CIBC 2019

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Molecular Breast Imaging (MBI): A Functional Breast Imaging Modality

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Disclosure

- Consultant, Philips Ultrasound
- Sub PI, Delphinus Inc.

MBI

- Gamma camera; high resolution, small field of view, detect > 3 mm cancers.
- Molecular (physiologic) imaging contrast to anatomical.
- Complements mammography & US.
- Close proximity of the small detectors (6 x 8 inch or 10 x 8 inch) to the breast provides excellent spatial resolution and allows same positioning as mammography.

MBI

- Two types of gamma camera; multicrystal [illegible]ing sodium iodide or cesium iodide seen in single head detectors & cadmium zinc telluride (CZT) direct conversion detectors used in the dual head units.
- Technology referred to both MBI & BSGI, depending on the camera.
- Dose can be reduced by a factor of 2 using a dual head detector.
- However, to have same photon sensitivity need to fuse these images increasing the cost of the dual head detectors systems.

Commercial MBI [illegible] available

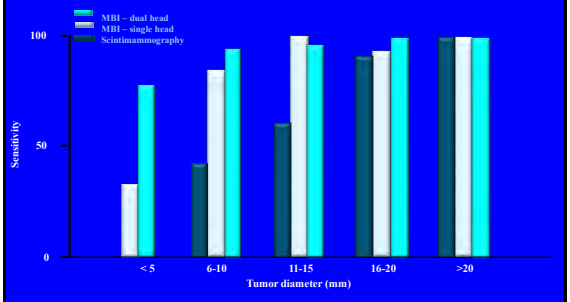
Dilon 6800
BSGI
3 mm pixels
20 x 15 cm FOV

CMR Naviscan (previous GammaMedica) LumaGem
MBI
1.6 mm pixels
20 x 16 cm FOV

Dilon/ GE Discovery NM 750b
MBI
2.5 mm pixels
24 x 16 cm FOV

BSGI was traditionally referring only to Single head but now we are calling both single & dual head as MBI. CMR Naviscan is making both, PEM and dual head MBI.

Sensitivity of Single & Dual head MBI detectors & Scintimammography



Clinical Data Summary (16 papers & presentations)

- Total patients 4156
- Overall Sensitivity 91.2%
- Overall Specificity 82.4% **
- Overall PPV 62.5%
- Overall NPV 97.0%

**Specificity is directly linked with pre-test probability of disease. BSGI is a problem-solving tool when MMG & US are insufficient or discordant.

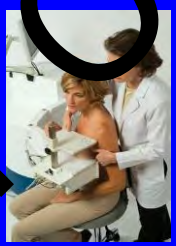
MBI: Technique

- No preparation; hydrated
- Source of error;
  - Infiltration in arm vein may cause FP uptake in the axillary lymph nodes.
  - Patient motion (rare) will decrease accuracy.
  - Sensitivity low for cancers < 3 mm.
- Contraindications;
  - Pregnancy
  - Known hypersensitivity to Tc-99m sestamibi (rare)

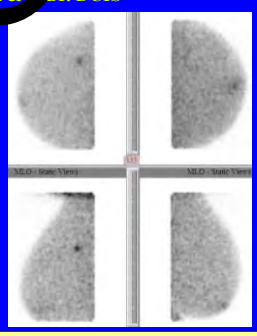
MBI:Technique

- IV injection of Tc99m Sestamibi (butterfly needle) followed immediately by imaging
  - 8 to 15 mCi (300 – 555 MBq)
- Tech trained in MMG positioning
- Pt seated, breast immobilized with gamma shield & detector. Gamma shield absorbs radiation from thyroid avoiding artifact
- CC & MLO views (10 min or less/view 175,000 counts)
  - Additional projections can be done.

ne camera can replicate any mammographic view.



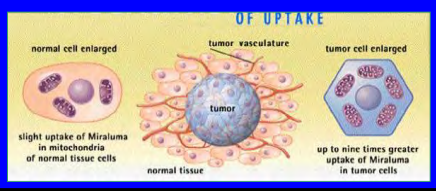
Mammogram & MBI: DCIS



Easy to compare both modalities and observe same area of suspicion.

