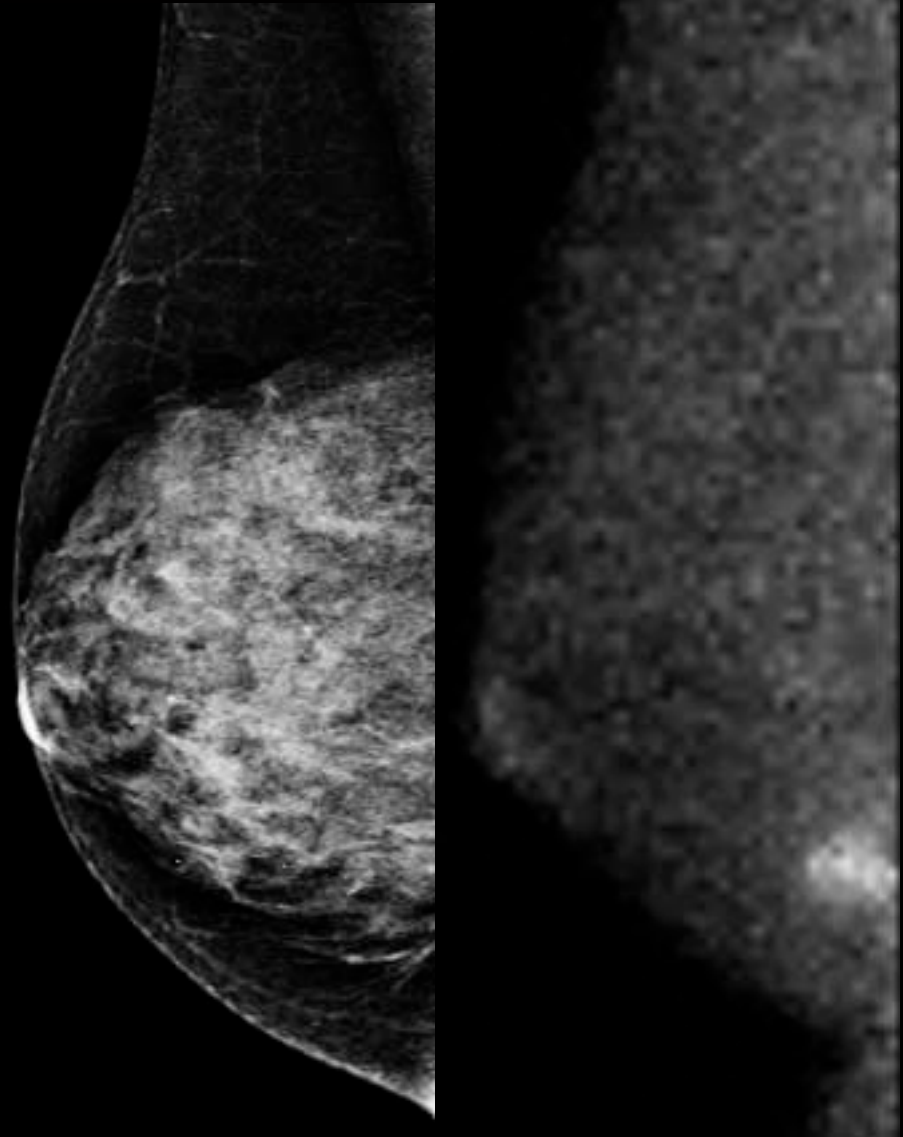
17 mm IDC with DCIS extension

# Patient Example: Ductal Carcinoma In Situ

Digital Screening  
Mammography  
(Negative)

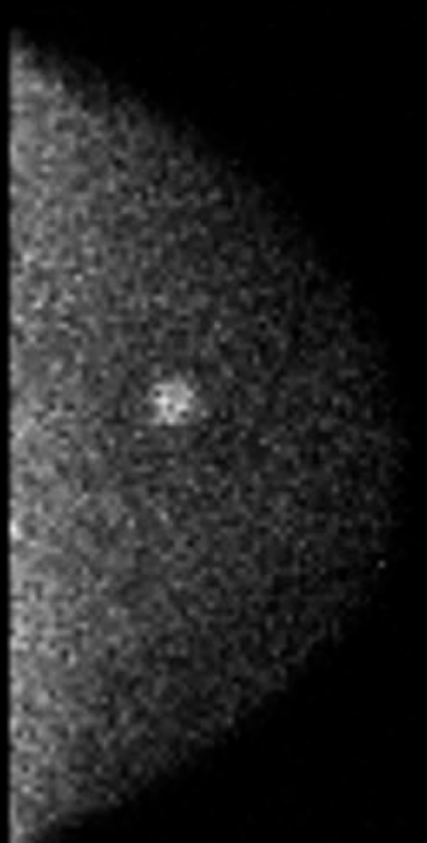
Molecular Breast Imaging  
(Positive)

9 mm Ductal Carcinoma In Situ

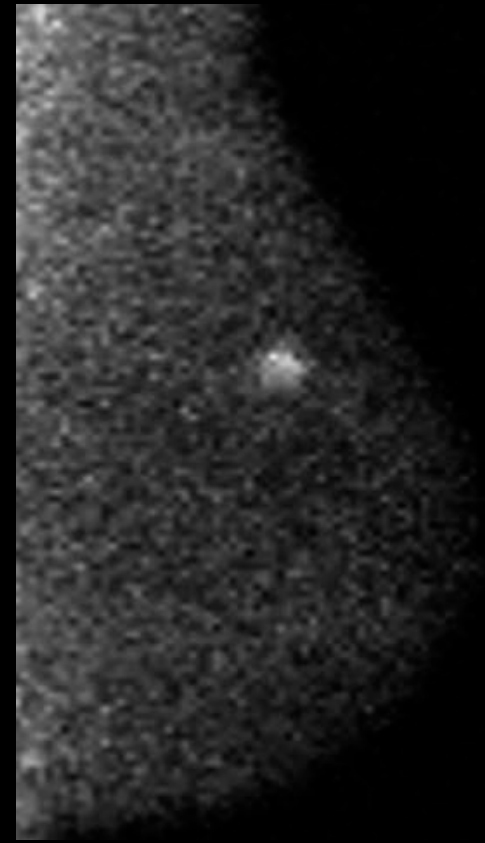
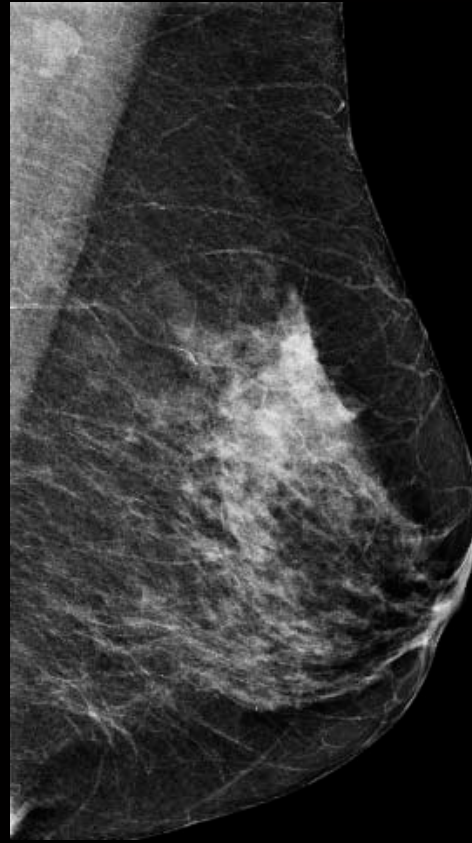


# Patient Example: Tubulolobular Carcinoma

Lt CC



Lt MLO



Digital Screening Mammography (Negative)

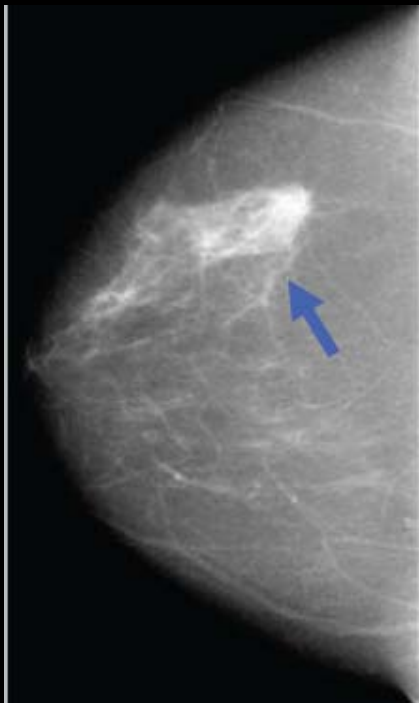
Molecular Breast Imaging (Positive)

7 mm Tubulolobular Carcinoma

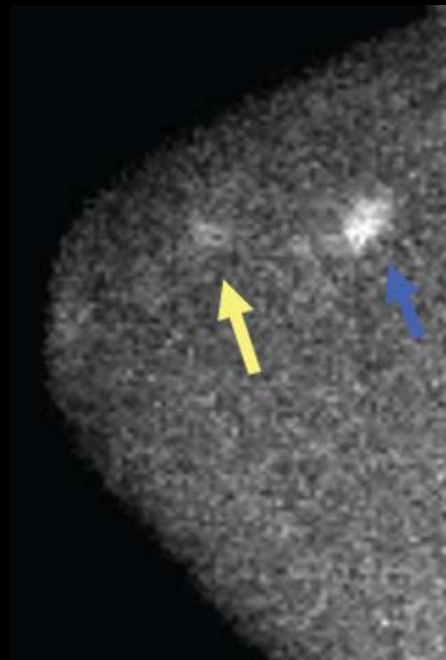
# Patient Example: MBI versus MRI

## Infiltrating Lobular Carcinoma

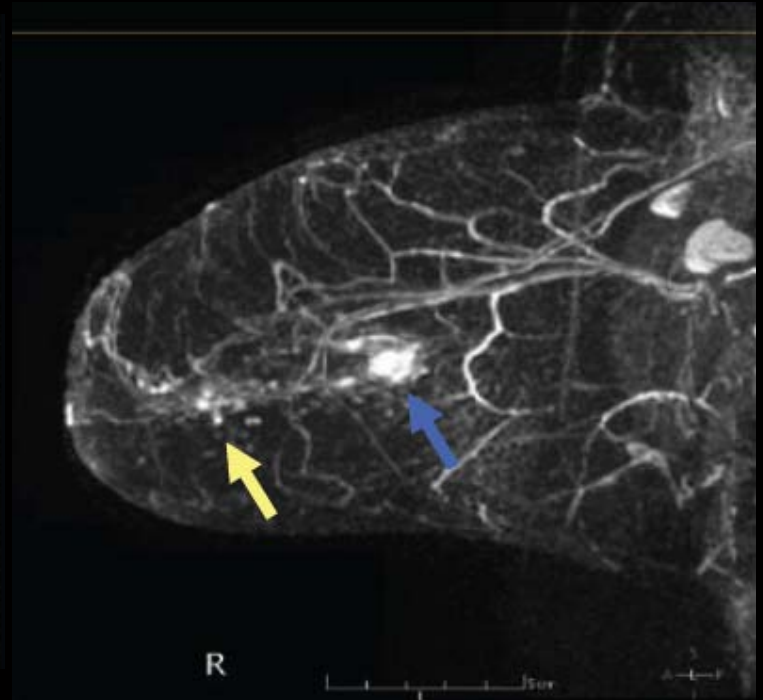
- Index lesion detected on mammography (blue arrows)
- Multifocal cancer detected by MBI and MRI only (yellow arrows)



