



Establishing a New Breast-Specific Gamma Imaging Program: Roles of the Medical Physicist

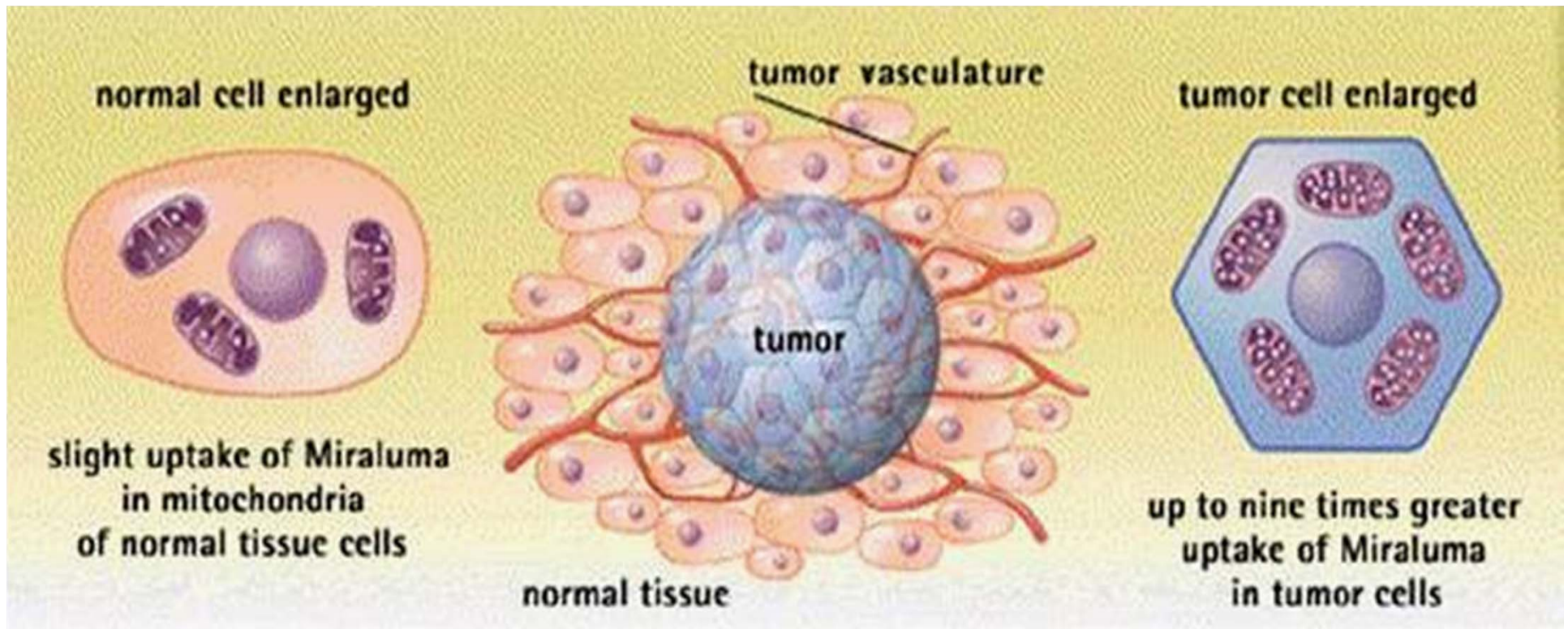
2013 AAPM Spring Clinical Meeting
Jessica Clements, M.S., DABR

Acknowledgements

- Dilon
 - Ben Welch, PhD
 - Cindy Ulmet

Objectives

- Review BSGI technology and clinical advantages
- Understand radioactive materials licensing issues and training for staff and physicians
- Learn about medical physics acceptance testing and QC procedures
- Understand the process to receive ACR accreditation



Conventional breast imaging techniques inspect the breast *anatomy* for irregular *structures*.

BSGI uses a mitochondrial binding pharmaceutical (Sestamibi) to inspect the *physiology* of the breast for increased *metabolic rate* relative to surrounding tissues.

Advantages

- Geometry
 - Reduced distance results in better resolution compared to standard gamma cameras (~ 3.5 mm)
 - Reduced background scatter and shine-through from other organs



Advantages

- Duplicates any mammographic view
- Immobilized breast

Understanding the Big Picture

- Patient care occurs in five phases
 - Screening – non-symptomatic patient
 - Diagnostics
 - Treatment planning
 - Treatment Monitoring
 - Surveillance

Clinical indications

- Dense breast tissue that is difficult to image - Indeterminate results from mammography and/or ultrasound
- Palpable mass not demonstrated in mammogram or ultrasound
- Patients where MRI is indicated, but not possible
- Evaluation of multiple lesions or clusters of microcalcifications to aid in biopsy target selection

Other uses

- Evaluating the axillary region for node status
- Determining the extent of primary lesion
- Detecting multicentric and multifocal disease for treatment planning
- Predicting chemotherapeutic response
- Monitor primary tumor response to neoadjuvant chemotherapy
- Screening high-risk population

The Cornerstone Study

International prospective evaluation of scintimammography with 99mTechnetium sestamibi. F.S. Sampalis et al. AmerJournSurg 185 544–549. 2003.

N = 1,734 patients

Sensitivity = 93%

Specificity = 87%

BSGI is Highly Sensitive for Breast Carcinoma Smaller than 5mm

146 patients with 167 lesions

Population:

- Palpable masses negative on mammogram
- Patients with biopsy proven cancer
- Areas of concern noted on mammography, but negative on ultrasound, MRI and clinical examination
- High Risk patients (greater than a 1.66% of breast cancer in the next 5 years)

Statistics

- Overall sensitivity 96.4%
- Sensitivity under 5 mm was 89%
- NPV: 94%
- PPV: 68.8%
- Smallest Cancers visualized were 1mm

Brem R, Floerke A, Rapelyea J, Teal C, Kelly T, Mathur V. Breast Specific Gamma Imaging as an Adjunct Imaging Modality for the Diagnosis of Breast Cancer. Radiology. 2008;247(3):651-57.



See What Matters™

Sensitivity Analysis

Overall	96%
Invasive Cancers	97%
Sub-centimeter lesions	89%
DCIS	94%

- The median size of DCIS was 7mm.
- BSGI detected 7 cancers which were occult in mammography

Brem R, Floerke A, Rapelyea J, Teal C, Kelly T, Mathur V. Breast Specific Gamma Imaging as an Adjunct Imaging Modality for the Diagnosis of Breast Cancer. Radiology. 2008; 247(3):651-57.

Real-World Application of BSGI, Initial Experience & Its Potential Impact On Clinical Care

- 176 patients
- Changed patient management in 14% of cases
- Detected cancer in 2% of patients with negative mammogram
- Detected additional cancer in 6% of patients with known primaries
- BSGI false positive rate was 6.3

Zhou M, Johnson N, Blanchard D, Bryn, S, Nelson J. Real-world application of breast-specific gamma imaging, initial experience at a community breast center and its potential impact on clinical care. The American Journal of Surgery (2008) 195, 631–635.

Clinical Utility of Breast Specific Gamma Imaging For Evaluating Disease Extent in the Newly Diagnosed Breast Cancer Patient

- 138 newly diagnosed cancers
- Found additional disease in 11% of cases
- Sensitivity = 91.4%
- Specificity = 94.2%

Zhou M, Johnson N, Gruner S, Ecklund GW, Muenier P, Bryn S, Green G, et al. Clinical Utility of Breast Specific Gamma Imaging For Evaluating Disease Extent in the Newly Diagnosed Breast Cancer Patient. The American Journal of Surgery, Vol 197, No 2, February 2009.

Detection of Ductal Carcinoma in-situ

Comparison of BSGI, MRI and Mammography

Sensitivity	
BSGI	91%
MRI	88%
Mammo	82%

- BSGI detected a 4mm DCIS that was negative on MRI.
- BSGI detected 2 mammographically occult contra-lateral DCIS lesions.
- BSGI detected 2 mammographically occult lesions in patients with bloody nipple discharge and negative mammograms.

Brem, et al. Detection of Ductal Carcinoma in-situ with mammography, Breast –Specific Gamma Imaging and MRI: a comparative study. Academic Radiology. August 2007

Detection of Ductal Carcinoma in-situ Comparison of BSGI, MRI and Mammography (cont)

- Smallest lesion size detected was 2mm
- BSGI detected 4 DCIS < 4mm
- In this study, there were 2 low-grade DCIS lesions and both were detected by BSGI.

Brem, et al. Detection of Ductal Carcinoma in-situ with mammography, Breast –Specific Gamma Imaging and MRI: a comparative study. Academic Radiology. August 2007

Invasive Lobular Carcinoma

Detection with Mammography, Ultrasound, Magnetic Resonance Imaging, and Breast-specific Gamma Imaging (BSGI)

26 women

SENSITIVITY

- BSGI 93%
- Mammography 79%
- US 68%
- MRI 83%

Brem R, et al. Breast Specific Gamma Imaging in Women with One Suspicious or Cancerous Breast Lesion. Invasive Lobular Carcinoma: Detection with Mammography, Ultrasound, Magnetic Resonance Imaging, and Breast-specific Gamma Imaging (BSGI). The American Journal of Roentgenology, 192, February 2009; Pages 379 – 383.

Results of a Multi-Center Patient Registry to Determine the Clinical Impact of Breast-Specific Gamma Imaging, a Molecular Breast Imaging Technique

Overall N = 1,042
Sensitivity 91%
Specificity 77%

Bertrand M, Lanzkowsky L, Stern L,
Weigert J. Podium Presentation
Radiologic Society of North America
Annual Meeting. November 29th –
December 4th 2009.

Compared to Mammography N=362

BSGI sensitivity = 93%

MMG Sensitivity = 71%

BSGI detected 30 malignant and 7 high-risk lesions in patients with negative or indeterminate mammograms.

Cost of BSGI per disease diagnosis was \$2,431.57.

Clinical experience with BSGI

Results: 512 patients

- Sensitivity of 89%, Specificity of 90% and NPV of 98%.
- No infiltrating lobular cancers were missed.
- BSGI detected several mammographically occult cancers

Weigert J. Breast Specific Gamma Imaging (High Resolution Molecular Imaging of the Breast): A Useful Adjunct to Breast Imaging. RSNA Poster Session. RSNA Annual Meeting. Chicago IL, November 2007.

Breast Specific Gamma Imaging Compared to Breast MRI in Patients with Inconclusive Mammographic and Ultrasonic Findings

- 63 lesions
- Sensitivity BSGI -96%, MRI 88%
- Specificity for BSGI was nearly 2 times greater than MRI
- BSGI resulted in 1/3 the number of indeterminate studies

Lanzkowsky L, et al. Breast Specific Gamma Imaging Compared to Breast MRI in Patients with Inconclusive Mammographic and Ultrasonic Findings. 2008 Radiological Society of North America Annual Meeting.

Breast-specific Gamma Imaging Compared to Breast US in Patients with Mammographic Abnormalities Requiring Diagnostic Evaluation

- 70 women
- BSGI and Ultrasound had 96% and 58% sensitivity respectively
- 55% and 43% specificity respectively
- Negative Predictive Value was 96% and 63% respectively

Weigert J, et al. Breast-specific Gamma Imaging Compared to Breast US in Patients with Mammographic Abnormalities Requiring Diagnostic Evaluation. 2008 Radiological Society of North America Annual Meeting

Breast-Specific Gamma Imaging compared to Breast MRI

Results: 122 Lesions

Performance in Breast Malignancies or High-Risk Lesions			
	Positive	Sensitivity	Indeterminate
BSGI	110/120	91.6%	3
MRI	106/117	90.6%	6

- BSGI has additional advantages over MRI in that the study generates 4-8 images as compared to up to 1000 images in MRI
- Can be utilized in all patients including those with ferromagnetic implants or renal insufficiency.
- BSGI is conducted at a fraction of the cost per procedure of breast MRI.

Kristin Brill, et al. Breast-Specific Gamma Imaging compared to Breast MRI in patients requiring diagnostic imaging after screening mammography. ASCO Annual Meeting, Washington D.C. Sept, 2006.