Tc-99m Sestamibi (Radiotracer)

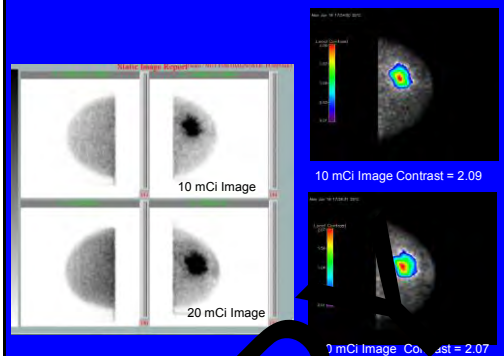
- Tc-99m a gamma-emitting radionuclide, peak radiation 140 keV, half life 6 hours, excreted by the biliary tract.
- Sestamibi (tracer) is a mitochondrial binding agent; 10x increase metabolic activity is seen mitochondria of cancer cells.



MBI / BSGI

- 20-30 mCi (700-1100 MBq) of Tc-99m sestamibi (FDA approved in 1997);
  - Radiation dose to breast similar to 4 view MMG
  - Total body radiation dose is 6-9 mSieverts
- Currently 4-8 mCi is used with dual head detectors (8 mCi = 2.4 mSieverts or 60% radiation dose reduction) & 10-15 mCi with single head detectors, both shown to provide good image quality.

Dose Reduction Case



Infiltrating Ductal Carci na

Requirements/ Guidelines/ Parameters

- Require NRC license, hot lab & ACR accreditation (Jan 2012), but no room shielding.
- SNM Procedure Guideline for Breast Scintigraphy with BSGI (June 2010)
- ACR Practice Parameter for the Performance of Molecular Breast Imaging (MBI) using a Dedicated Gamma Cam (August 2017)

Meta-analysis of articles

- BSGI sensitivity 95%, specificity 80%, NPV
  - <1 cm cancer & DCIS sensitivity 84% & 88%
- BSGI dx 4% of cancers in pts with nl MMG, 6% additional cancers in those with a bx proven cancer.

– Sun Y, Wei W et al. Clinical usefulness of BSGI as an adjunct modality to MMG for dx of breast cancer; a systemic review and meta-analysis. Eur J Med Mol Imaging, Nov 14, 2012

Clinical Role of MBI

- 224 patients with a total of 244 lesions who had MMG, US and MBI with subsequent biopsy or a 6 months follow up.
- The combined sensitivity of MMG and MBI detected 42/44 lesions; 95.
- MBI contributed to the detection of malignant and high-risk lesions missed by MMG and US.
- Nearly all of the MBI(-) lesions detected by MMG presented as suspicious calcifications on MMG.
- *MBI can improve cancer detection when included as part of the diagnostic work-up of patients.*
- *MBI can not rule out the need for biopsy of suspicious calcifications or when indicated by conventional imaging.*

-The Role of MBI in Breast Patient Management; Its Impact in a Community Breast Center, RSNA 2012

BSGI Sensitivity in Patients with Dense Breast – A Korean Population

662 patients with 665 lesions
- 192 malignant, 473 benign lesions
- Specificity = 87.9%

	Overall	Nondense	Dense
BSGI	95.3%	95.7%	95.1%
MMG	75.1%	82.9%	70.7%

Anbok L, Jihyun L, MD, et al The efficacy of BSGI with 99mTc-sestamibi in the diagnosis of breast cancer according to breast density for Korean women. RSNA 2011

BSGI Compared to Mammography and Sonography in the Diagnostic Breast Patient

N = 329	MMG	US	BSGI
Sensitivity	74%	84%	93%
Specificity	79%	62%	70%
PPV	71%	60%	68%
NPV	82%	85%	93%

BSGI provided a statistically significant improvement in sensitivity and NPV ($p < 0.000001$ using the McNemar test).