Screen Mammogram



MBI



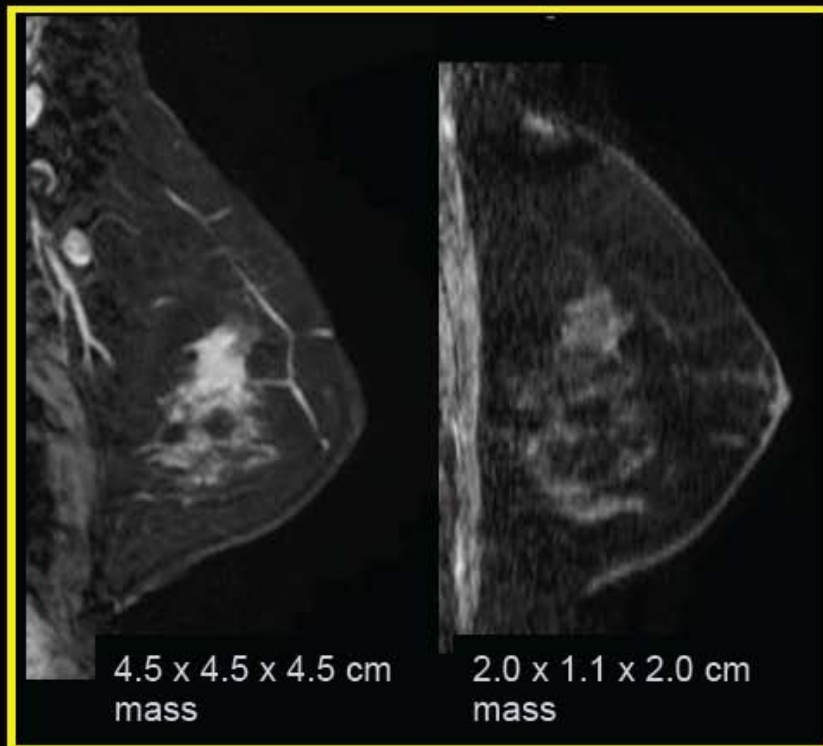
Breast MRI

*Courtesy of Mayo Clinic.*

# Patient Example: MBI versus MRI

Pre and Post Neoadjuvant Chemotherapy

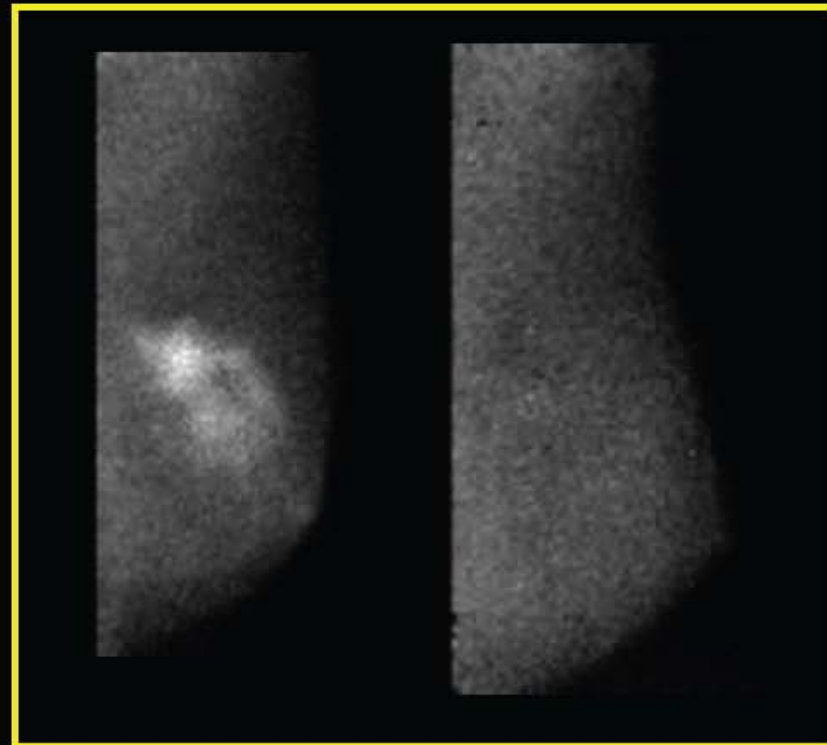
MRI



Pre-therapy

Post-therapy

Molecular Breast Imaging



Pre-therapy

Post-therapy

Initial diagnosis: IDC with large Area of DCIS

MRI: indicated residual disease

Left Mastectomy: Surgical Pathology indicated no residual viable cancer

*False Positive from MRI → Unnecessary Mastectomy*

*Courtesy of Mayo Clinic*

# MBI Lexicon, Teaching Files, & CME Course

## Gamma Camera Molecular Breast Imaging Lexicon: A Pictorial Review

Robert W. Maxwell, M.D.  
Amy L. Conners, M.D.  
Cindy L. Tortorelli, M.D.  
Carrie B. Hruska, PhD  
Deborah J Rhodes, M.D.  
Judy C Boughey, M.D.  
Wendie A Berg, M.D., PhD

In revision

## Lexicon for Standardized Interpretation of Gamma Camera Molecular Breast Imaging: Observer Agreement and Diagnostic Accuracy

Amy L. Conners, M.D.  
Carrie B. Hruska, PhD  
Cindy L. Tortorelli, M.D.  
Robert W Maxwell, M.D.  
Deborah J. Rhodes, M.D.  
Judy C. Boughey, M.D.  
Wendie A. Berg, M.D., PhD

In press

2012, *European Journal of Nuclear Medicine and Molecular Imaging*, epub & in press

The same Mayo Clinic authors have compiled **teaching files** and recorded a **video CME course** on “**Molecular Breast Imaging Interpretation**” – soon to be released.

# Published MBI Screening Clinical Data

## High-Risk Screening Study

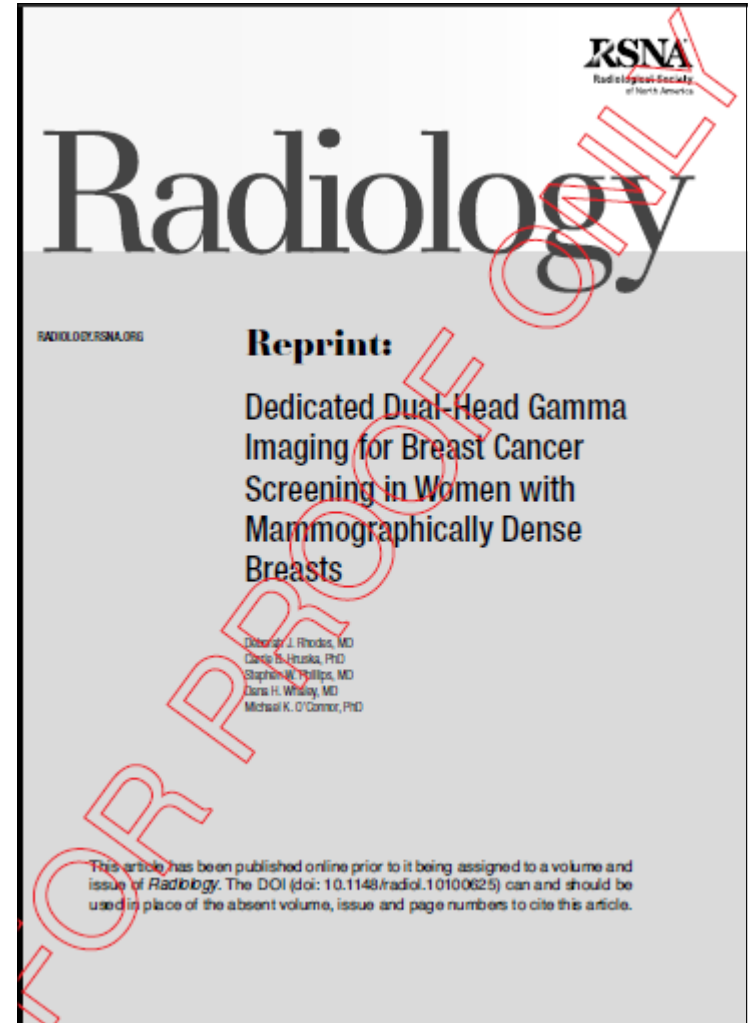


Inclusion Criteria: Dense Breast  
+ another high risk factor

1,007 patient study shows:

- ❖ 91% Sensitivity (MMG+MBI)
- ❖ 93% Specificity (MBI alone)

Includes one year follow up



Jan. 2011 *Radiology*

# Low-Dose Dense-Breast MBI Screening

Funded by Susan G. Komen Foundation



Inclusion Criterion: > 50% Dense Breast on prior year's MMG

**8 mCi <sup>99m</sup>Tc-sestamibi** (analyzed as 4 mCi – half acquisition time)

1,700 patient study ended cohort enrollment in February 2012 with one year follow up

**Full report at RSNA 2012**

Interim results (reported RSNA 2011):

Diagnostic performance characteristics at participant level:

Characteristic	Incident MMG	Prevalent MBI	Combination
Sensitivity	3/15 (30%)	13/15 (87%)	14/15 (93%)
Recall Rate	137/1252 (11%)	128/1252 (10%)	221/1252 (18%)
Biopsies	13/1252 ( 1%)	38/1252 ( 3%)	48/1252 ( 4%)
PPV	3/137 ( 2%)	13/128 (10%)	14/221 ( 6%)

*Courtesy Deborah J. Rhodes, MD, Mayo Clinic*

Q3: The SNM recommends for BSGI a 925 MBq (25 mCi)  $^{99m}\text{Tc}$ -Sestamibi dose; what is the dose currently used by the Mayo Clinic for MBI?