BSGI compared to Ultrasound and MRI the diagnostic population

Results: 98 lesions

- The combination of MMG and BSGI was the only imaging combination which would have resulted in 100% sensitivity in this group.
- Due to the lower cost and higher patient compliance compared to breast MRI, it may be used to improve detection while lowering healthcare costs.
- Based on this group of 75 patients who had both studies, a work up of BSGI alone would have saved \$58,107 health care dollars
- BSGI detected cancer in 4 women who could not comply with the MRI order.

Bertrand M. First Year's Experience using Breast-Specific Gamma Imaging: A comparative analysis with Mammography, Ultrasound and MRI in the Detection of Breast Cancer. Miami Breast Cancer Conference. Orlando Florida. February 20 -23, 2008.



Photo courtesy of Dilon Diagnostics

Detector

- Pixelated NaI(Tl) crystals and Position Sensitive Photomultiplier Tubes (48)
- Images are 64x48 pixels, centered in an 80x80 matrix (Pixels outside the active matrix are set to zero)

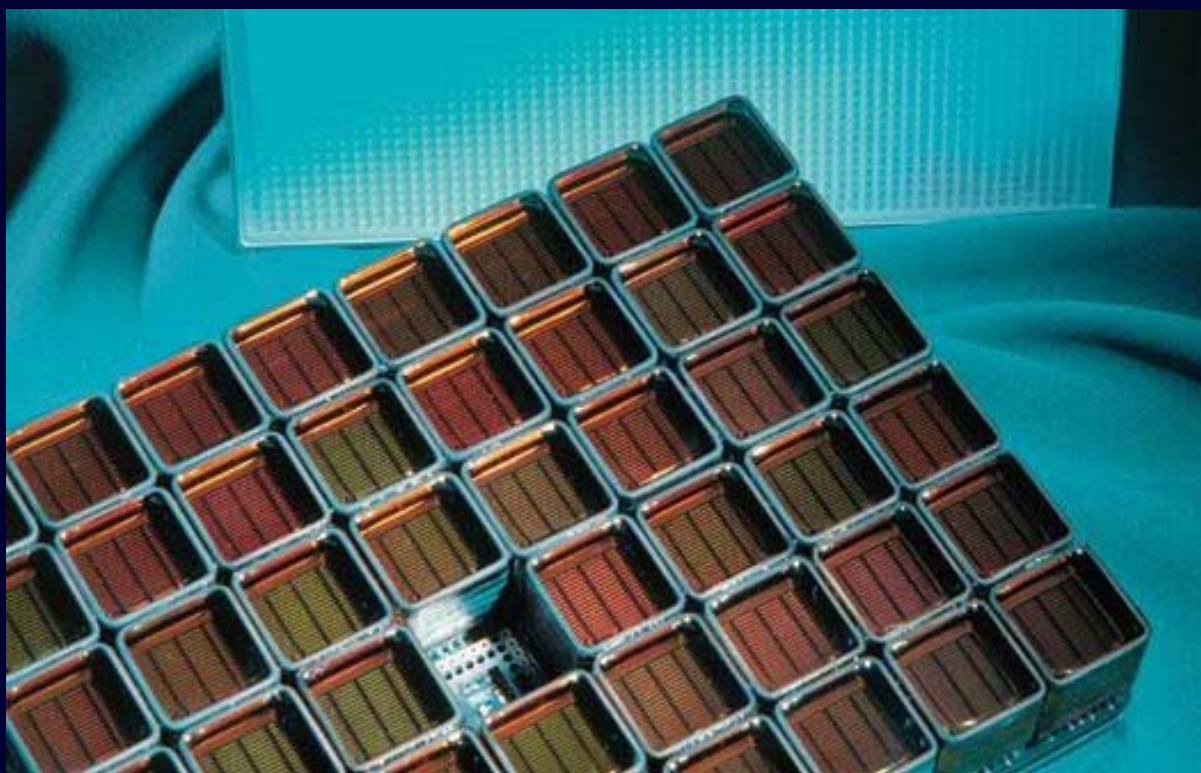


Photo courtesy of Dilon Diagnostics

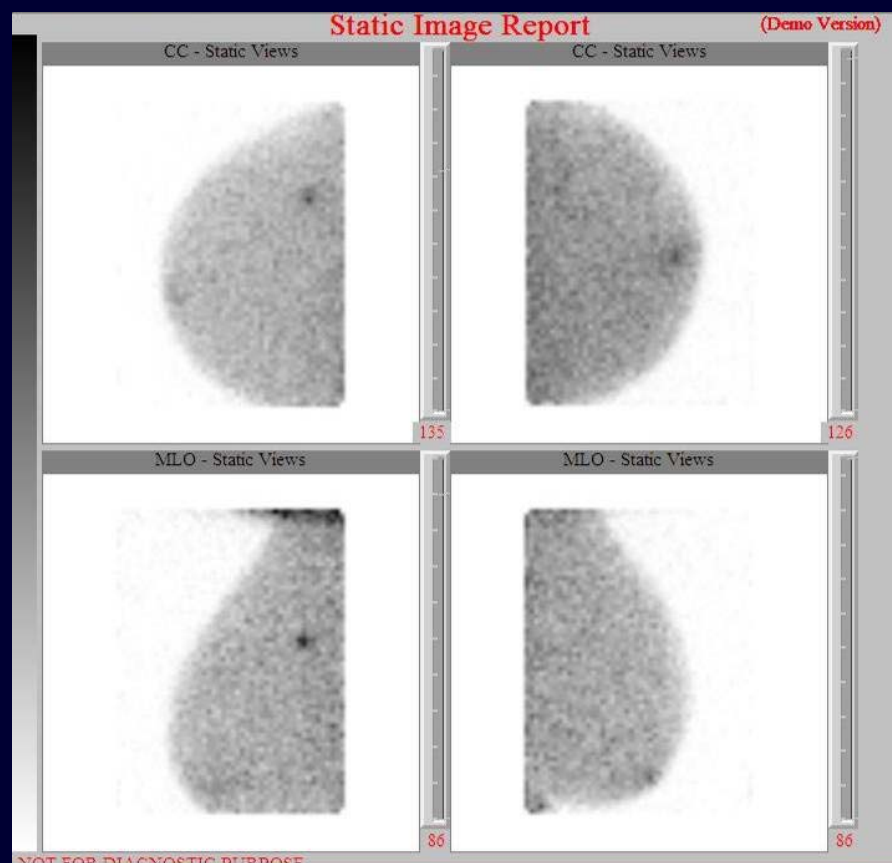
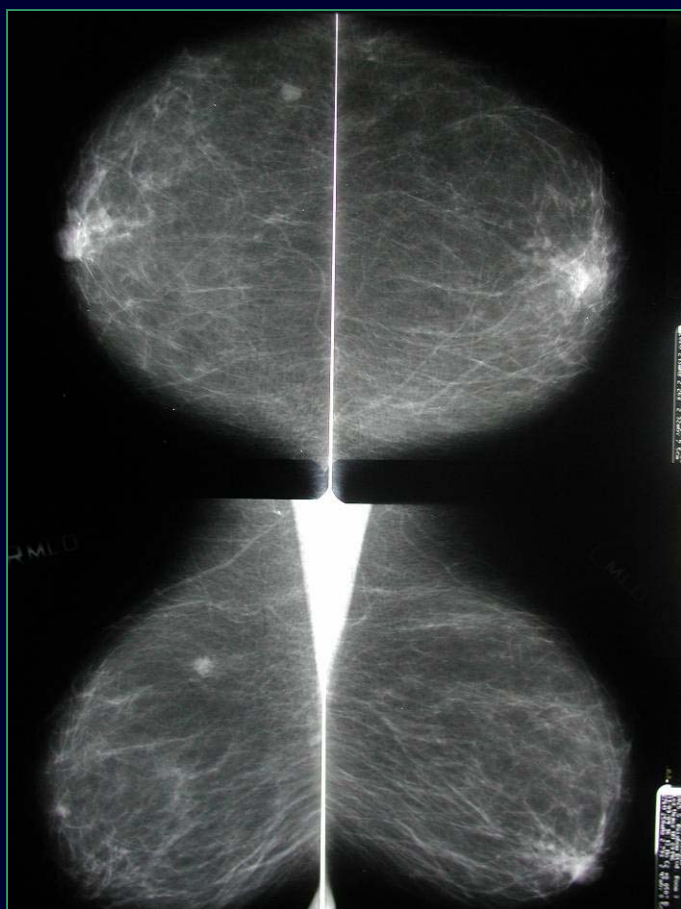
Detector

- Pixel size is 2.96 mm x 2.96 mm
- Crystal thickness – 6 mm
- 3072 crystals
- 48 PMTs
- 5 mm Pb shielding
- FOV = 6 x 8 inches

Imaging Specifications

- Intrinsic spatial resolution 3.3 mm
- Energy Resolution 13.5%
- Uniformity +/- 10% across full FOV
- Image event rate 10kcts/sec (max)

Ductal Carcinoma and Positive BSGI

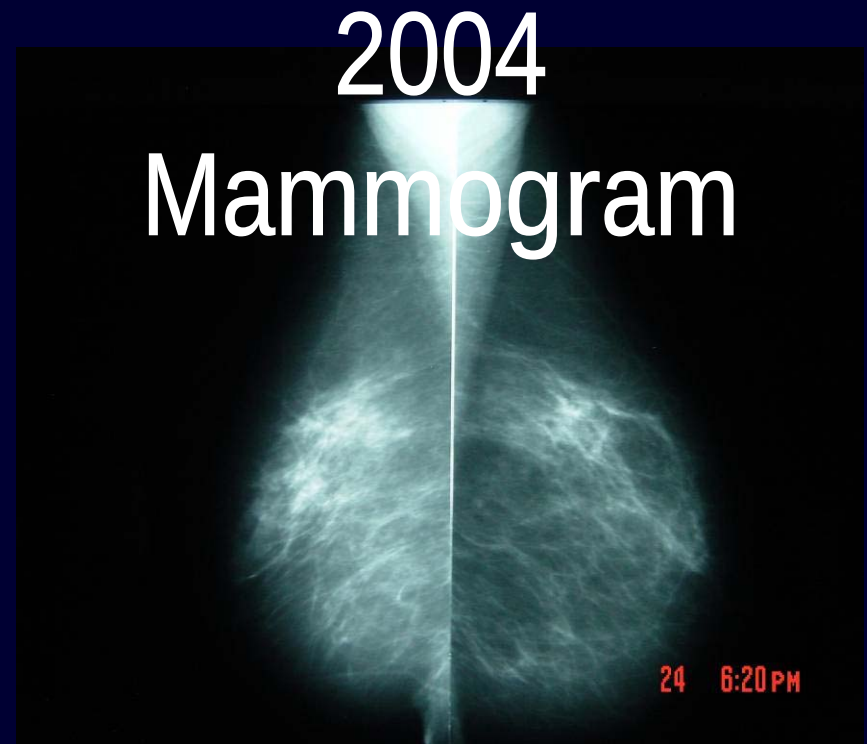
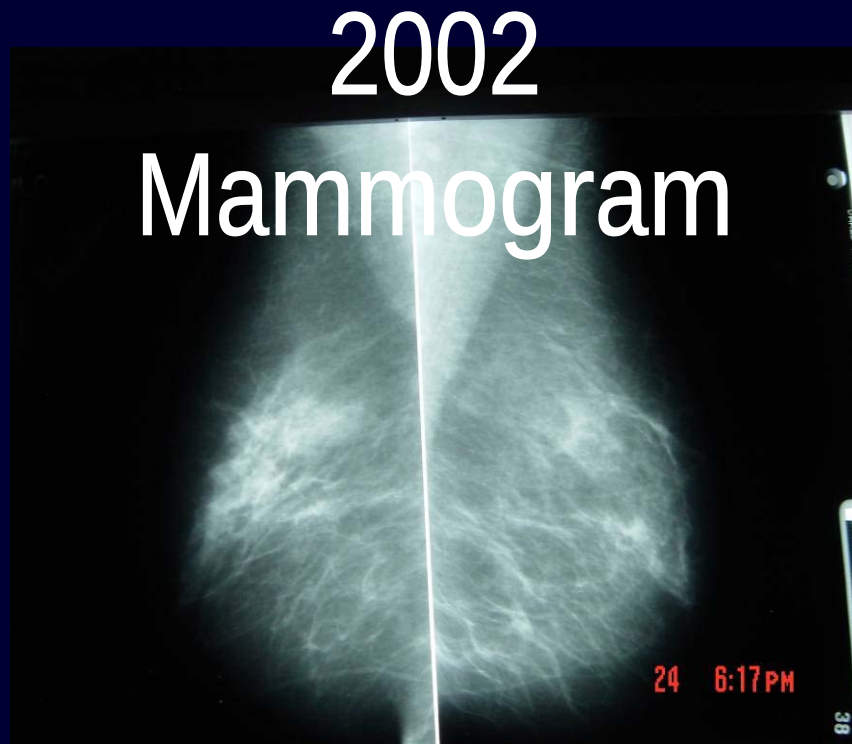