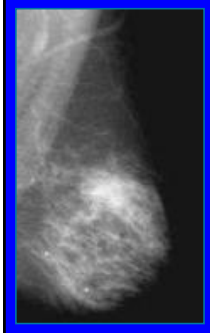
Weigert J, Bertrand M, Stern L, Kieper D. Results of a Multicenter Patient Registry to Determine the Clinical Impact of BSGI, a MBI Technique. AJR:198, January 2012

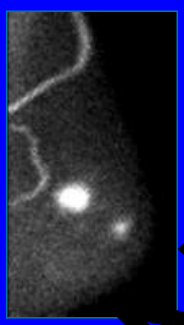
BSGI in patients with one suspicious mammographic or clinical finding

- 159 women who had one suspicious breast lesion on physical exam and/or mammography
- BSGI identified occult cancer in 14 of the 159 (9%)
  - 9 ipsilateral lesions (6%)
  - 5 contralateral lesions (3%).
- 50% of the lesions detected were smaller than 1 cm

Brem, RF, Shahan,C, Rapleyea, J et al. Detection of Occult Foci of Breast Cancer Using BSGI in Women with One Mammographic or Clinically Suspicious Breast Lesion. Radiol 2010; 735–743.

Greater Clinical Confidence





Additional 10 cancers lesions only on

Dual head MBI detected

BSGI compared to Breast MRI

122 Malignant and high-risk lesions requiring excision

	Positive	Sensitivity	Indeterminate
BSGI	110/120	91.6%	3
MRI	106/117	90.6%	6

BSGI advantages over MRI;

- generates 4-8 images as compared to up to 1000 images in MRI making interpretation time much less.
- can be utilized in all patients including those claustrophobic, with ferromagnetic implants or renal insufficiency.
- conducted at a fraction of the cost.

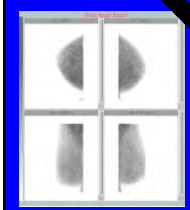
Brill, K et al. BSGI compared to Breast MRI in patients requiring diagnostic imaging after screening mammography. ASCO Annual Meeting, Washington D.C. Sept, 2008

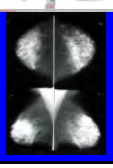
MBI: Criteria for Interpretation

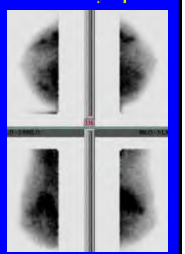
BI-RADS 1: Normal Homogeneous uptake

BI-RADS 2: Benign Minimal patchy update

BI-RADS 3: Probably benign Patchy update

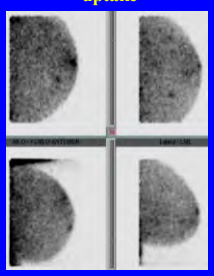


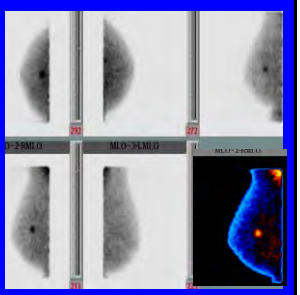




BI-RADS 4: Probable abnormal Mild focal increase uptake

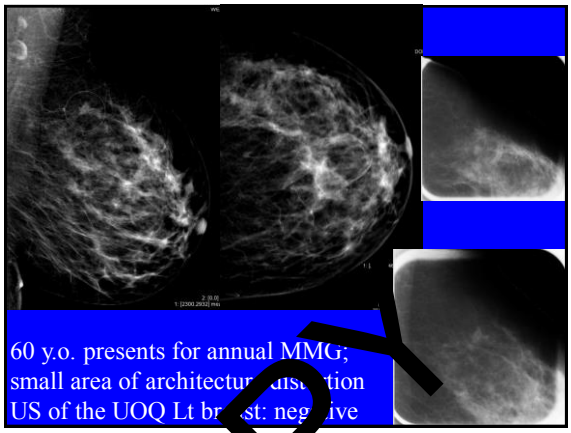
BI-RADS 5: Abnormal Focal increase uptake