- 0% a) 148 MBq (4 mCi)
- 0% b) 296 MBq (8 mCi)
- 0% c) 370 MBq (10 mCi)
- 0% d) 555 MBq (15 mCi)
- 0% e) 740 MBq (20 mCi)

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d) 555 MBq (15 mCi)

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References: SJ Goldsmith, et al, SNM Practice Guideline for Breast Scintigraphy with Breast-Specific  $\gamma$ -Cameras 1.0, *J Nuc Med Tech* 2010; 38; 219-224.

MK O'Connor, et al, Comparison of radiation exposure and associated radiation-induced cancer risks from mammography and molecular imaging of the breast, *Med Phys* 2010; 37: 6187-98.

# Breast Cancer Imaging Market Segments

## 1. General Screening

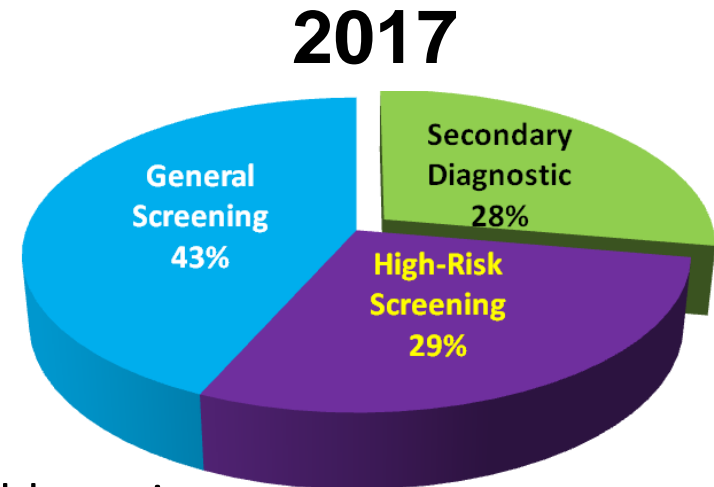
- Recommended for women over 40 (or 50?)
- Biggest player: Digital Mammography
- Future players: TomoSynthesis , Counting mode MMG (MicroDose), Color CT

## 2. Secondary Diagnostic

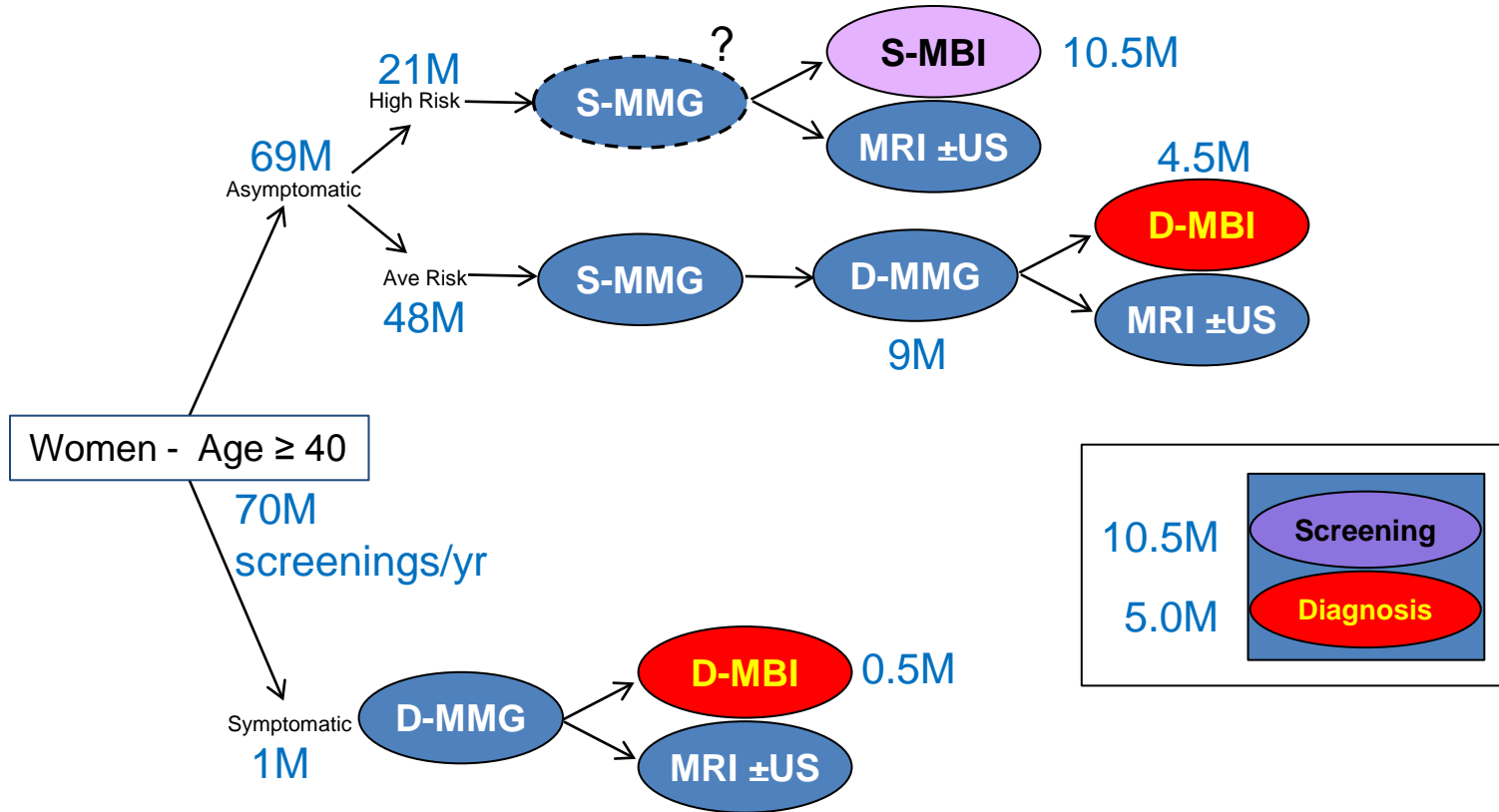
- MMG equivocal; for surgical staging & treatment monitoring
- Emerging, growing market beginning ~2005
- Biggest player: MRI
- Other players: Ultrasound, **MBI**

## 3. High-Risk Screening

- Brand-new field
- Dense breasts, family history, BRCA genes, Ashkenazi
- Biggest players: Ultrasound, MRI
- Future players: **MBI**

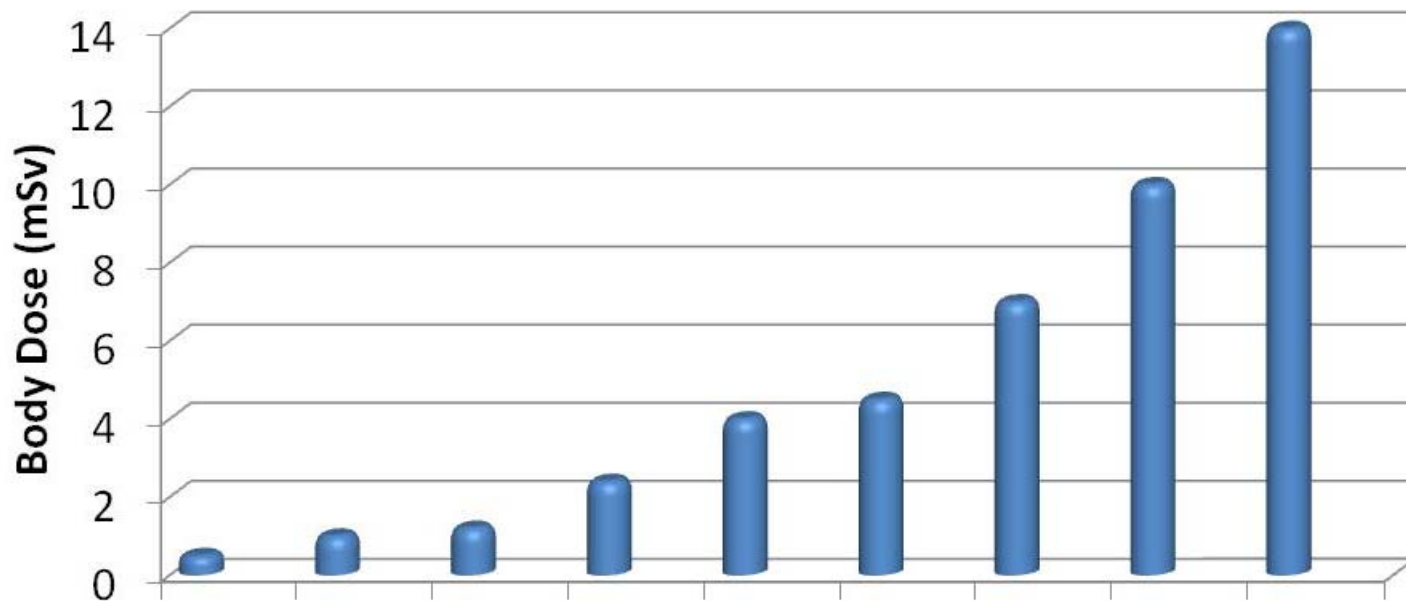


# Clinical Flowchart: MBI Screening & Diagnosis



High Risk (Dense Breast) Screening: MBI becomes standard  
2<sup>nd</sup>ary Diagnosis: MBI with MBI-guided Biopsy competes with MRI, US

# Radiation dose reduction



# Radiation Dose Reduction

Consider the exam-time/dose tradeoff yield from improving technology:

- detector & collimator optimization
- energy window optimization
- noise reduction algorithms
- fusion image from two detectors

Initial dose for BSGI and MBI was 20-30 mCi  $^{99m}\text{Tc}$ -sestamibi

MBI dose has been lowered to 8 mCi and ongoing development promises to lower it further to 2-4 mCi.