BSGI is capable of detecting very small cancers such as the 5mm ductal carcinoma in this case. Note the normal, bilateral nipple uptake

Courtesy of West Valley Imaging

Negative Mammogram

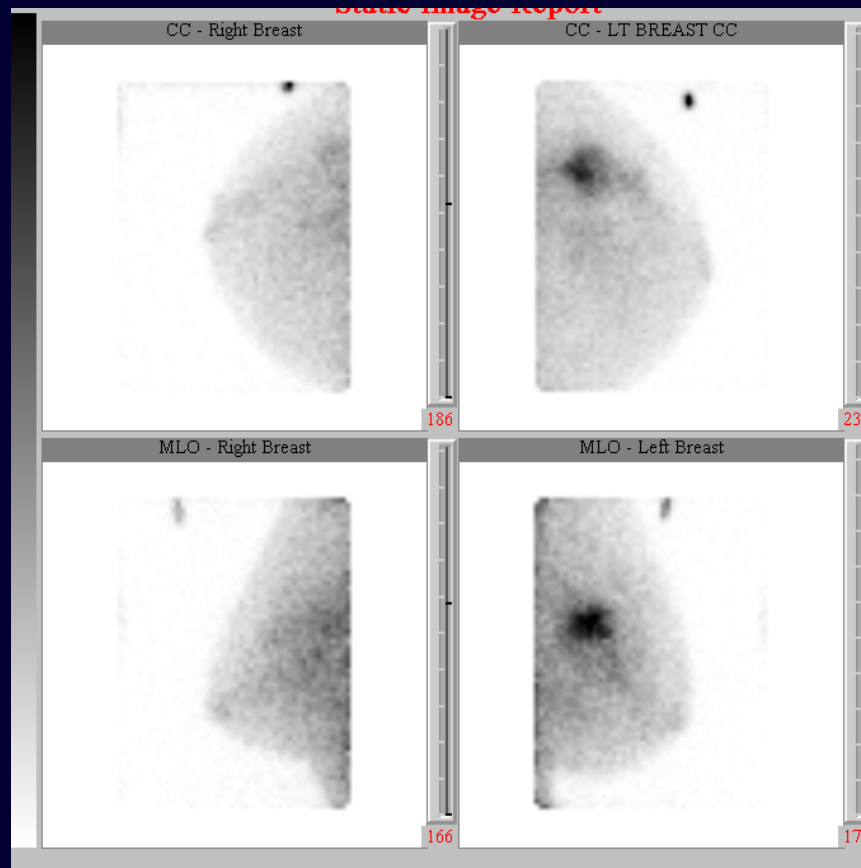
Patient presents with an ill-defined palpable thickening 2 months after the 2004 examination



Recommend BSGI for evaluation of thickening

Positive BSGI

Study reveals focal area of uptake in left breast



Procedure followed with ultrasound

Clinical History

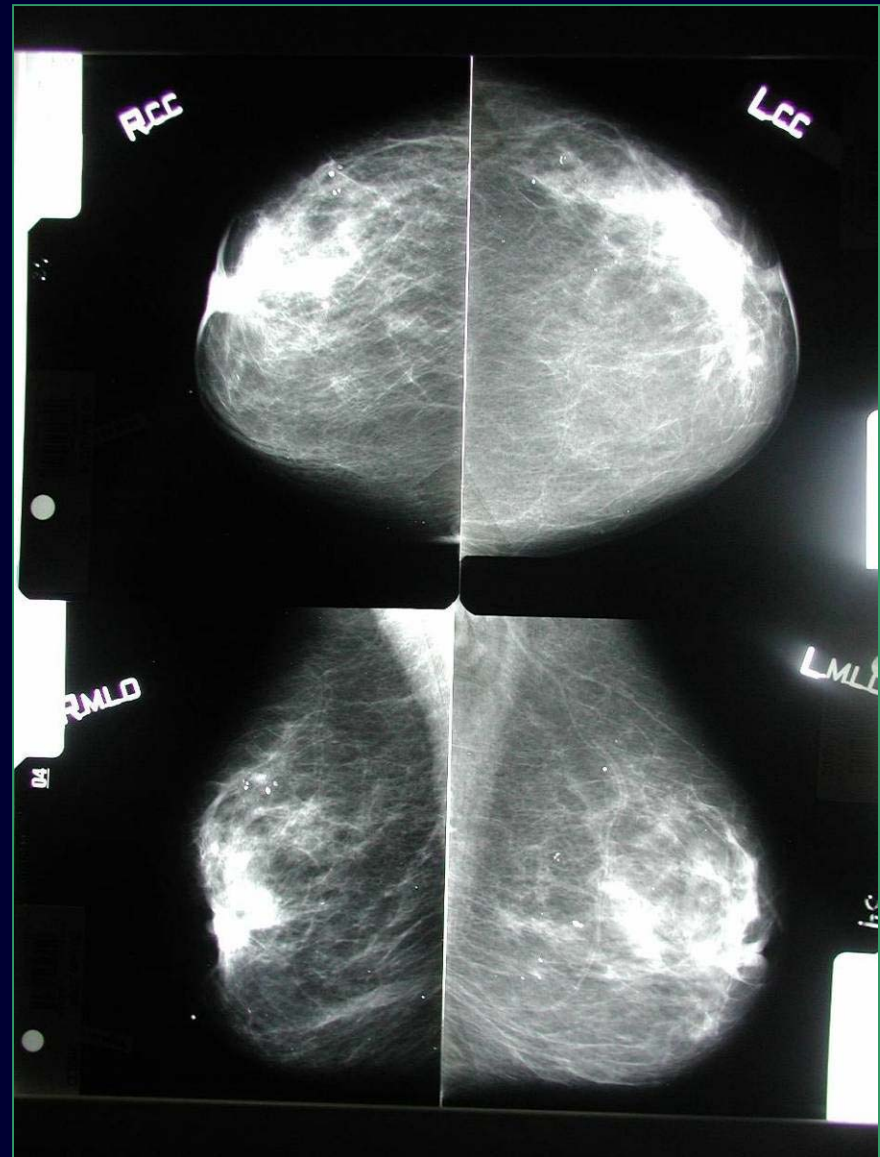
62 year-old female with a history of relatively fatty breast tissue with somewhat dense bilateral parenchyma.

Mammogram

Irregular mass in the retroareolar portion of the right breast with skin thickening and nipple retraction. BIRADS 5.

Ultrasound

Solid mass noted corresponding to the mammographic density measuring 1.8 cm x 1.7 cm x 1.6 cm.



Papillary Carcinoma with Second Focus

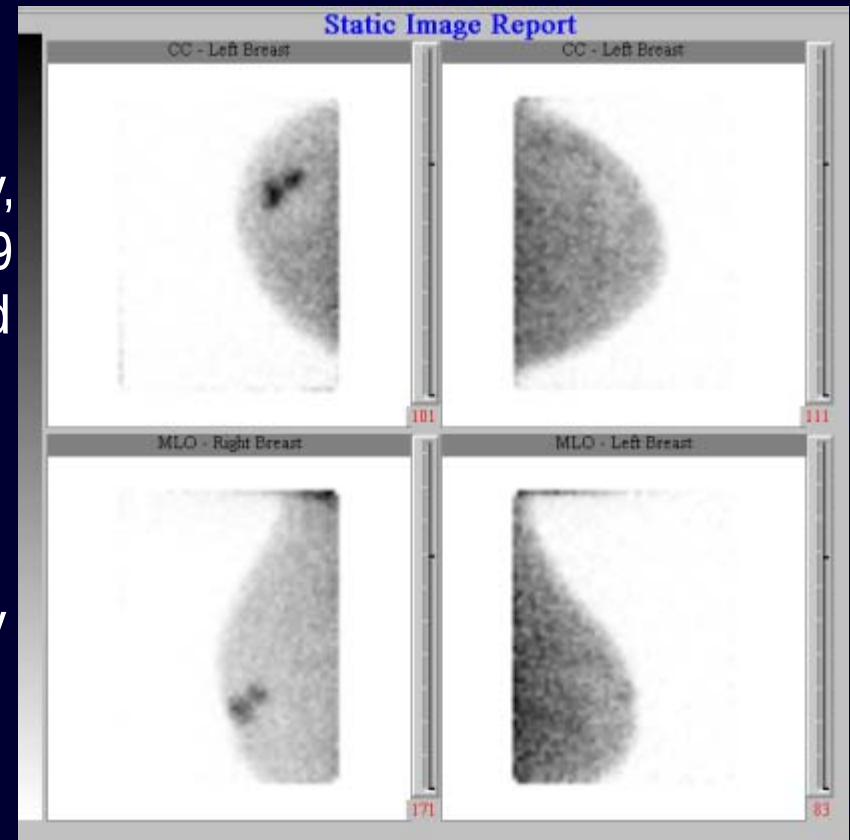
Breast-Specific Gamma Imaging

Two areas of focal uptake noted. The first focus corresponds to the sonographic density, measuring approximately 1.6 cm x 1.3 cm x 1.9 cm. The second focus proximal to the first and slightly superior and posterior measuring approximately 1.3 cm x 0.7 cm x 1.2 cm.

Histopathology Findings

Both areas are confirmed as invasive papillary carcinoma.

Courtesy of West Valley Imaging



BSGI confirmed an extension of disease to the superior lateral aspect of the primary lesion and ruled out disease in the opposite breast.

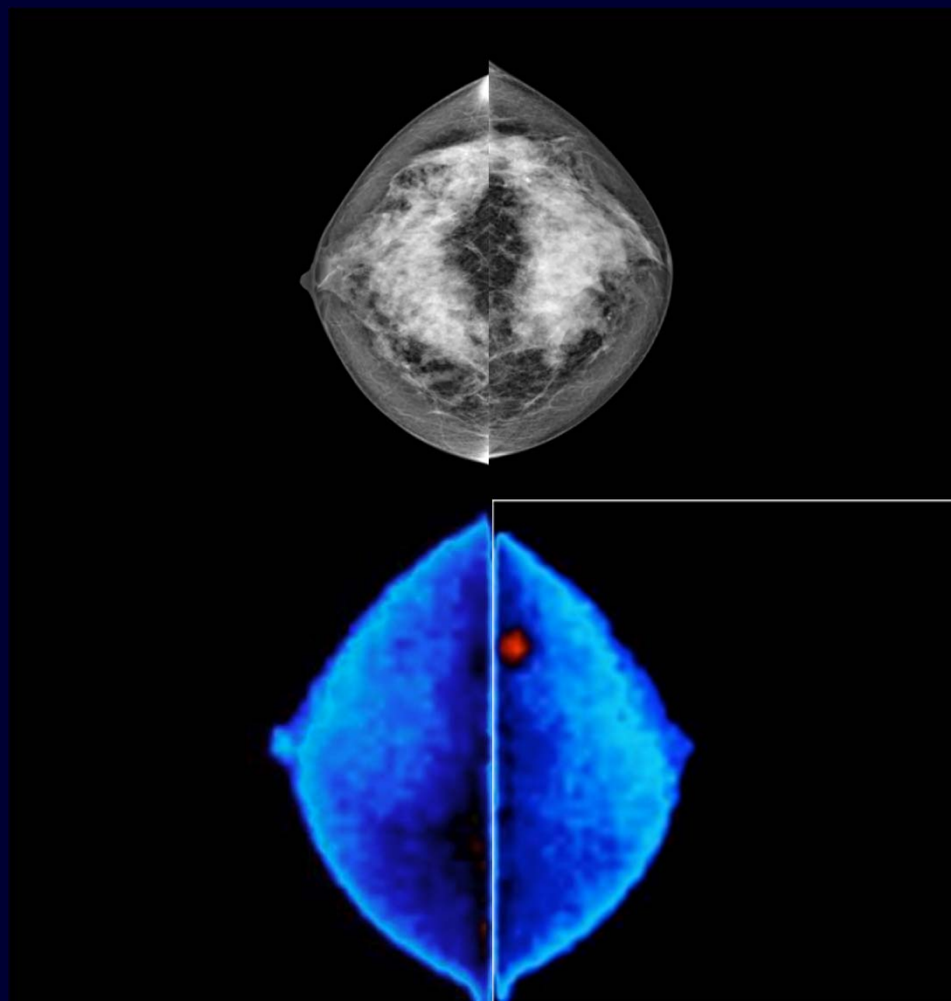
HISTORY

67 year-old with difficult to interpret mammogram due to dense breast tissue. Mammographically benign architectural distortion interpreted as scar tissue.