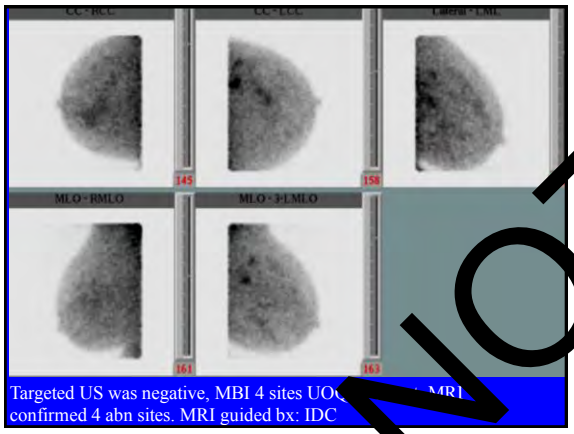


MBI: Indications

- Complements mammography & US for patients who are difficult to image; dense breast tissue, implants, post surgical, silicone & paraffin injections.
- Patients with known cancer:
  - determine extent of disease
  - evaluate for multifocal/ multicentric/ bilateral disease.
- Questionable areas found on mammography or US; reassurance for BI-RADS 3.
- Clinical abnormality such palpable mass or nipple discharge with nl mammogram & US.
- Scar vs recurrent cancer.

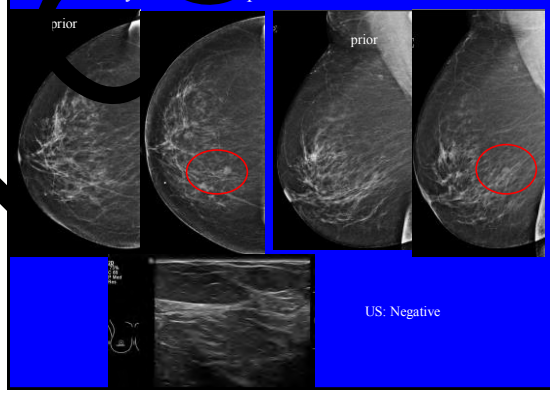


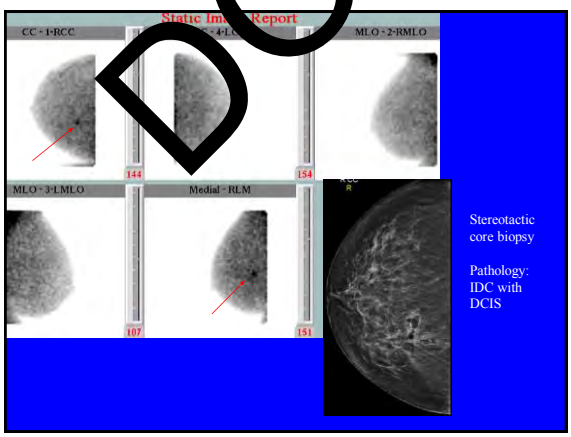
60 y.o. presents for annual MMG; small area of architectural distortion US of the UOQ Lt breast: negative



Targeted US was negative, MBI 4 sites UOQ MRI confirmed 4 abn sites. MRI guided bx: IDC