# Radiation Dose - Perspective

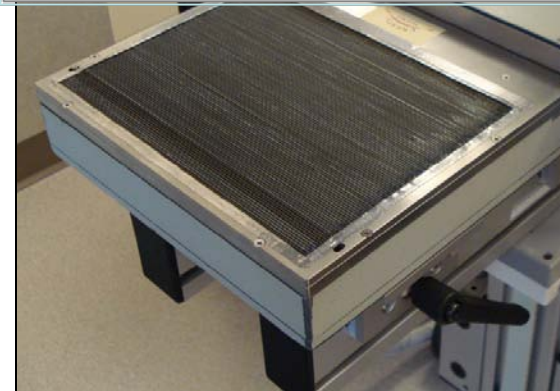
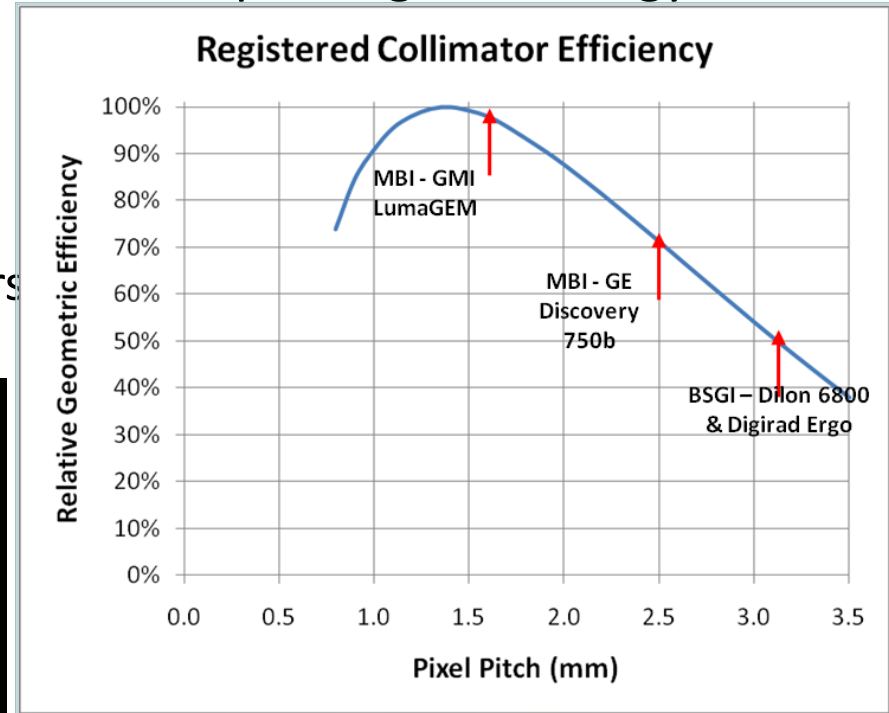
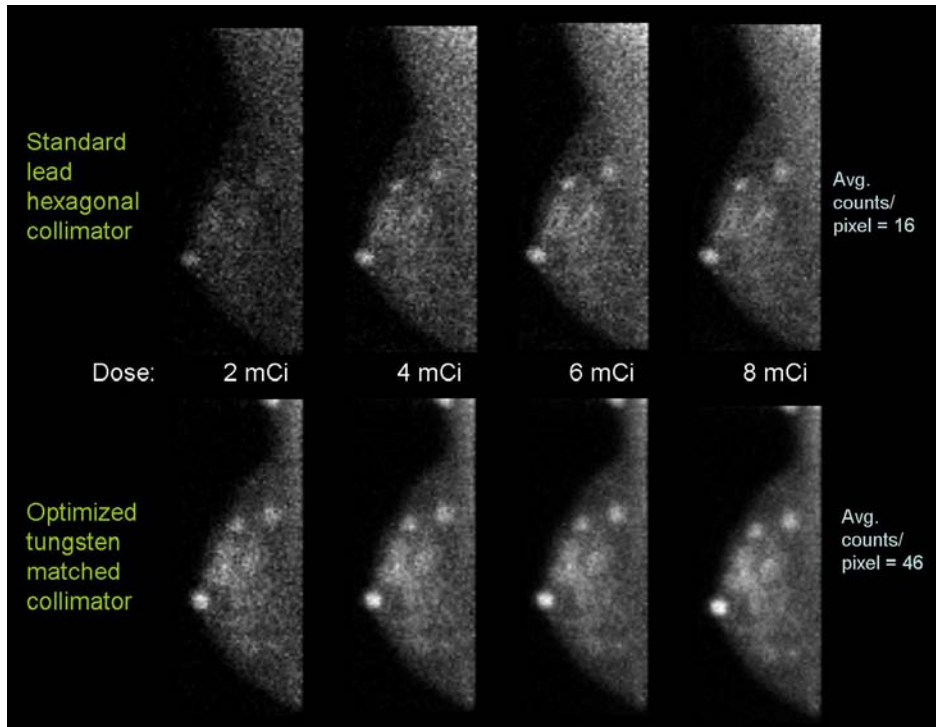
## Typical Radiation Doses (From Various Sources)\*

Watching television <sup>2</sup>	0.01 mSv/year
Air travel (roundtrip from Washington, D.C., to Los Angeles, Calif.) <sup>3</sup>	0.05 mSv
Medical chest X-ray (one film) <sup>4</sup>	0.1 mSv
Nuclear medicine thyroid scan <sup>2</sup>	0.14 mSv
Full set of dental X-rays <sup>3</sup>	0.4 mSv/year
Mammogram (four views) <sup>1</sup> <b>MBI</b>	0.7 mSv
Average annual exposure living in the United States <sup>6</sup>	3 mSv/year
Average annual exposure from breathing radon gas <sup>5</sup>	2 mSv
Nuclear medicine lung scan <sup>1</sup>	2 mSv
<hr style="border-top: 1px dashed black;"/>	
Nuclear medicine bone scan <sup>1</sup>	4.2 mSv
Nuclear cardiac diagnostic test (technetium or Tc-99m) <sup>4</sup>	10 mSv
Abdominal CT scan <sup>1</sup>	10 mSv
Various PET studies (18F FDG) <sup>1</sup> <b>Airline Crew</b>	14 mSv
Tobacco products (amount for a smoker's lungs from 20 cigarettes a day) <sup>5</sup>	53 mSv/year
Cancer treatment (tumor receives) <sup>5</sup>	50,000 mSv

\*Radiation doses are estimated; obtained from various sources.

# Radiation Dose Reduction

- Consider the time-dose tradeoff yield from improving technology:
  - detector / collimator optimization
  - energy window optimization
  - noise reduction algorithms
  - composite image from two detectors



Tungsten square holes registered to detector pixels

# System sensitivity – effect of collimation and energy window

Study performed by Mayo Clinic on LumaGEM & GE MBI system

Detector	Collimator	Energy Window	counts/ min/ $\mu$ Ci	Relative gain in counts/pixel
<b>CZT 1.6 mm Pixel (GMI)</b>	Standard	Standard, 140 $\pm$ 10%	312	1.0
	Standard	Wide, 112 – 154 keV	391	1.3
	Tungsten design	Standard 140 $\pm$ 10%	905	2.9
	Tungsten design	Wide, 112 – 154 keV	1132	3.6
<b>CZT 2.5 mm Pixel (GE)</b>	Standard	Standard, 140 $\pm$ 10%	254	1.0
	Standard	Wide, 112 – 154 keV	331	1.3
	optimized design	Standard 140 $\pm$ 10%	534	2.1
	optimized design	Wide, 112 – 154 keV	705	2.8

62%

# Radiation Dose Reduction

- Consider the time-dose tradeoff yield from improving technology:
  - detector / collimator optimization
  - energy window optimization
  - noise reduction algorithms
  - composite image from two detector

CZT spectral tail:  
charge-sharing (10%) &  
hole-trapping

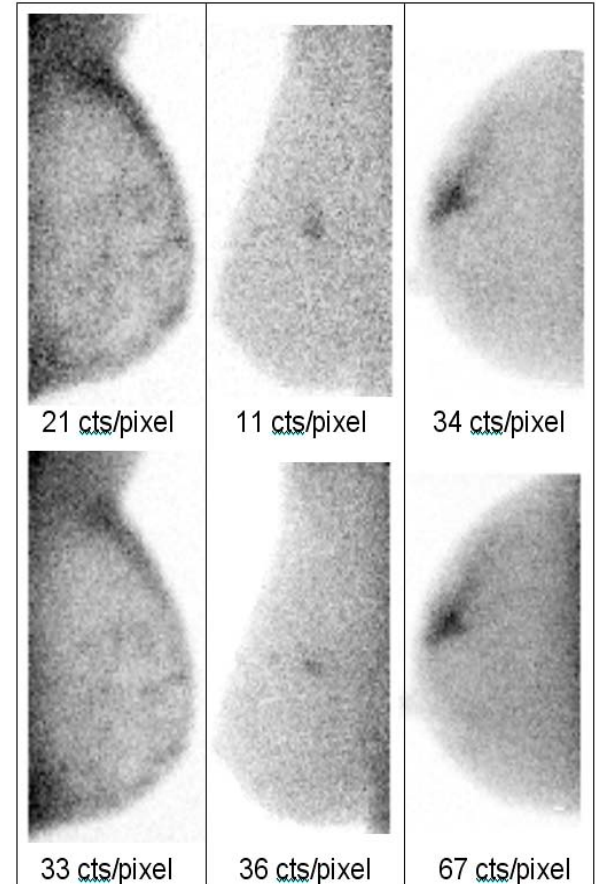
Very little scatter in breast

Wide energy  
Window (20%)  
(110-154 keV)

~1.4 gain in  
sensitivity

Standard  
energy  
window (126-  
154 keV)

Wide energy  
window (110-  
154 keV)

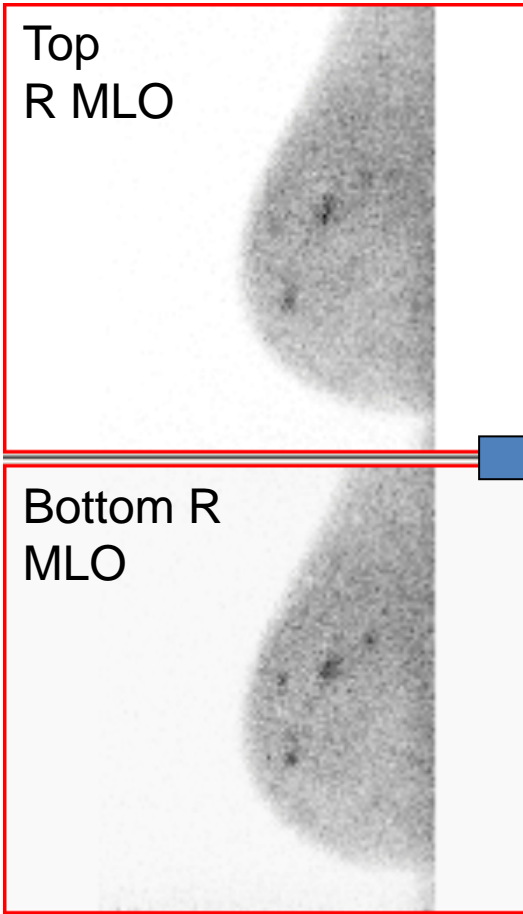


Courtesy of Mayo Clinic

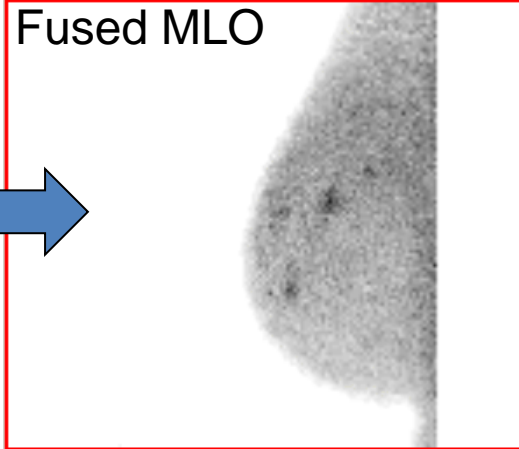
# Dual-Image Fusion & Noise Reduction - WIP