Courtesy of Eisenhower Medical Center

BSGI IMPACT

BSGI detected a lobular carcinoma in a region of previously benign biopsy in a patient with dense breasts. Second-look ultrasound core biopsy revealed a 1.4 cm Lobular Carcinoma.



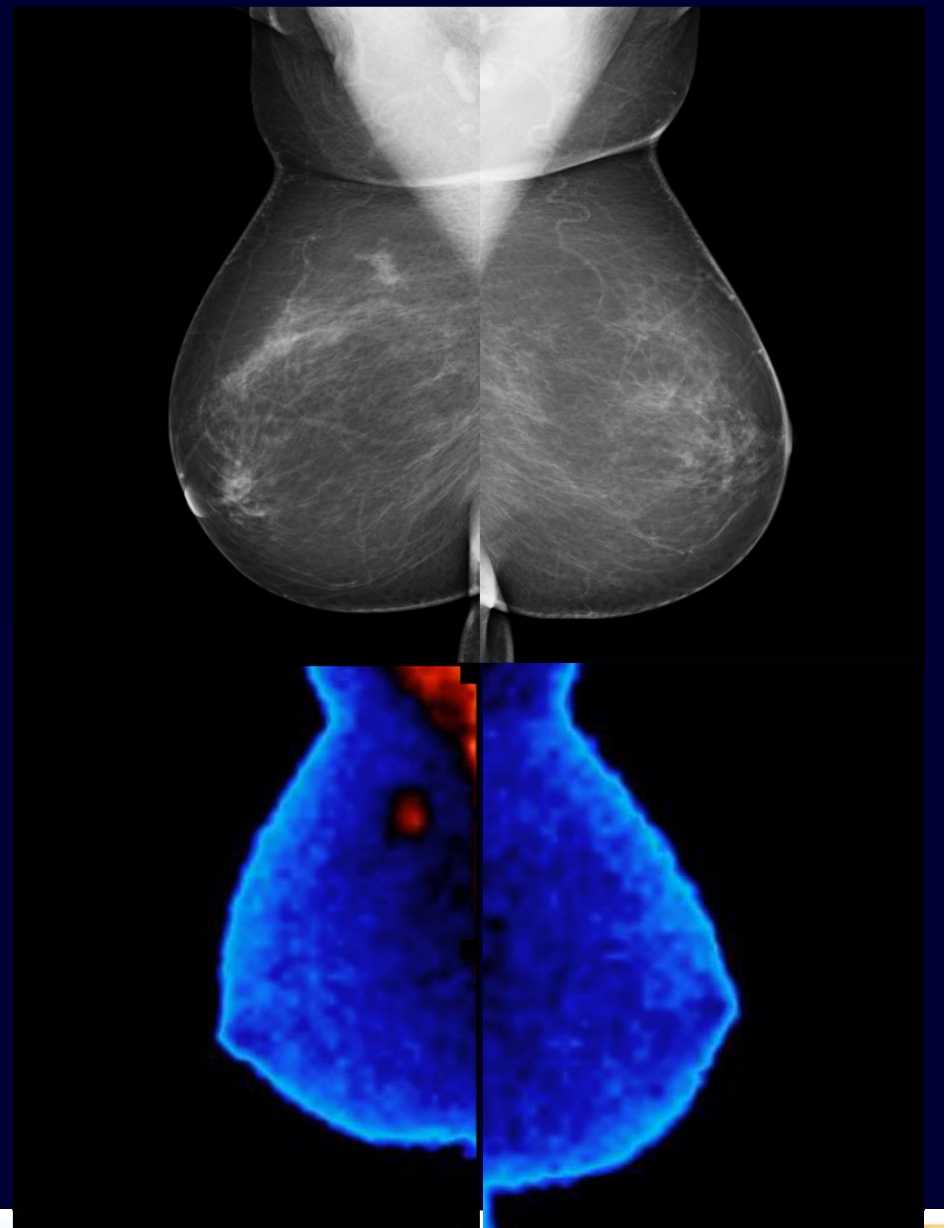
HISTORY

72 year old patient undergoing a routine annual screening. A suspicious mass seen in the mammogram at 10:00 o' clock

Courtesy of Methodist Hospital, Philadelphia, Pennsylvania

BSGI IMPACT

BSGI is excellent in differentiating infiltrating lobular carcinoma from normal asymmetric fibroglandular tissue.



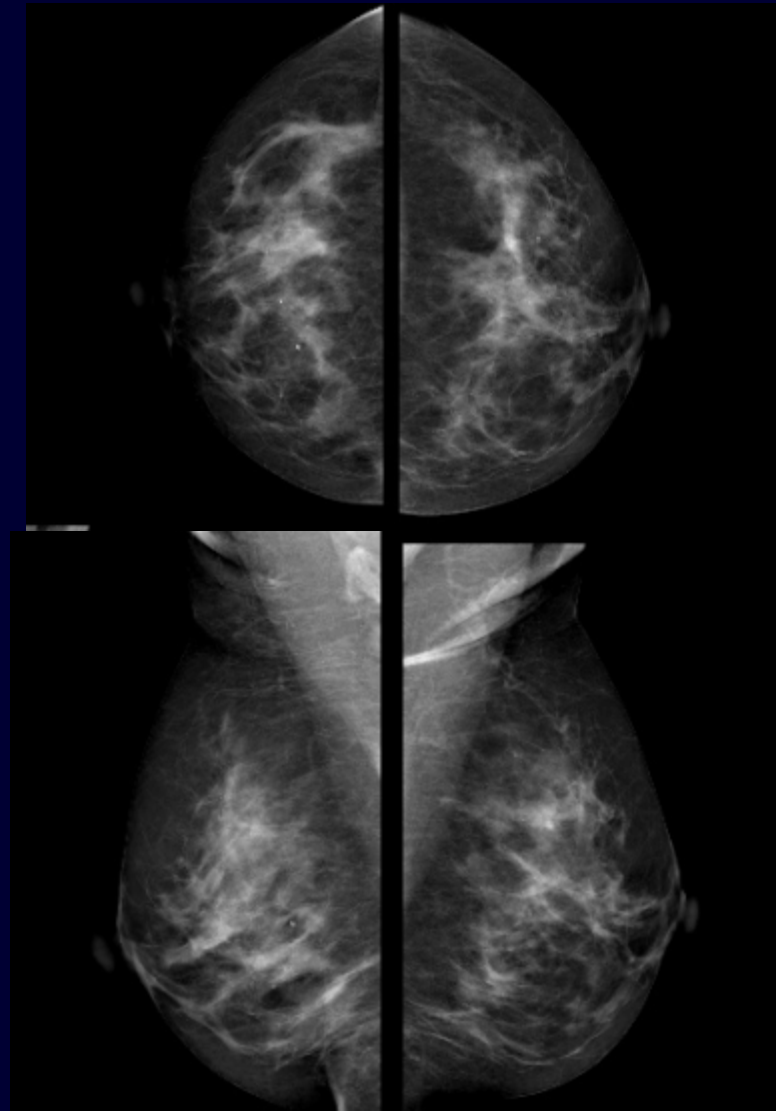
HISTORY

Prior benign biopsy of calcifications in the left breast in for annual screening mammogram.

SCREENING MAMMOGRAM

Mammographic findings show continued calcifications in both breasts. There are however, still some calcifications in the left breast that are slightly indeterminate in appearance, but similar to the ones that were biopsied in the past. BIRADS 4, BSGI is recommended.

Courtesy of Methodist Hospital, Philadelphia, Pennsylvania



BSGI:

Left Breast - no intense in the site of the calcifications.

Right breast – unanticipated focal intensity in the lower outer quadrant.

Ultrasound:

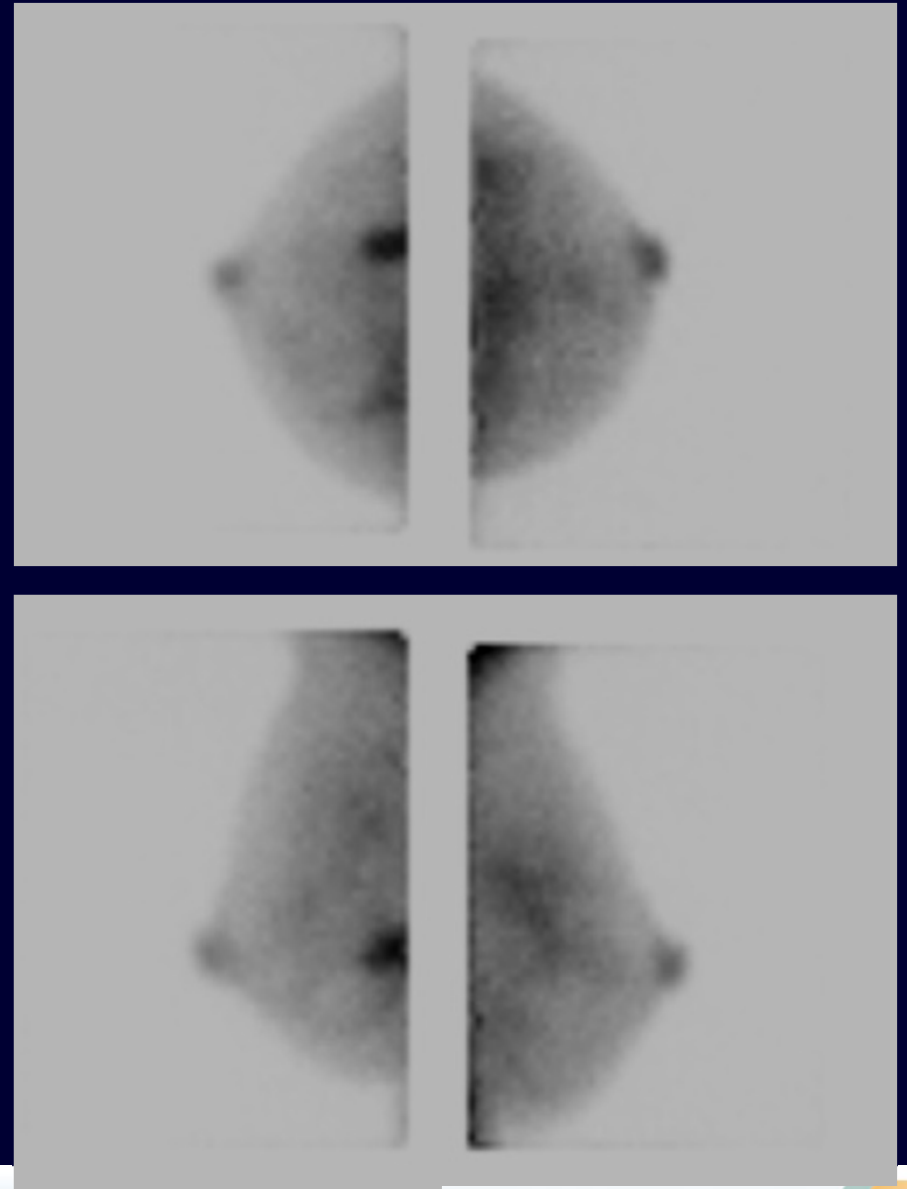
US guided core biopsy: poorly differentiated Infiltrating Ductal Carcinoma.