73 year old asymptomatic woman

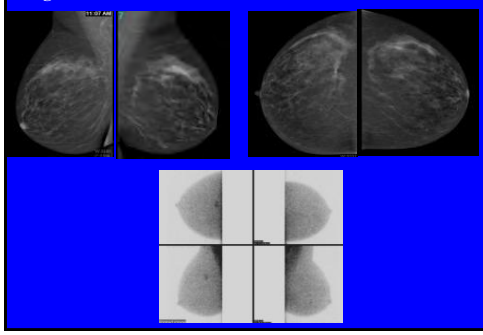


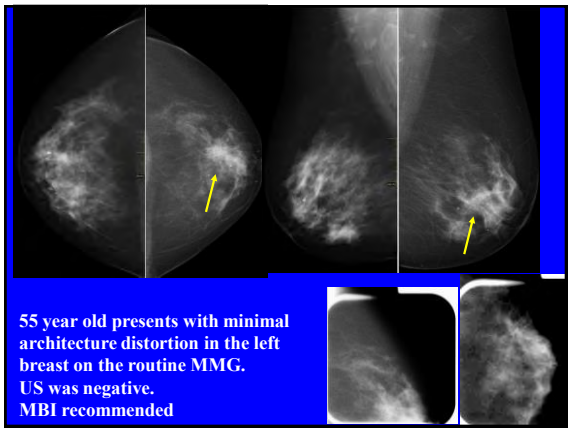


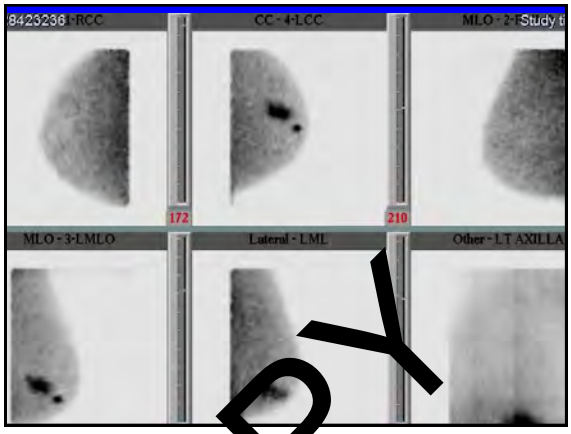
Stereotactic core biopsy

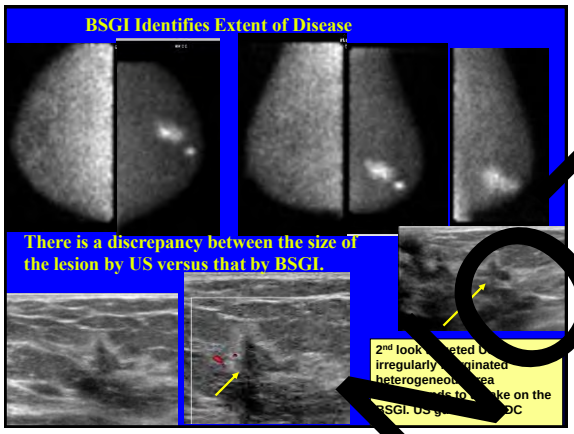
Pathology: IDC with DCIS

A 65-year old patient. Maternal aunt, grandmother and paternal cousin with breast cancer. Patient had LCIS in RtUOQ with excisional biopsy, presents with new palpable abn RtUOQ. US neg. MBI abn. Stereotactic bx: IDC







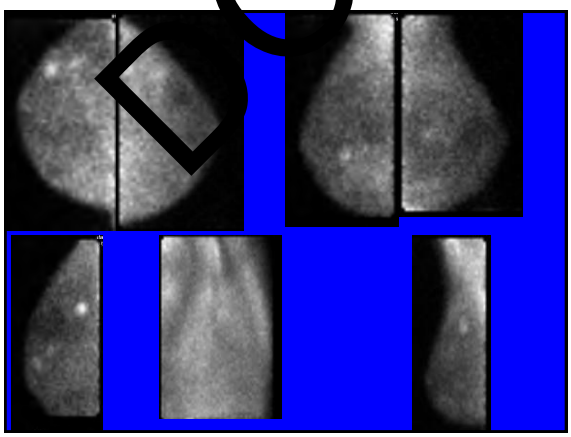


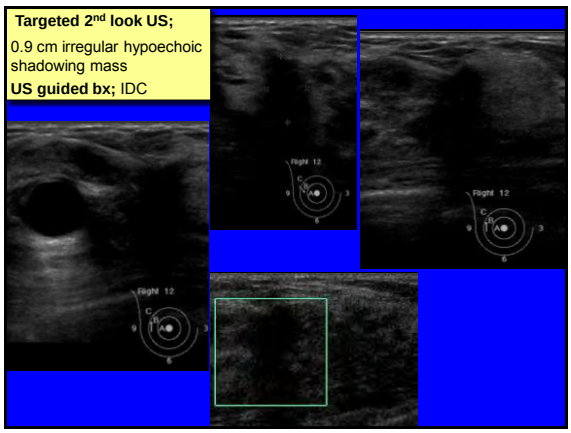
55 year old female with no risk factors for breast cancer, except very dense breasts.