20 mCi (old protocol)

- noise reduction algorithms
- fusion image from two detectors



**4 mCi** (new WIP protocol)

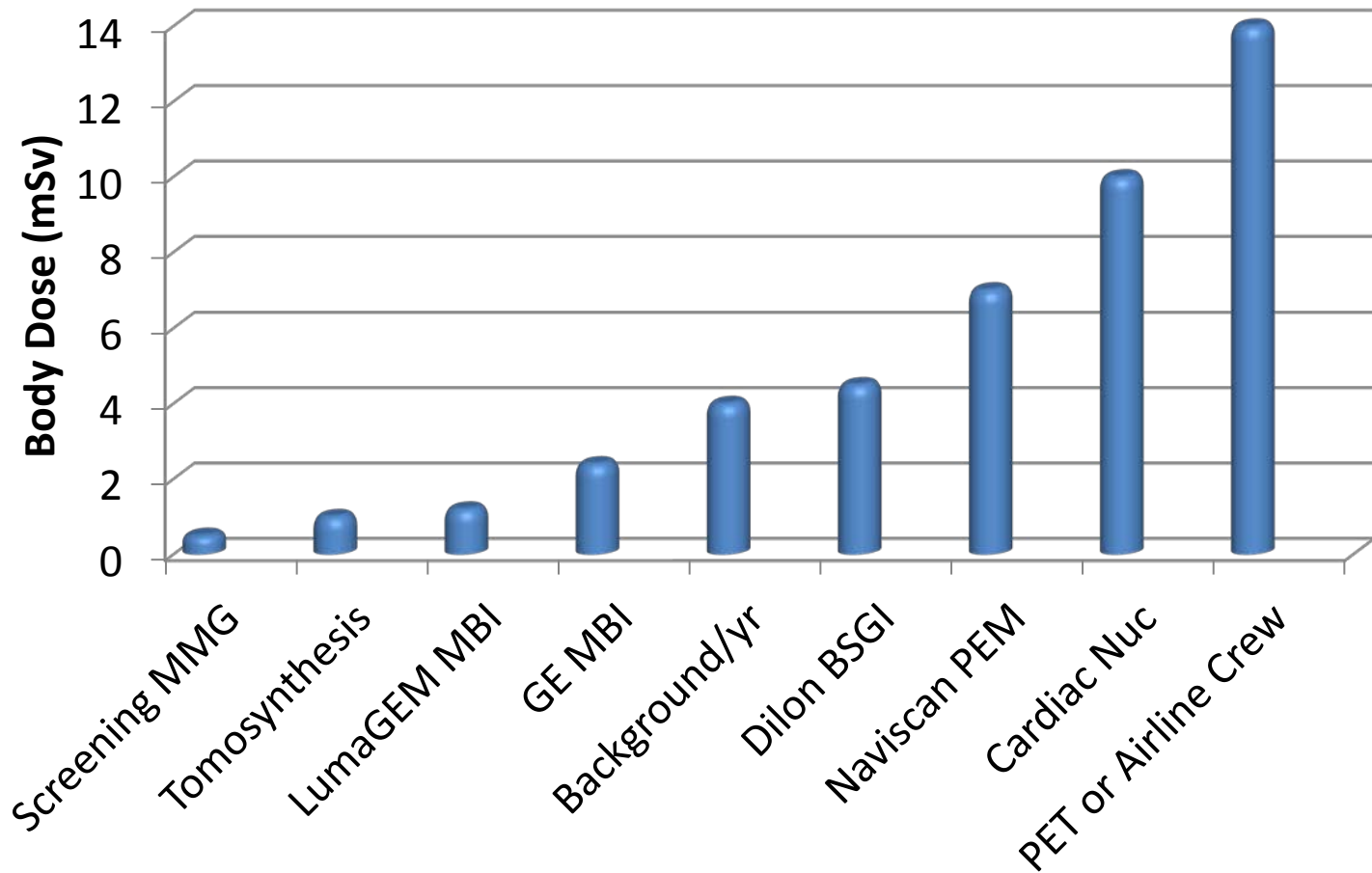


The top and bottom planar images are fused with use of an adaptive, edge-preserving, noise-reduction filter

Mayo Clinic is validating use of 4 mCi  $^{99m}\text{Tc}$ -sestamibi protocol in clinical studies  
This low dose is equivalent to screening MMG

*Courtesy of Mayo Clinic*

# Radiation Dose Comparisons



MBI at 2-4 mCi essentially equivalent to screening MMG

# Breast Imaging Radiation Dose

\*Dense-breast

Modality	Radiation	Dose / year	Risk*: Attributable Deaths / 100,000	Benefit*: Lives Saved / 100,000	Benefit / Risk
MBI – Gamma Medica LumaGEM	2-4 mCi <sup>99m</sup> Tc-MIBI	~0.6 - 1.2 mSv	36-72	2408	34-67:1
Digital Mammography	X-rays	~0.5 mSv	15	845	56:1
Tomosynthesis	X-rays	~1 mSv	40	~1600	~40:1
PEM - Naviscan	10 mCi <sup>18</sup> FDG	~7 mSv	408	~2000	~5:1
BSGI – Dilon 6800 & Digirad Ergo	15 mCi <sup>99m</sup> Tc-MIBI	~4.5 mSv	270	~1800	~7:1
MBI - GE Discovery 750b	8 mCi <sup>99m</sup> Tc-MIBI	~2.4 mSv	140	~2200	~16:1

\* Assumes annual breast screening for ages 40-80  
 ~ Calculated capability – no clinical trial evidence

Based on: Hendrick, *Radiology*, 2010;257:246-253  
 & O'Connor, *Med Phys*, 2010;37:6187-98

# Shorter Exam Times

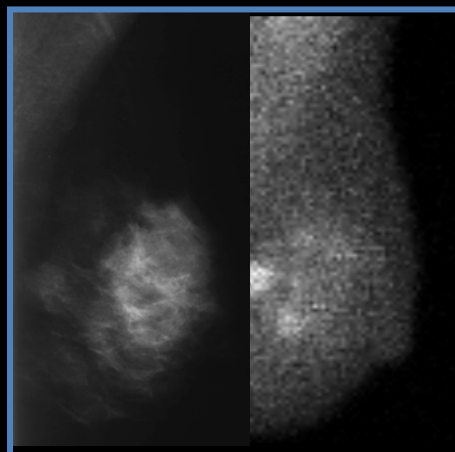
After dose reduction to MMG level:

GMI & Mayo Clinic are developing new technology (electronics and software algorithms) to achieve by mid-2013:

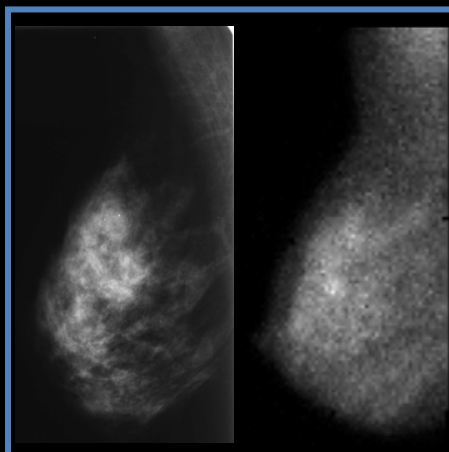
- 3 - 5 min/view @ 4mCi *or*
- 6 - 8 min/view @ 2 mCi

Result: 15 – 35 min total screening exam time

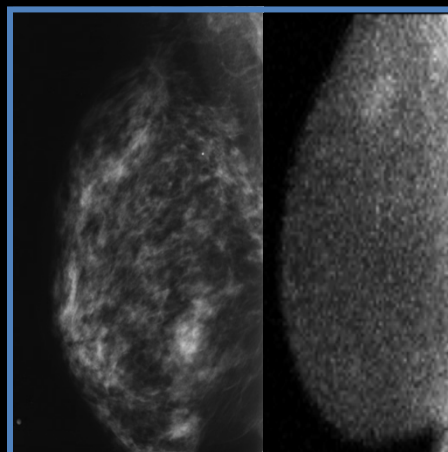
# Mammographically Occult Cancers Detected on MBI