Preop MRI:

2 areas of enhancement on the left breast

Bilateral Mastectomy:

No cancer found in the left breast and only one site of Infiltrating Ductal Carcinoma was found in the right breast detected by BSGI



Courtesy of Methodist Hospital, Philadelphia, Pennsylvania



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HISTORY

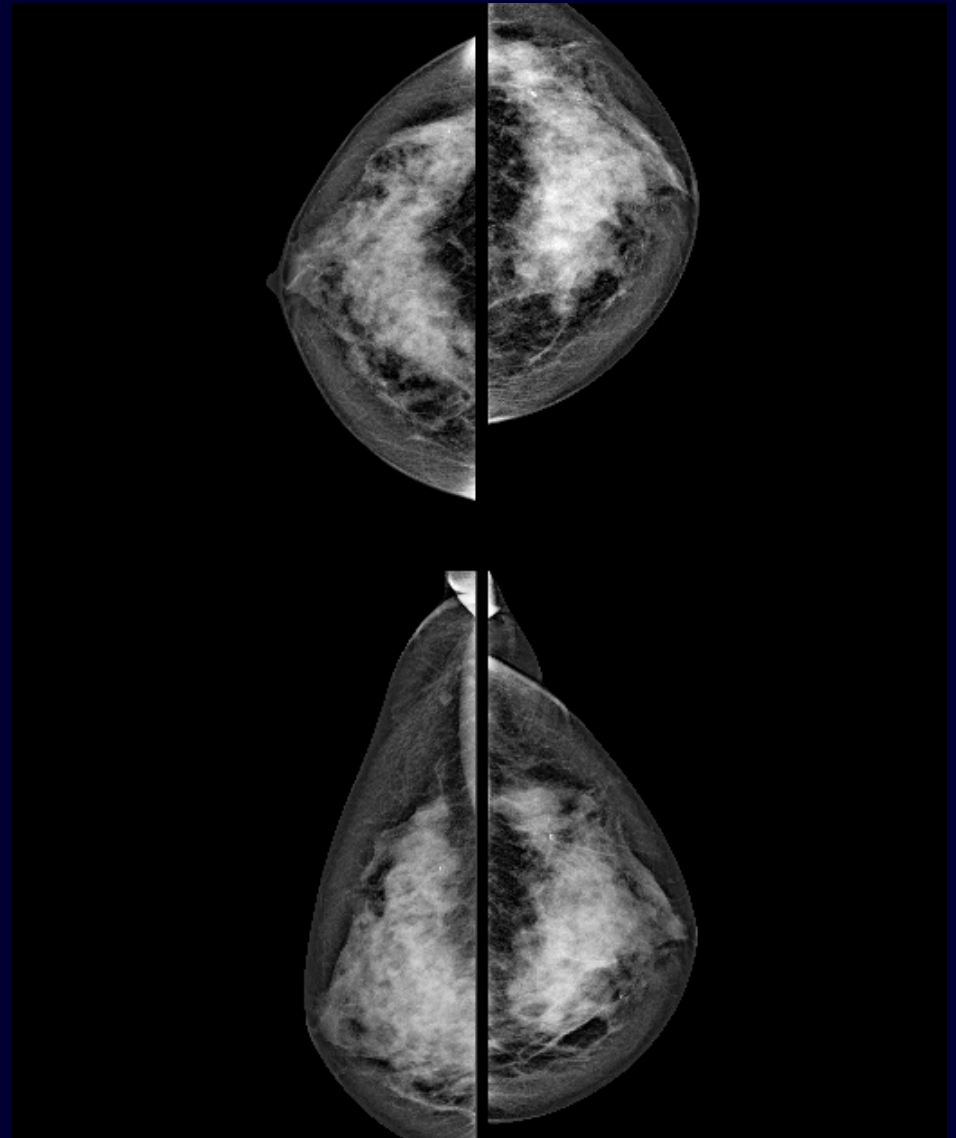
67 year old with extremely dense breast and a history of benign breast biopsy, 22 years prior, of the left breast at 1 o' clock in for screening mammogram.

MAMMOGRAM

Films are difficult to interpret due to density. There is asymmetry in the right breast, inferior region at anterior depth. Left breast: architectural distortion at 1 o' clock position and focal asymmetry at 8 o' clock position middle depth.

DIAGNOSTIC MAMMOGRAM

Prior density in the right is no longer apparent. Left breast 8 o' clock is not noted. Left breast 1 o' clock is consistent with previous surgery. Due to the prior surgery, breast density and previously noted bilateral densities, BSGI is recommended.



Courtesy of Eisenhower Medical Center, Rancho Mirage, CA

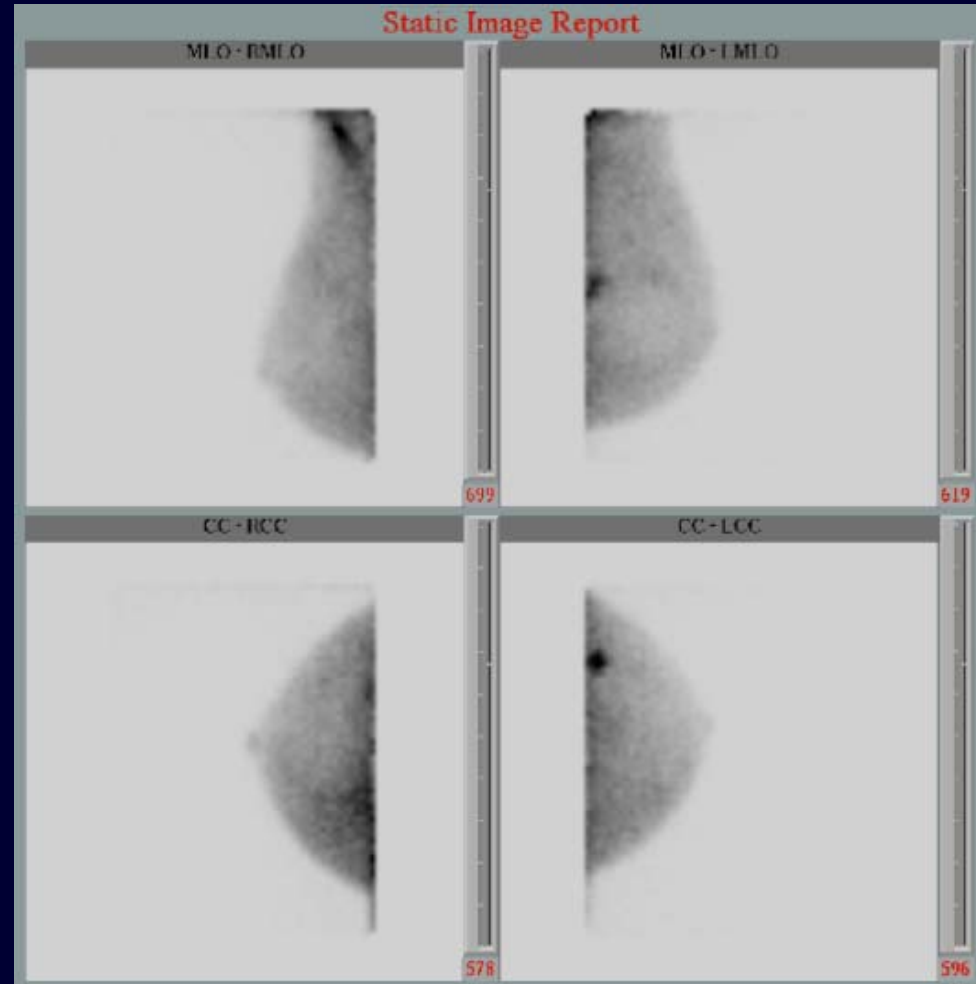


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BSGI detected a 1.4cm focal intensity
in the left breast

Subsequent second-look US guided
biopsy revealed a 1.4cm lobular
carcinoma

*Courtesy of Eisenhower Medical Center, Rancho
Mirage, CA*



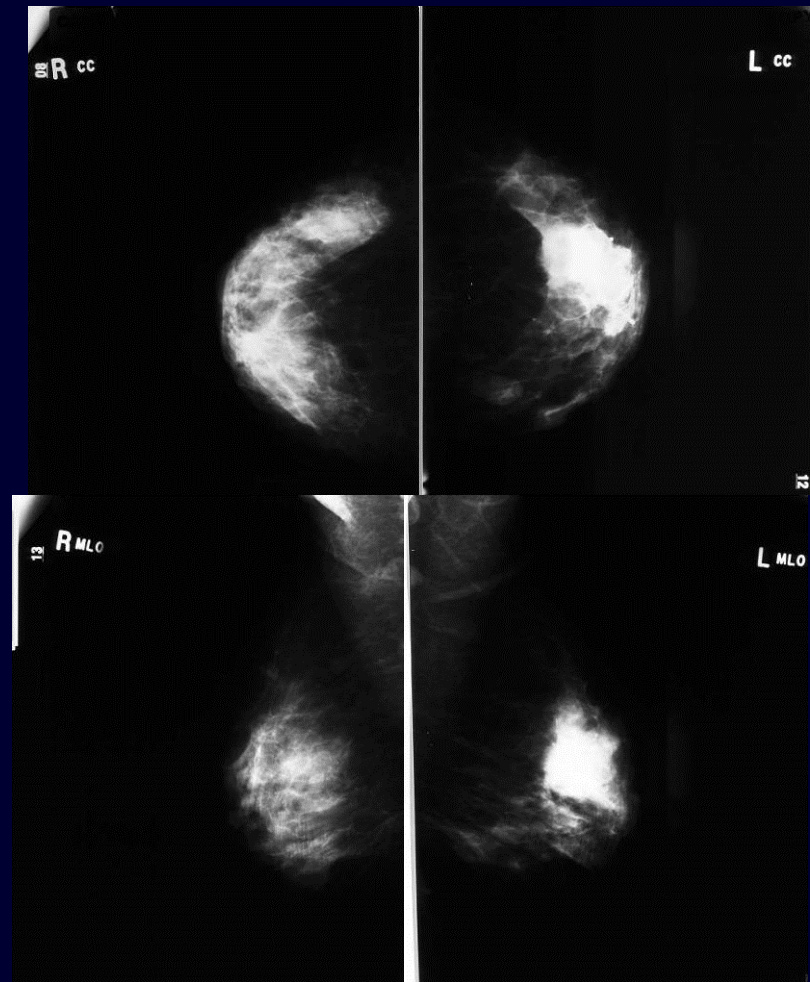
History

61 year-old with no previous cancer history.

Mammogram

Multiple bilateral masses and microcalcifications suspicious for malignancy, including a 1cm mass in the right breast at 9 o' clock, 3cm mass in the left breast at 12 o' clock and a 1.5 cm mass in the left breast at 8 o' clock. Further evaluation with ultrasound is recommended. BIRADS 0.