Mammogram very limited due to dense fibroglandular tissue.

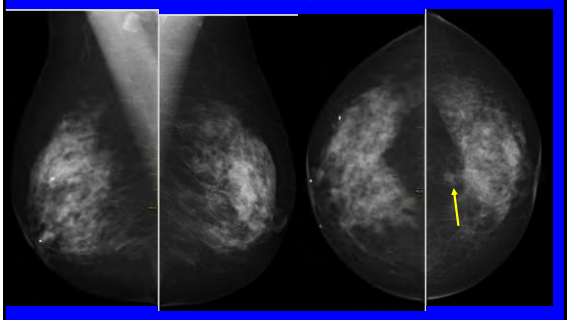
US showed multiple cysts (simple and debri-containing).

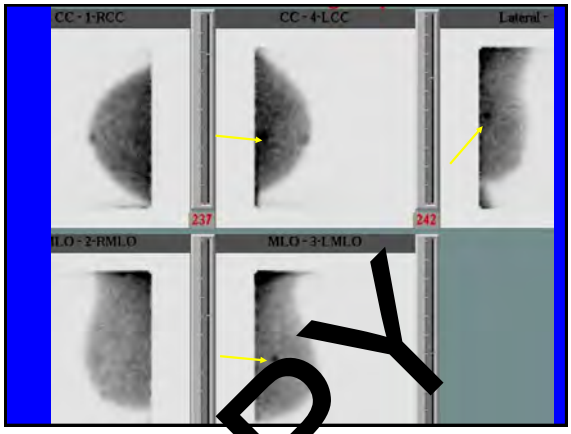
She had a mammogram and US every 6 months.

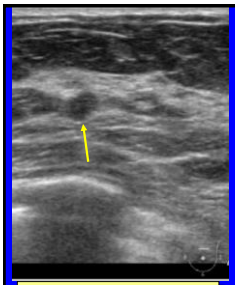


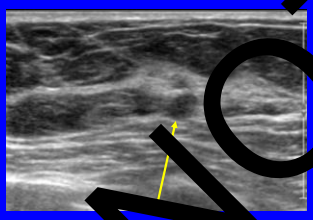


69 y.o. woman presents for annual MMG. MMG showed an asymmetry center Lt breast only in the CC view. US neg. BSGI recommended to evaluate asymmetry.









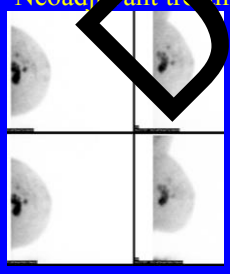
Targeted 2nd look US; left breast 12 o'clock 3 mm hypoechoic mass.

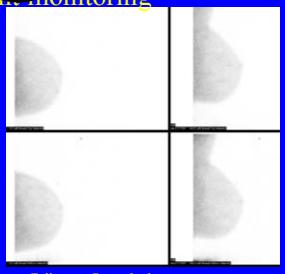
US guided bx; IDC

MBI: Indications

- **Evaluating axillary region for lymph node status in breast cancer pts.**
- **Predicting chemotherapeutic response.**
- **Monitoring primary tumor response to neoadjuvant therapy.**
- **Evaluation of multiple lesions or clusters of microcalcifications to aid in bx targeted selection.**
- **Evaluation in women with indeterminate/ malignant type Ca++ before stereotactic core bx.**

Neoadjuvant treatment monitoring





Baseline

Follow up 7 months later

50 yo patient with dense breast, biopsy proven IDC ng III & metastases in axillary lymph nodes. Following neoadjuvant treatment, tumor was reduced in size on US. MBI showed no enhancement indicating successful treatment. Post neoadjuvant Lt lumpectomy, axillary dissection: Fibrosis, scarring and sclerosing adenosis, no residual tumor seen.