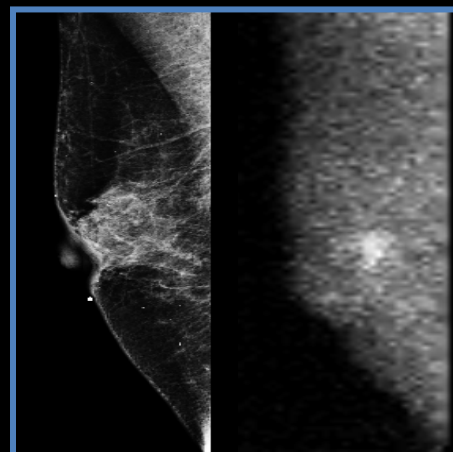
10 mm + 16 mm IDC



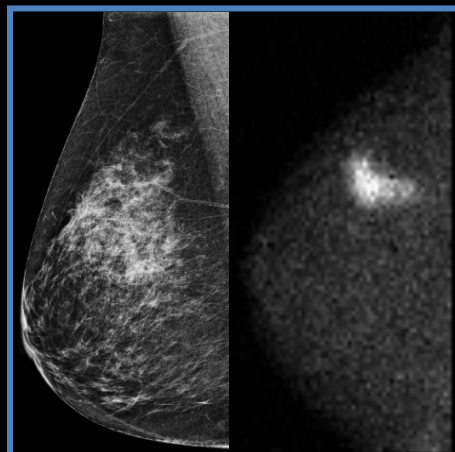
8 mm DCIS



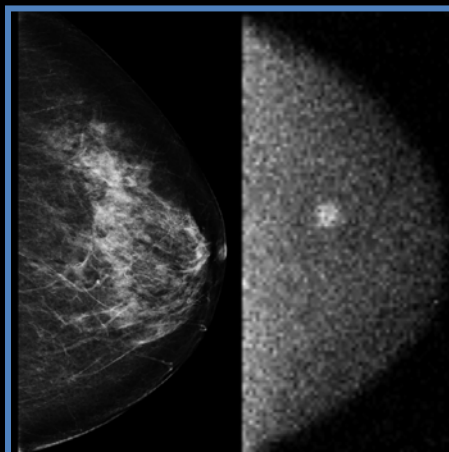
9 mm ILC



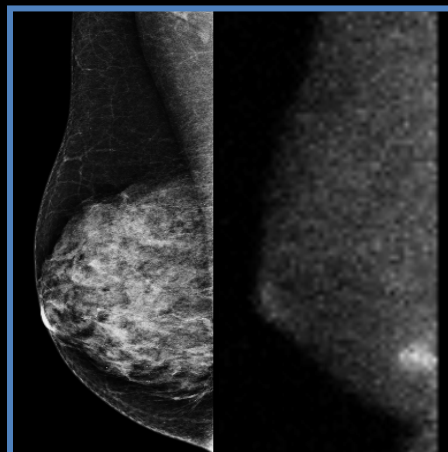
9 mm IDC



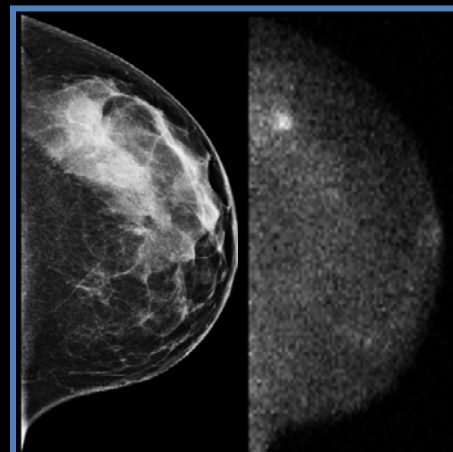
17 mm IDC + DCIS



7 mm tubulolobular ca



9 mm DCIS



13.5 mm ILC (total extent 5.1 cm)

## Q4: What are the most important factors leading to a dose reduction in MBI?

- 0% a) Quantum efficiency of the detector, LEHS collimator
- 0% b) Patient prep (fasting, delay for background washout), LEHS collimator
- 0% c) LEHS collimator, noise reduction filter, CZT detectors
- 0% d) Optimal pixel size, registered collimator, two detector heads, noise reduction filter
- 0% e) Registered tungsten collimator, CZT detectors

## Q4: What are the most important factors leading to a dose reduction in MBI?

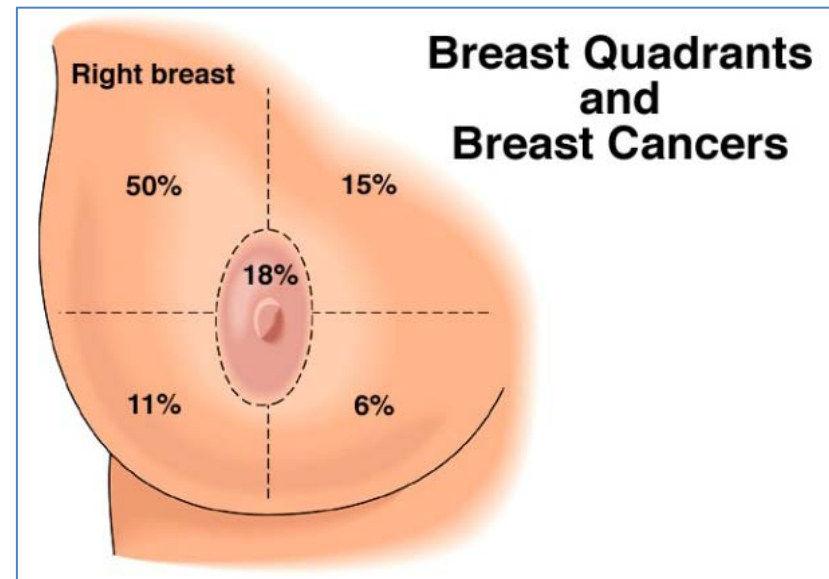
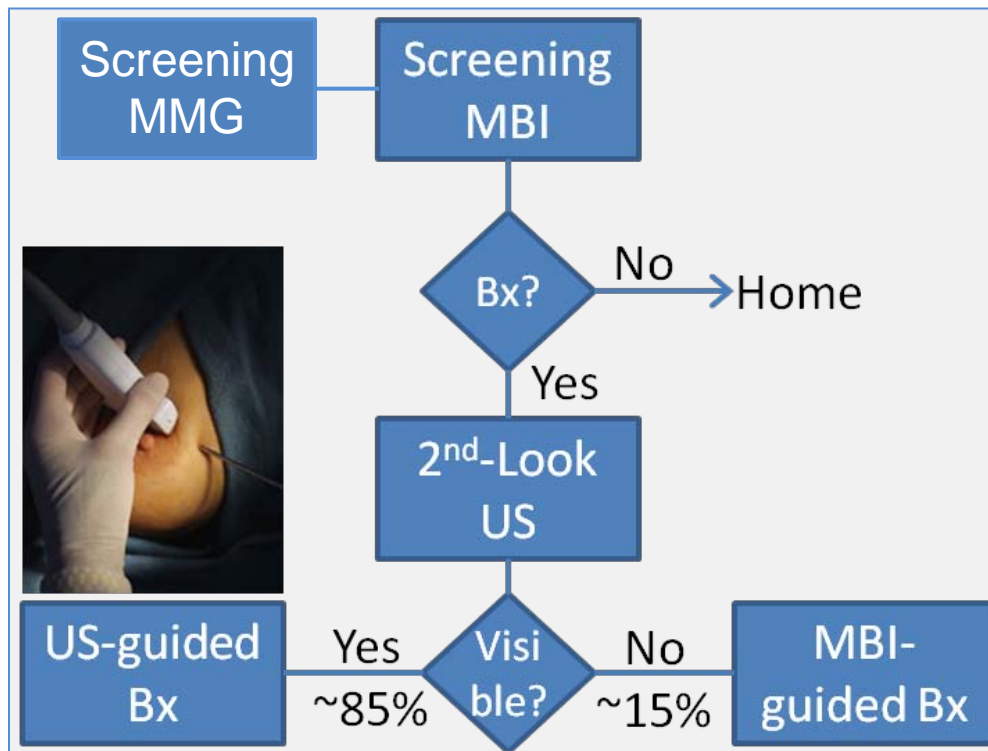
- a) Quantum efficiency of the detector, LEHS collimator
- b) Patient prep (fasting, delay for background washout), LEHS collimator
- c) LEHS collimator, noise reduction filter, CZT detectors
- d) Optimal pixel size, registered collimator, two detector heads, noise reduction filter
- e) Registered tungsten collimator, CZT detectors

Reference: AL Weinmann, et al, Design of optimal collimation for dedicated molecular breast imaging systems, *Med Phys* 2009; 36: 845-56.

# Pre-requisite to screening: MBI-guided Biopsy

MBI-guided biopsy on LumaGEM<sup>®</sup> is being developed

- Clinical trials at beta sites mid-2012
- Stereotactic targeting
- Lateral access to breast between detectors
- **Specimen verification**