Courtesy of The Rose -Houston, Texas



Bilateral Lobular Carcinoma

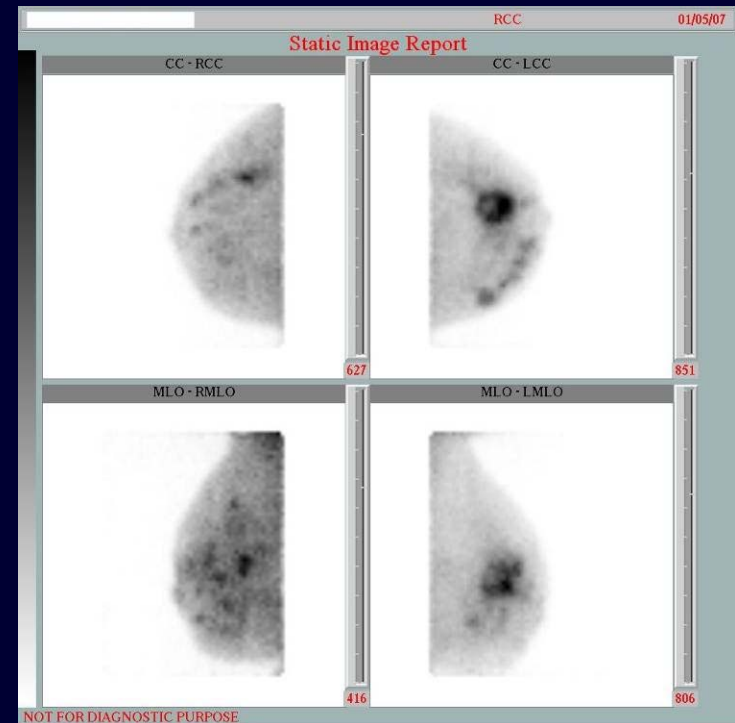
BSGI

Multiple bilateral foci of uptake indicating high suspicion of the masses indicated by US and a large number of smaller satellites. At least 5 new satellites are noted in the left breast and 4 in the right. There is also a focal enhancement in the axillary tail of the right breast possible indicating an involved node. Highly suggestive of broad-spread bilateral malignancy.

Surgical pathology

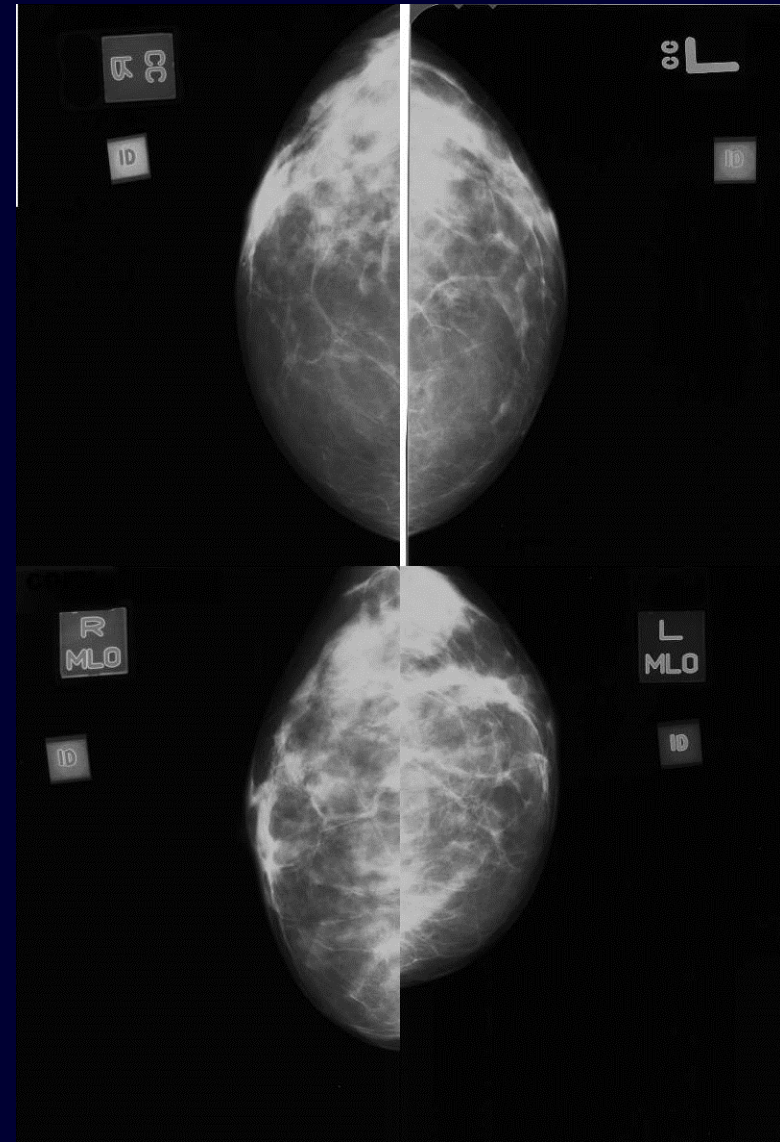
Broad- spread bilateral lobular carcinoma.

Courtesy of The Rose - Houston, Texas

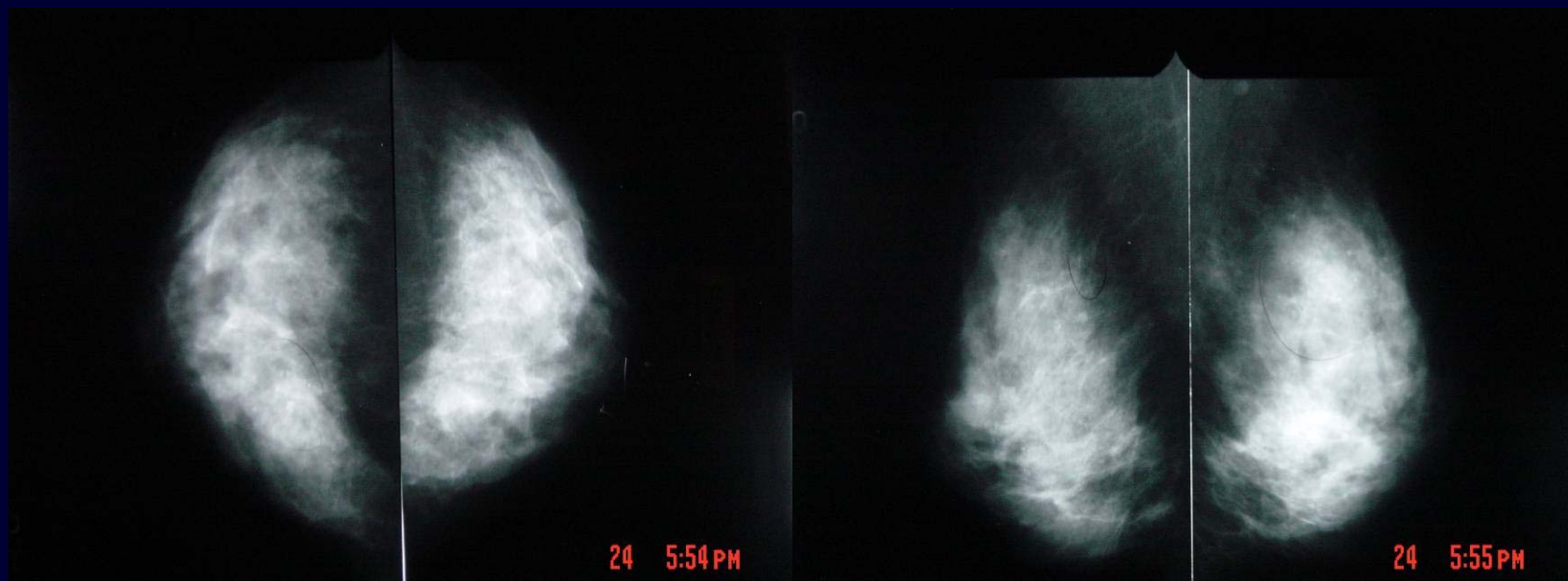


Mammogram (cont.)
Push-back views do not reveal an
obvious correlate.

Courtesy of The Rose Breast Diagnostic Center



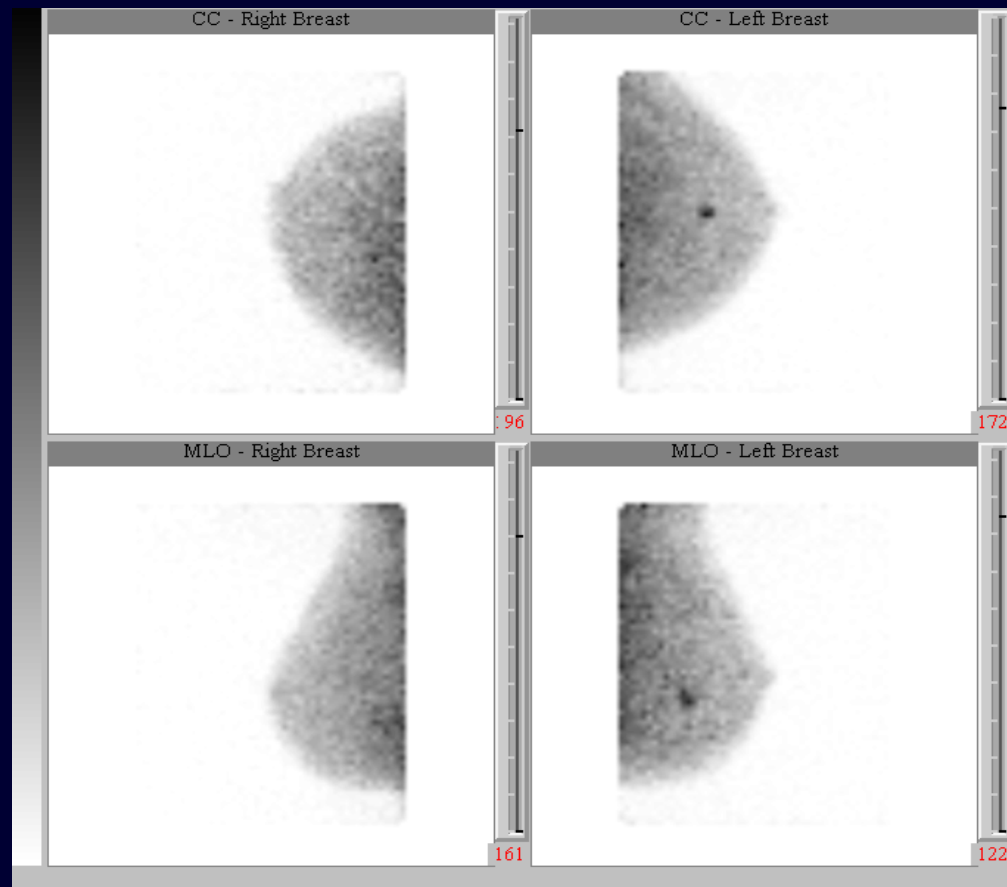
50 year old with positive family history



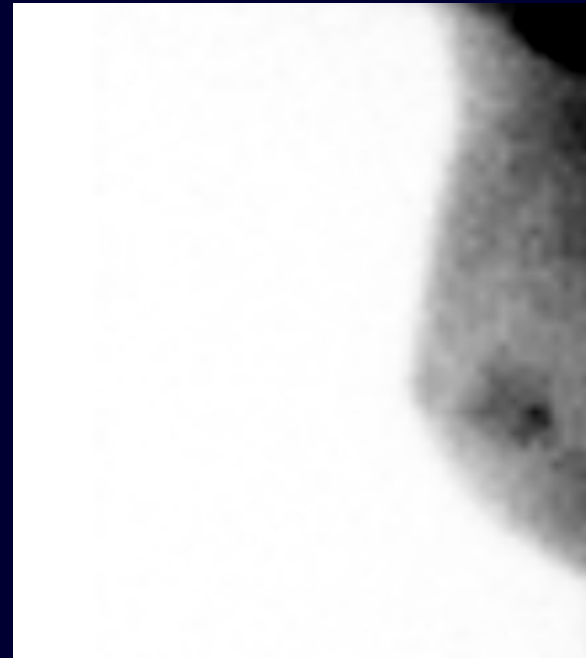
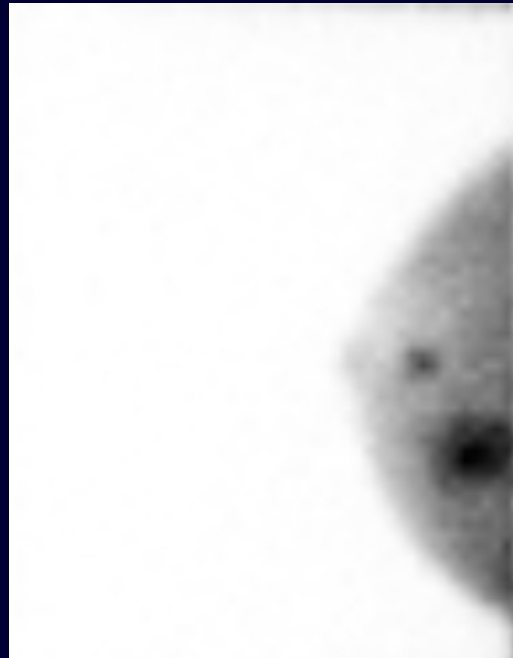
Mammogram reveals dense breast with fibroglandular changes

Recommended BSGI based on family history

Courtesy of West Houston Radiology



BSGI Study demonstrates a focal area of increased activity in the left breast.
Second Look US biopsy – 3mm Ductal Ca



BSGI

Left breast – normal uniform distribution. Right breast – a large area of asymmetric focal area of increased uptake in the upper-inner quadrant of the breast, measuring approximately 2 cm. A second, smaller and more intense focus located retroareolar, measuring about 1 cm at the 6 o'clock position. In addition, there are areas of increased activity in the right axilla which may be node activity. Multifocal positive in the right breast and possible positive findings in the right axilla.