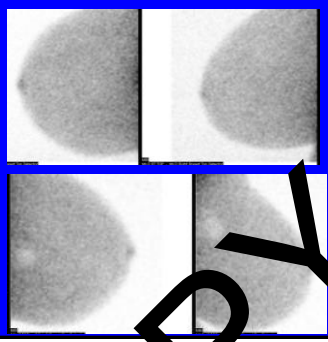
BSGI vs MRI Comparing the Dx Performance in Assessing Tx Response After NAC in Pts with Breast Cancer

- 114 breast cancer patients had BSGI & MRI prior and after NAC, 112 had subsequent surgery, 30 /114 had complete pathologic response to NAC.
- BSGI & MRI had comparable sensitivity in detecting residual tumor (70% vs 83%).
- BSGI had higher specificity than MRI in determining complete response (90% vs 60%).
- BSGI may be a useful adjunct tool for predicting complete pathologic response.
  - *Kim, S et al, AJR 212; 696- 705, March 2019*

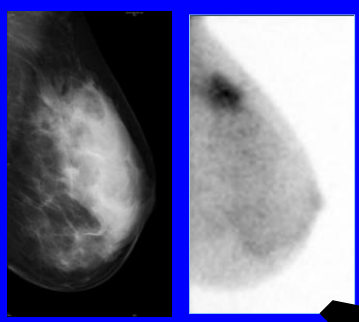
MBI: Indications

- **Patients which MRI is indicated and those who MRI is not technically possible (ferromagnetic implants, renal insufficiency or are claustrophobic).**
- **In high risk patients similar to the MRI screening criteria:**
  - **BRCA1, BRCA2 mutations**
  - **Parent, child, sibling BRCA+**
  - **Established lifetime risk > 20-25%**
  - **Chest radiation between 10 and 30 years old.**

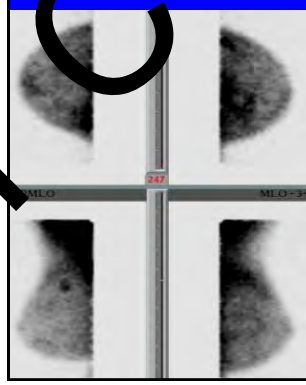
High-risk large patient with pacemaker cannot have MRI



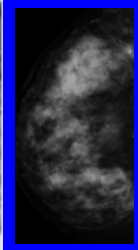
Screening the Dense Breast

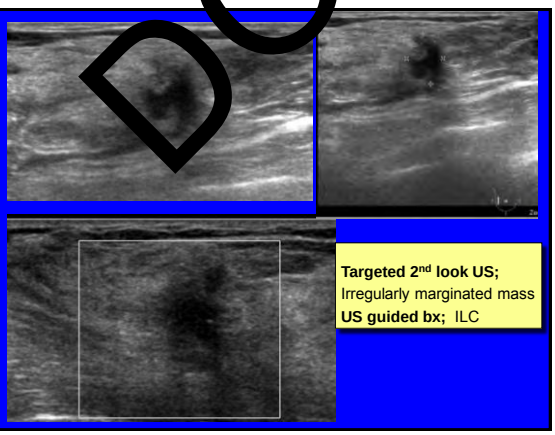


•40% of women have dense breast tissue.
•Dense breasts a 4 to 6 fold increased risk of developing breast cancer.
•Breast density is a strong predictor of the failure of MMG to detect cancer, missing every other cancer in dense breasts.



High risk patient. Mammogram; dense fibroglandular tissue, Screening US negative.





Targeted 2nd look US; Irregularly marginated mass **US guided bx;** ILC

Screening Study	Tc99m Sestamibi	N	ICDR to 2D IDC + DCIS	relative MMG IDC only	Size of Cancer by MBI Medium (range)	Recall rate by MBI	PPV 3 MBI
Rhodes 2011 Dense breasts+ risk factor	20 mCi	936	7.5	5.3	1.1 cm (0.4-5.1)	5.9%	28%
Rhodes 2015 Dense breast	8 mCi	1585	8.8	6.9	0.9 cm (0.5-4.1 cm)	6.6%	33%
Shermis 2016 Neg MMG, dense breasts, <20% risk	8 mCi	1696	7.7	6.5	1.0 cm (0.6-2.4 cm)	8.4%	19%
Brem 2016 BSGI, MMG neg, risk factor	7-32 mCi	849	16.5	7.1	2.5 (0.3-4.0)	25%	14%