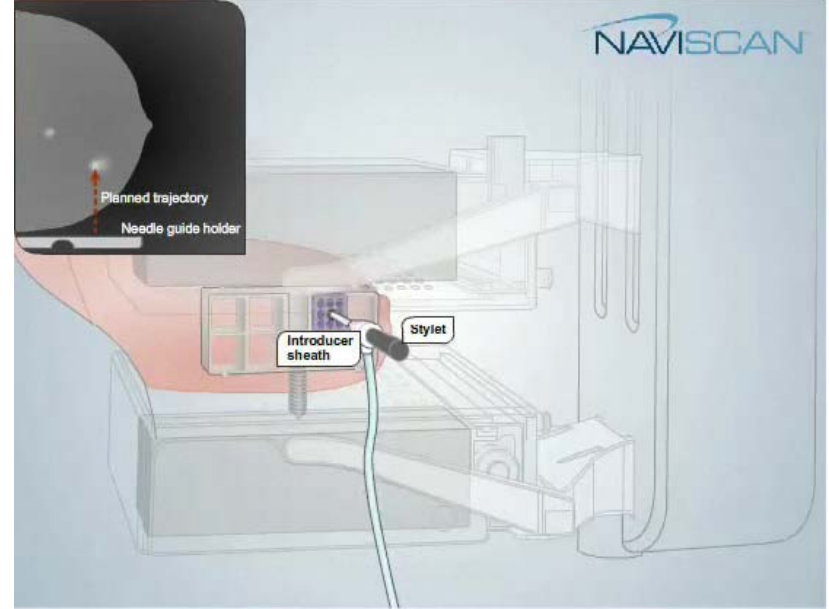


Visualize occult lesions with higher specificity

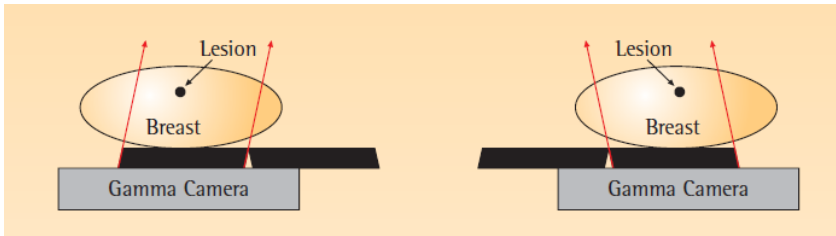
# BSGI- & PEM-guided Biopsy



Dilon – top approach



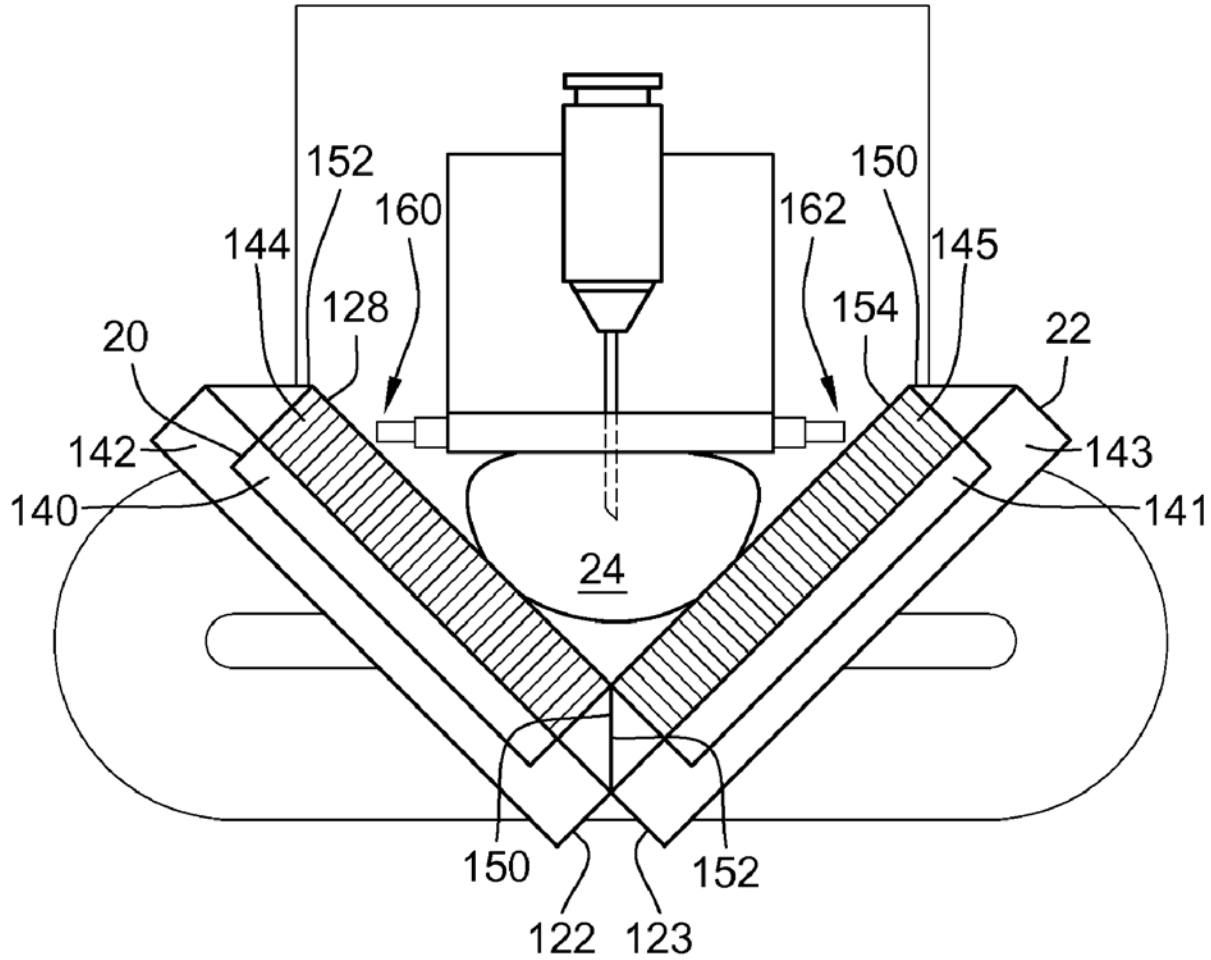
Naviscan – lateral approach



Sliding slant-hole collimator for stereo 3D lesion location

PEM limited angle tomography produces 12 slices (5 mm thick for average mildly compressed breast): inherent 3D lesion location

# GE MBI-guided Biopsy Patent Application



Bleviss, US2010/0329419

Q5: What advantages does MBI-guided biopsy (MBI-Bx) have over mammography-guided biopsy in women with dense breast tissue?

MBI-Bx has:

- 0% a) higher resolution, higher reimbursement, and is faster
- 0% b) higher specificity, instant specimen verification, and visualizes occult lesions
- 0% c) higher photon energy, lower radiation dose, and higher reimbursement
- 0% d) higher sensitivity, specificity, and resolution
- 0% e) lower radiation dose, instant specimen verification, and higher reimbursement

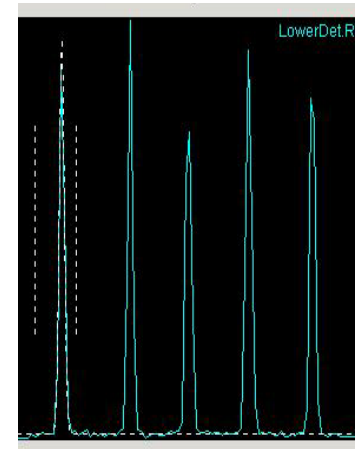
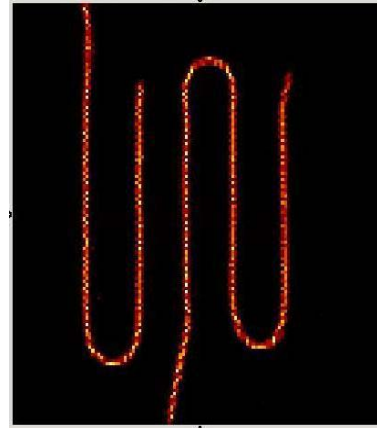
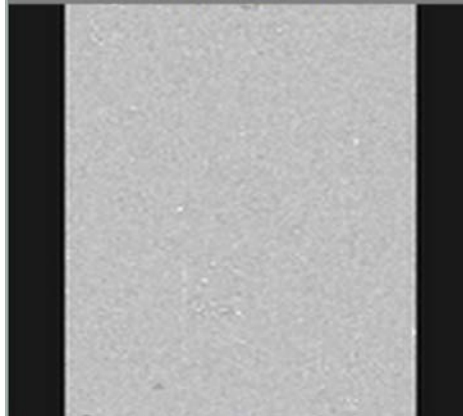
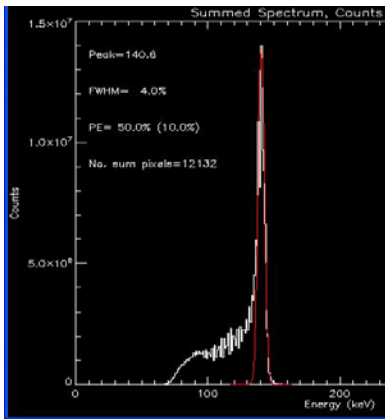
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- c) higher photon energy, lower radiation dose, and higher reimbursement
- d) higher sensitivity, specificity, and resolution
- e) lower radiation dose, instant specimen verification, and higher reimbursement

Reference: M O'Connor, et al, Molecular Breast Imaging, *Expert Reviews Anticancer Ther* 2009; 9: 1073-80.

# Performance of MBI, BSGI, & PEM



# Performance tests

Several NEMA NU1 tests can be adapted to characterize the performance of the small-FOV planar gamma cameras of MBI and BSGI.

Collimators in place (extrinsic) for all:

- Energy Resolution
- Uniformity
- Spatial Resolution
- Sensitivity (Geometric Efficiency)

# Energy Resolution

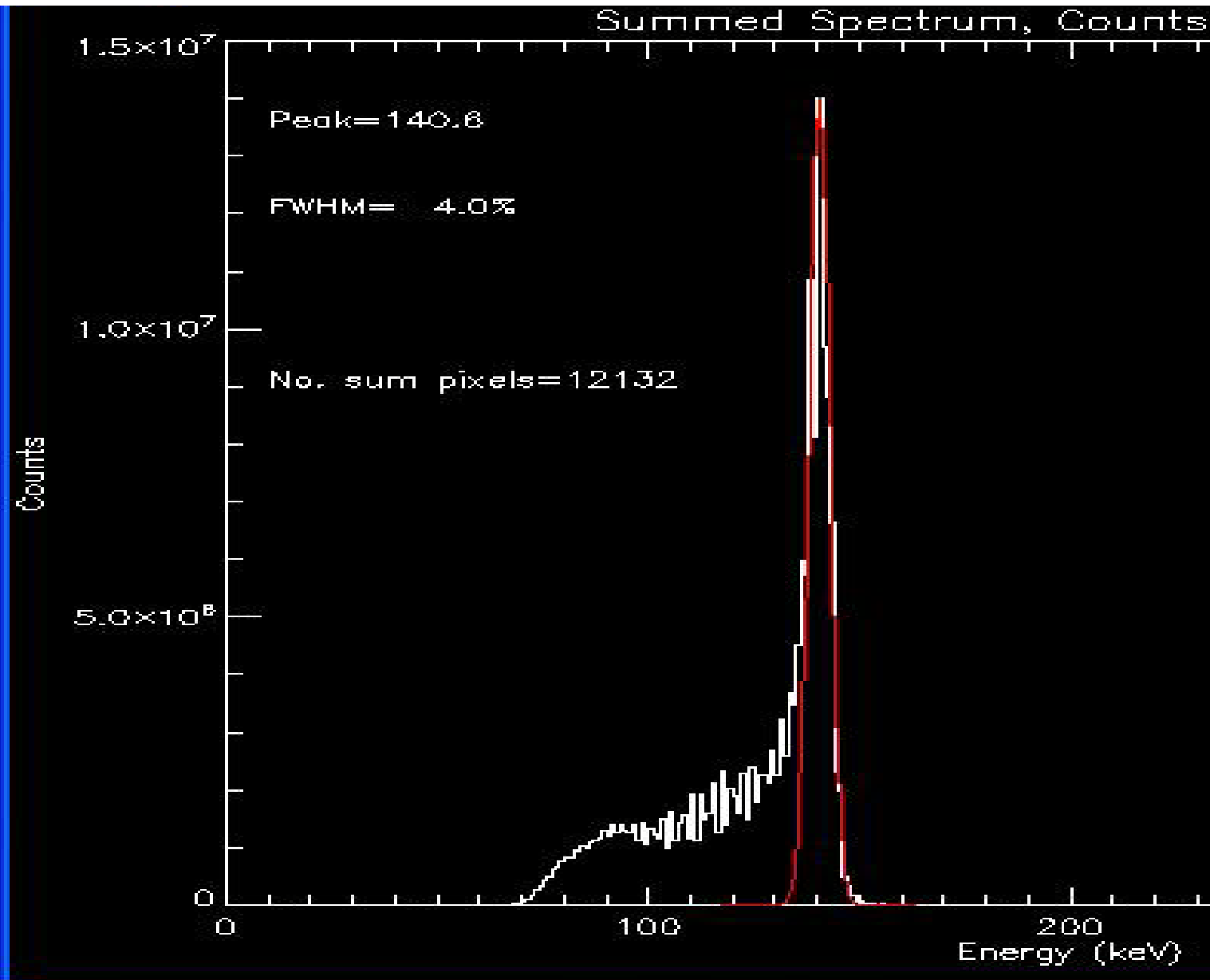
Planar  $^{57}\text{Co}$  or Flood  $^{99\text{m}}\text{Tc}$  source placed  
between two detector heads