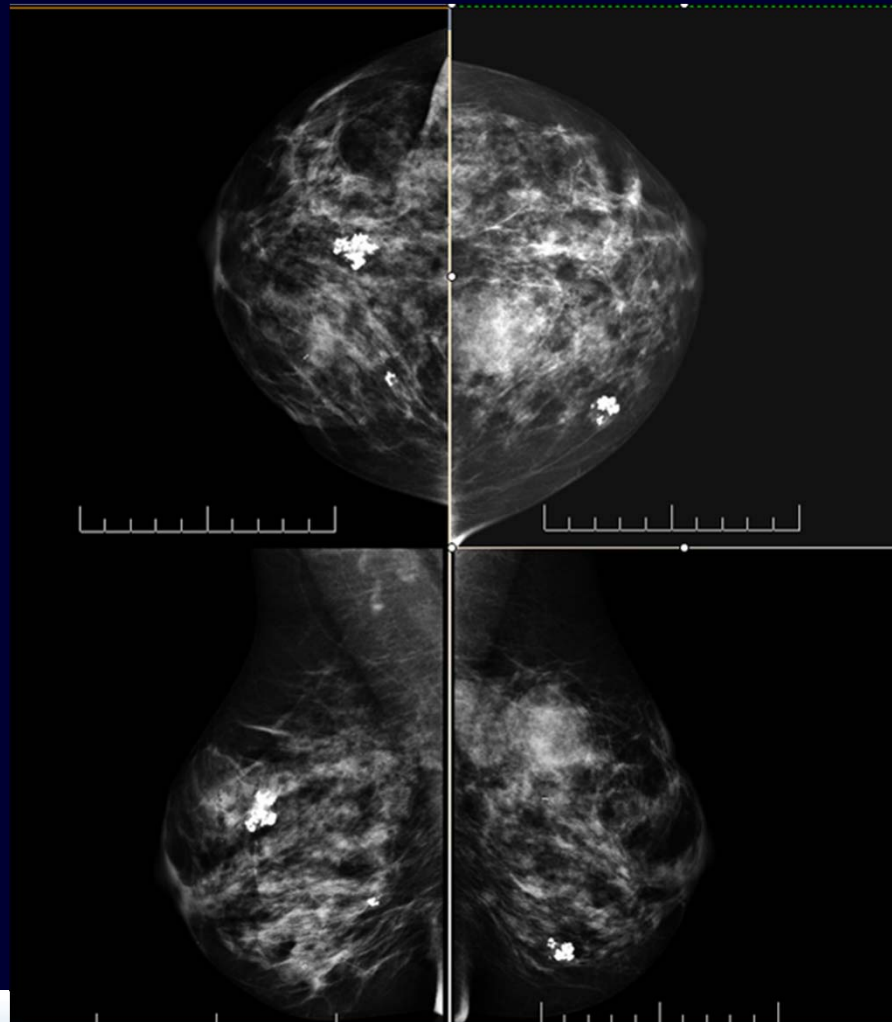
Courtesy of Legacy Good Samaritan Hospital

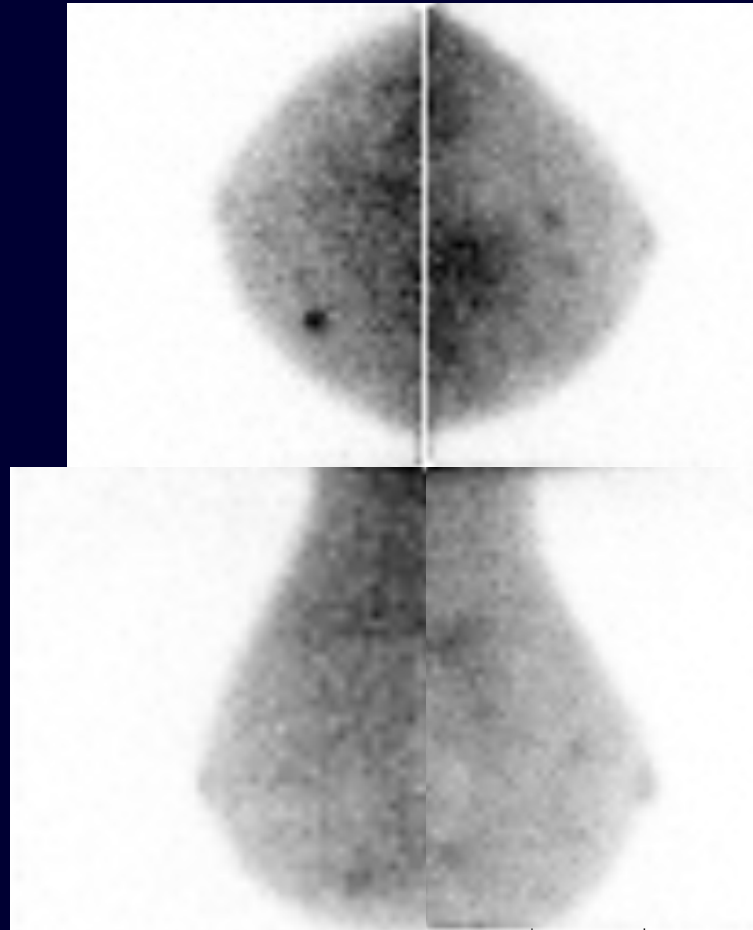


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Screening Mammogram

45 year old with no history or significant risk factors.



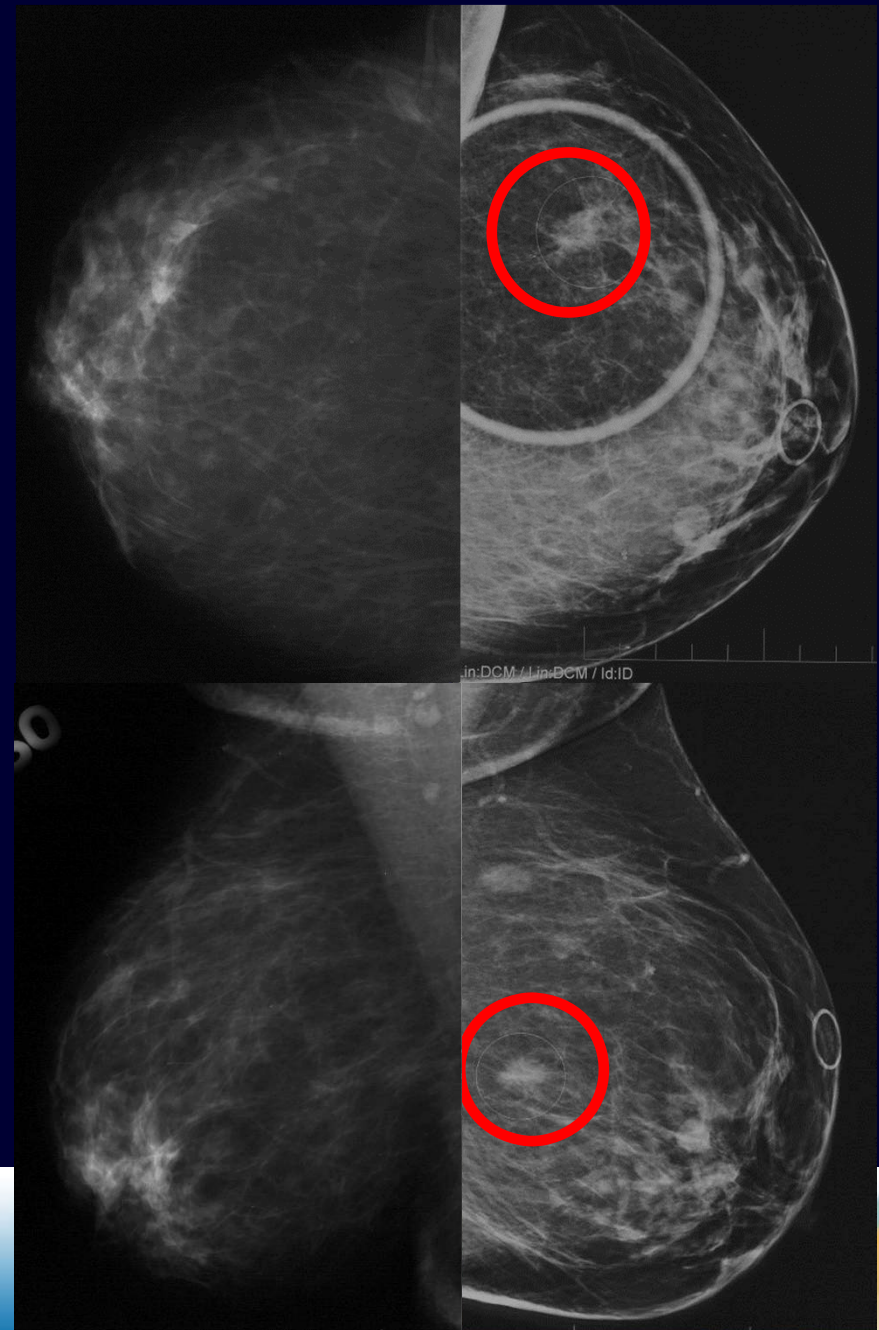


Bilateral US biopsy, left - 3 fibroadenoma right - ductal CA

Newly diagnosed breast cancer
requiring preoperative work-up.

Patient is claustrophobic and
refused MRI leading to a
recommendation for BSGI.