Individual CZT pixel energy calibrations (linear)  
applied

Summation of energy spectrum of all pixels

Fit Gaussian to photopeak

# Energy Resolution - Example



4.0%  
FWHM  
140.5 keV

Typical:  
 $4.7 \pm 0.4\%$

# Uniformity

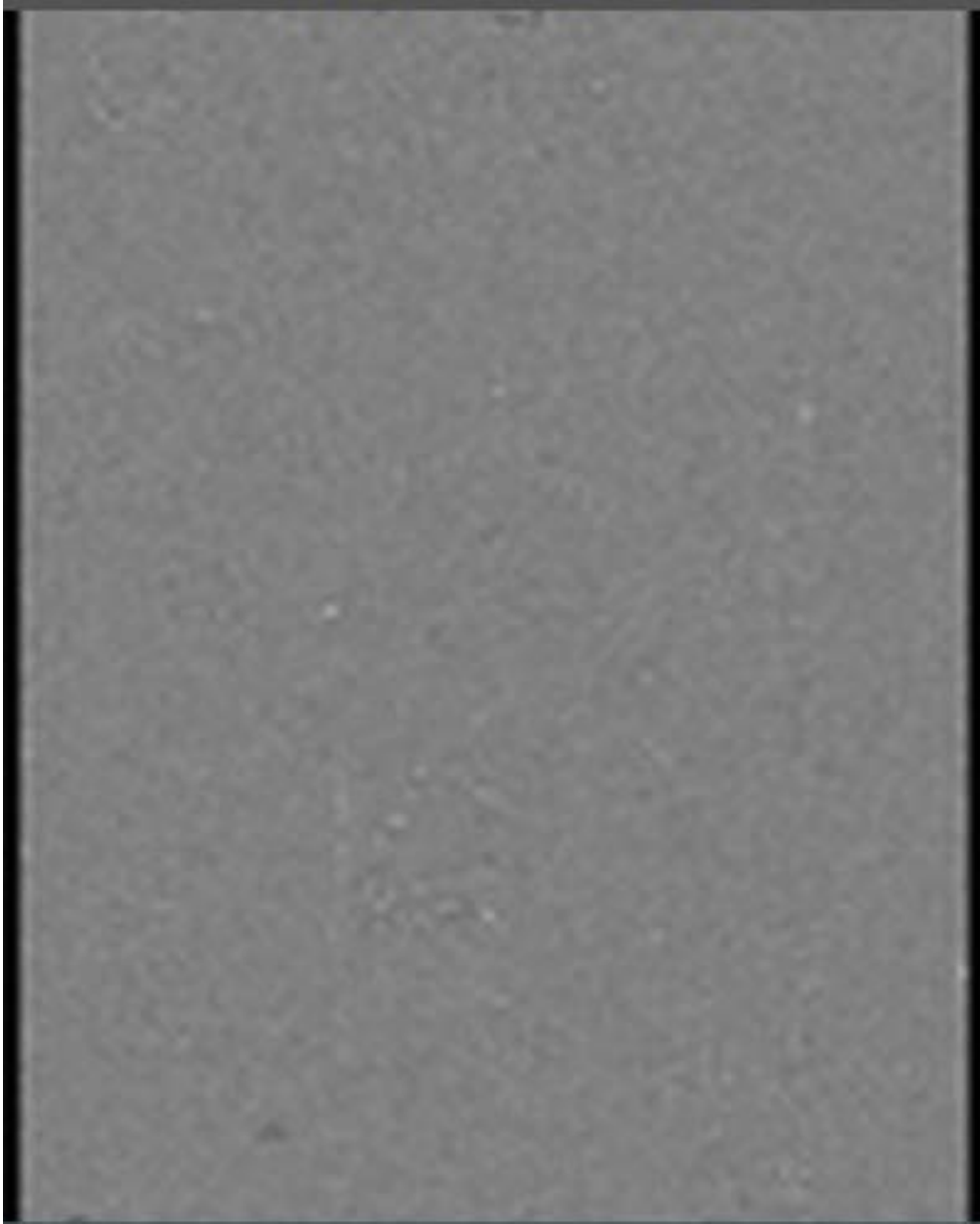
Planar  $^{57}\text{Co}$  or Flood  $^{99\text{m}}\text{Tc}$  source placed  
between two detector heads

Uniformity map measured (1 wk – 1 mo)

Uniformity corrections applied

Calculate NEMA integral & differential  
uniformity for entire FOV

# Uniformity - Example



Typical:

$1.1 \pm 0.2\%$  integral

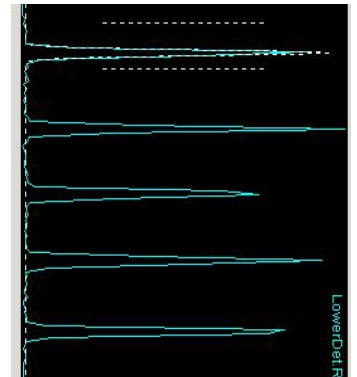
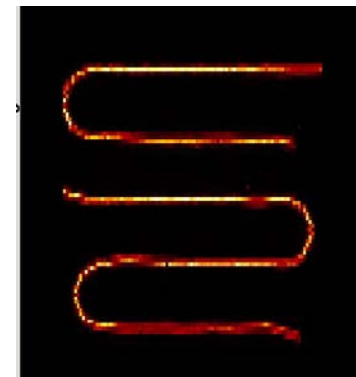
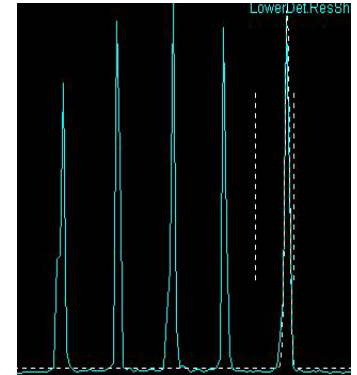
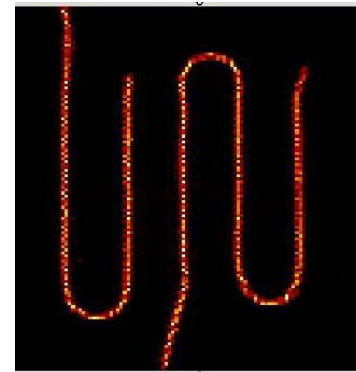
$0.9 \pm 0.1\%$  differential

Displayed to show very  
small differences

# Spatial Resolution (No scatter)

Thin tubing filled with  $^{99m}\text{Tc}$   
Offset 3 cm from detector  
cover

Detector separation 6 cm  
Measure in x&y orientations  
Measure profiles,  
deconvolve ID of tubing



Typical:

$5.0 \pm 0.9$  mm FWHM

$9.1 \pm 1.6$  mm FWTM

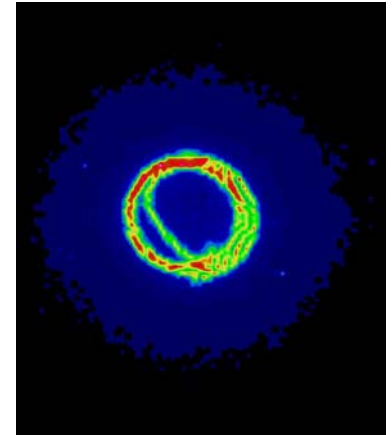
# Sensitivity (Geometric Efficiency)

Tubing filled with  $^{99m}\text{Tc}$ , coiled  
to fit dose calibrator

Place between detector heads

Count 10 minutes

Calculate



Typical:

$$667 \pm 56 \text{ cps/MBq/head} =$$
$$1482 \pm 124 \text{ cpm/mCi/head}$$

# PEM Performance

NEMA 2 measurements can be adapted to characterize PEM performance

I have had no access to a PEM, so I have no examples.

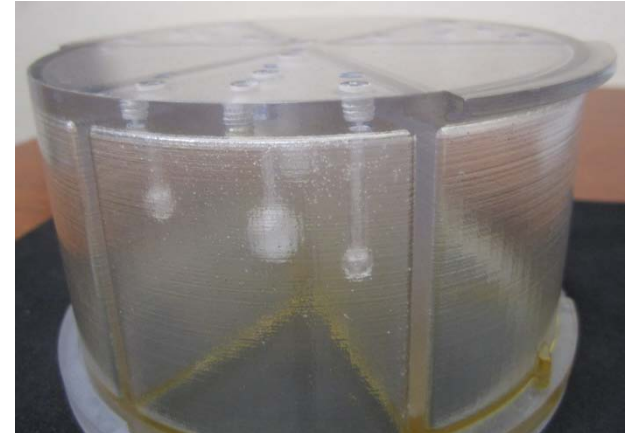
# Breast Lesion Phantom - WIP

GMI is developing a breast lesion phantom with Frank DiFilippo (Cleveland Clinic) & Michael O'Connor (Mayo Clinic), to measure:

- Lesion detectability
- Contrast recovery

Validation on multiple vendor systems  
(MBI & PEM)

Goal: to specify phantom and procedure  
for ACR accreditation



Based on DiFilippo, *et al*, *Phys. Med. Biol.* **55** (2010) 5363–5381

# Conclusions

- Every MBI, BSGI, or PEM system is more sensitive than screening MMG in dense breasts
- Dose must be reduced to match screening MMG (LumaGEM has demonstrated this low-dose capability)
- MBI-guided biopsy must be demonstrated (LumaGEM will provide biopsy guidance in mid-2012)
- Exam time must be reduced to under 30 minutes (LumaGEM will achieve this by mid-2013)
- Clinical trials must demonstrate value of dense-breast MBI screening (Mayo Clinic / LumaGEM trial will be published mid-2013)

# Learning Objectives

- Understand the physics of MBI, BSGI, and PEM breast imaging.
- Understand how radiation dose can be lowered in MBI, BSGI, and PEM.
- Understand how to characterize the performance of MBI, BSGI, and PEM systems.