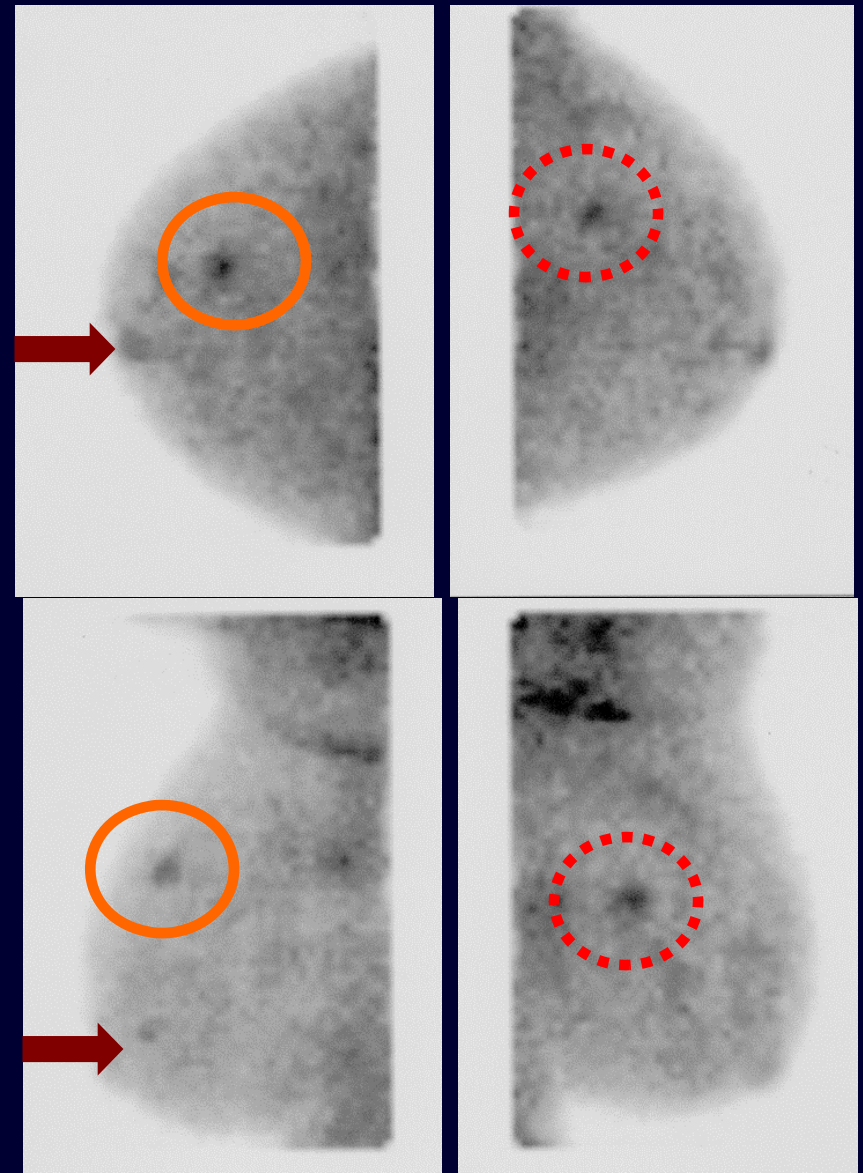
*Courtesy of Dr. Mike Linver, X-ray Associates of
New Mexico, Albuquerque, NM*



Newly diagnosed breast cancer
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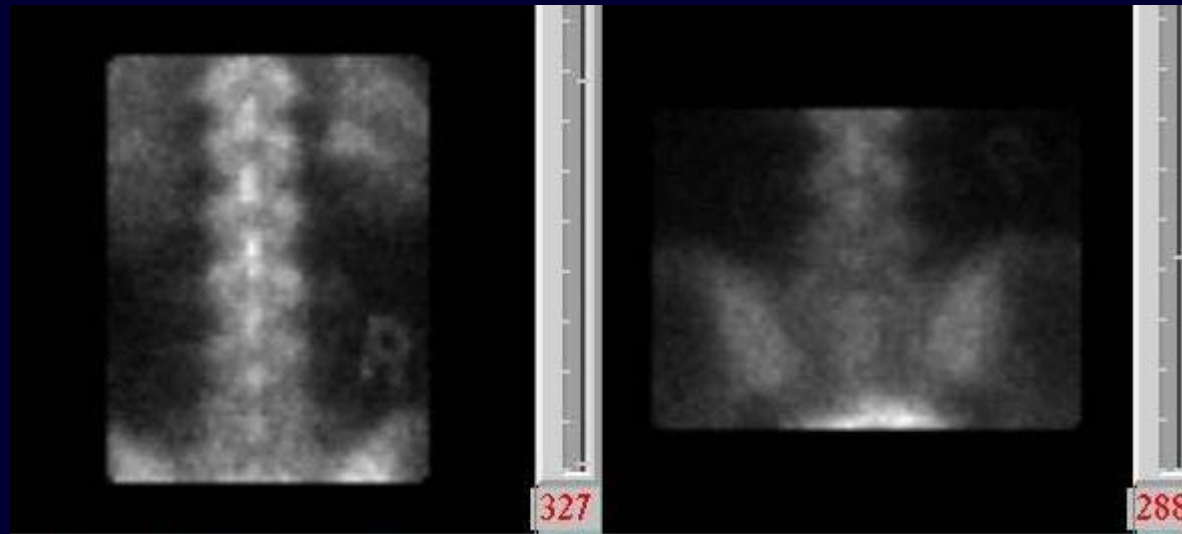
*Courtesy of Dr. Mike Linver, X-ray Associates of
New Mexico, Albuquerque, NM*



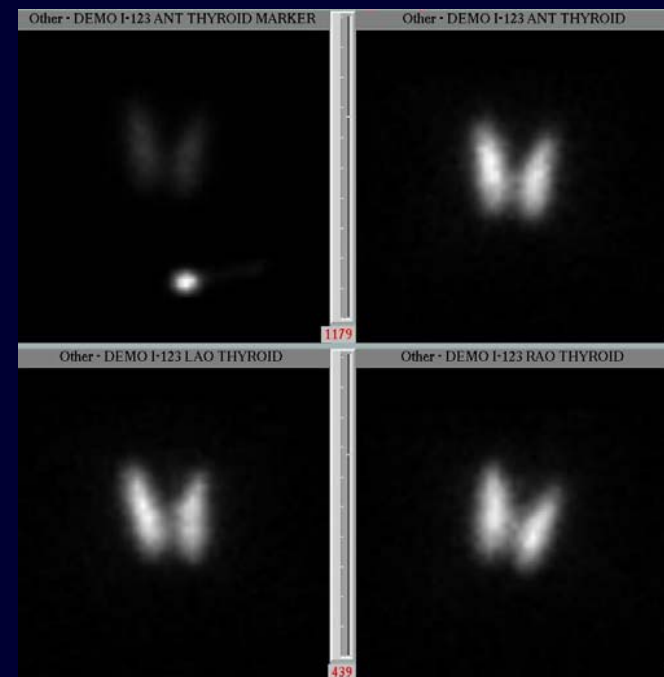
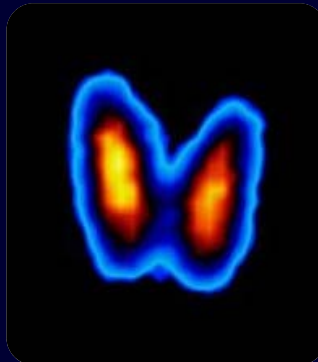
Collimators

- High Res
- General Purpose
- Slant 15

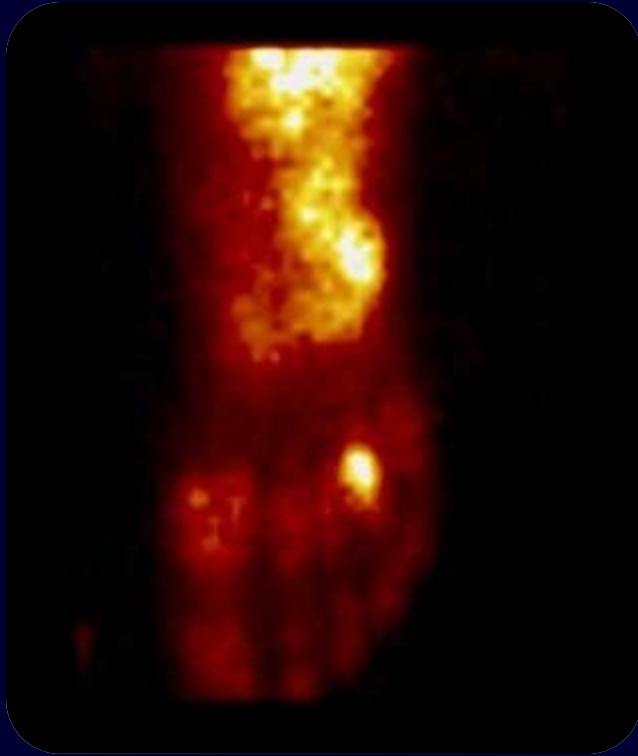
General Nuclear Medicine Utilization



Thyroid Processing



Bone Planar Imaging



**Osteomyelitis 4th
metatarsal**



**Hand resting on top of
the detector - 5 minute
image**

RAM License

- Where will the camera be used?
 - Nuclear Medicine
 - Oncology
 - Breast Center
 - Other?
- Who will be
 - Injecting
 - Positioning/Imaging
 - Interpreting images?

Licensing

- RAM license
 - Authorized users
 - Pharmaceuticals or sealed sources
- Isotopes
 - Co-57 for QC
 - Tc-99m for patient injections
 - Sestamibi for breast
 - Others for bone
 - I-123 for thyroid imaging (general NM only)

Training for physicians

- Online CME course
- Online webinar
- On-site physician follow-up training (1 day)
- Recommended 30-60 days post BSGI applications training or approximately 25-30 patient studies. May be coupled with general nuc med training.

Training for technologists

- Can be NM technologist or mammographer
- 2.5 – 3 full days
 - Day 1 lecture
 - Day 2 (3-4 patients)
 - Day 3 (2 patients)

BSGI Protocol

- Contraindications: menses cycle day 2-14, must have mammogram within the past 6 months, must be at least 48-72 hours after a biopsy, 6 months after lumpectomy, no inflammation in breast.
- 25 mCi Tc99m Sestamibi injected intravenously in the hand opposite of the diagnosed cancer

BSGI Protocol

- Uptake time = 5-10 minutes up to 90 minutes
- Planar images collected for 10 minutes each or 175kcts (RCC, LCC, RMLO, LMLO) and other views as needed

Acceptance or Annual Testing

- Intrinsic Tests
 - Uniformity
 - Spatial Resolution and Linearity
 - Energy Resolution
- Extrinsic Tests
 - Count Rate Parameters
 - System Uniformity
 - System Spatial Resolution
 - Relative Sensitivity

Intrinsic Uniformity

- Fillable flood
- 500 uCi Tc-99m
- ~ 8 kcps
- Total counts at least 5M
- Manufacturer Specification < 10%

Intrinsic Spatial Resolution

- 500 uCi Tc-99m point source
- ~ 5 FOV away
- 3M counts
- 4 Quadrant bar pattern
 - ROI of smallest resolved quadrant
 - Est. FWHM (mm) from mean counts and variance
- Manufacturer Specification 3.3 mm

Energy Resolution

- Performed to verify that scatter rejection is sufficient to provide optimal contrast in clinical studies
- Manufacturer Specification 13.5%

Count Rate Parameters

- Ensures that the time to process an event is sufficient to maintain spatial resolution and uniformity in clinical images acquired at high count rates
- Two source method to estimate dead time

System Uniformity

- 3 mCi Co-57 source
- 5M counts
- <10%

System Spatial Resolution 1

- SPECT Phantom
- 500 uCi Tc-99m
- 600,000 counts
- General Purpose Collimator
 - Satisfactory: 9.5 mm rods resolved with high contrast
 - Marginal: 9.5 mm rods resolved with low contrast
- High Resolution Parallel Hole Collimator
 - Satisfactory: 7.9 mm rods resolved with high contrast
 - Marginal: 7.9 mm rods resolved with low contrast

System Spatial Resolution 2

- 4 Quadrant bar phantom
- Up to 3 mCi Co-57 flood source
- 3M counts
- Criteria
 - Satisfactory: 3 – 3.4 mm bars resolved
 - Marginal: 3.5 – 3.9 mm bars resolved

Relative Sensitivity

- Performed to verify that the count rate per unit activity is satisfactory to maintain image quality and preserve the integrity of quantitative studies
- 500 uCi Tc-99m in a dish
- Collect counts for 1 minute, 10 times
- Average source CPM / source activity

Ongoing Quality Control

- Daily uniformity prior to patient imaging
 - 500-700 uCi Tc99m Fillable Flood
- OR
- 3 mCi Co-57 sheet source
- Open window count rate must be $< 7\text{kcp/s}$
- Uniformity must be $< 10\%$
- Note, weekly bars not recommended

Accreditation from the American College of Radiology

- NMAP - Planar
- Choose two hepatobiliary exams
- Specific questions? Carolyn Richards MacFarlane, ACR Program Manager for NM/PET. 800-227-5463 x 4563 or cmacfarlane@acr.org

Submitted Items - Clinical

- Two clinical studies
- Written protocol
- Radiologist's report
- Imaging parameters

Submitted Items - Physics

- Annual or Acceptance Report
- Field Uniformity
 - Intrinsic or system
 - 5M counts
- Spatial Resolution
 - Intrinsic or system
 - 3M counts
 - Four quadrant or ACR phantom (planar resolution)

Don't Forget:

- Also include an 8x11" sheet in the envelope that states "NM Breast Exams" so the submission can be flagged for specific breast reviewers

Questions?