ILC: Mammography, US, MRI & BSGI

- 26 pts (28 bx proven ILC)
- NI mammogram 6/28 (21%), abn mammogram 22/28
- US 17/25 had hypoechoic areas, 12 pts had MRI
- BSGI had the greatest sensitivity for the detection of ILC of 93% (26/28)
  -Mammography; 79% (22/28), US; 68% & MRI; 83%

Brem, R. Invasive Lobular Carcinoma: Detection with Mammography, Ultrasound, MRI and BSGI. AJR;192; February 2009; 379-383

Detection of DCIS: 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 occu[lt] lesions in patients with bloody nipple discharge and negative [m]ammograms.

Brem, et al. Detection of DC[IS] with M[a]mmography, BSGI and MRI: a comparative stuay. [A]cademic Radiology. August 200[7]

BSGI: DCIS

BSGI shows a second site of DCIS

BSGI: Extent of disease

- 138 pts [w]ith cancer
- 25 pts (18%) had + BSGI at a site remote from known cancer or more extensive disease.
- 10.9 % additional cancer converted 7 pts to mastectomy, 1 to neoadjuvant tx, 7 diagnosed contralateral cancer.
  - PPV; 92.9%

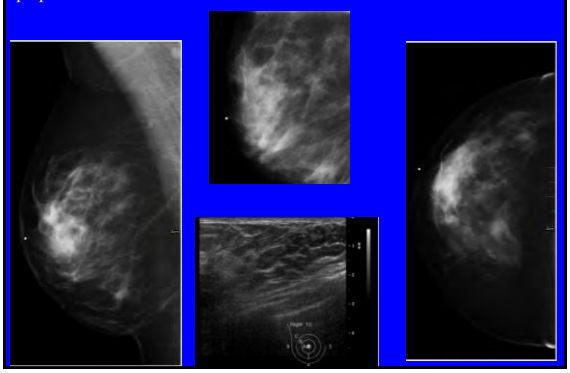
Zhou M et al. AJS, 2009;197 (2), 159-163.

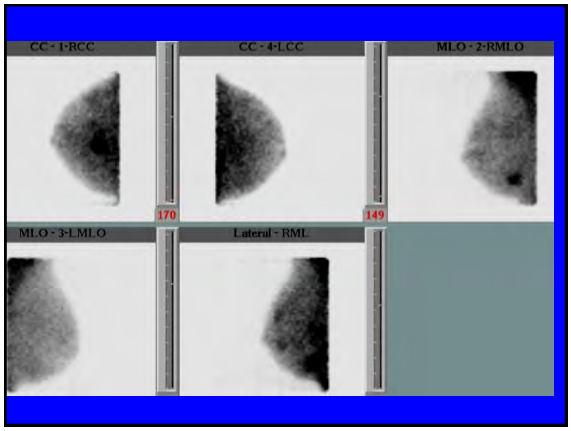
Post-s[u]rgical Breast

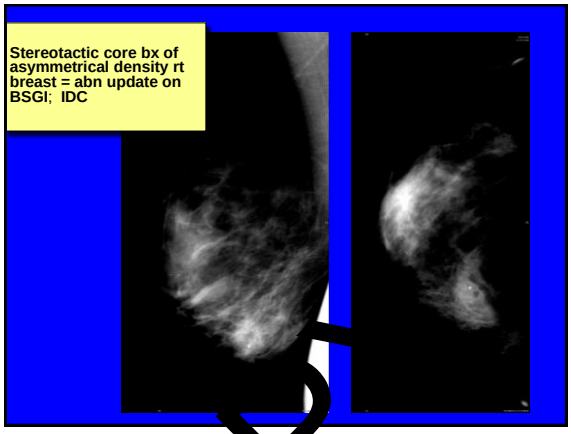
- **No increa[se] radiotracer uptake in women 6 months following lumpectomy or reduction mammoplasty.**

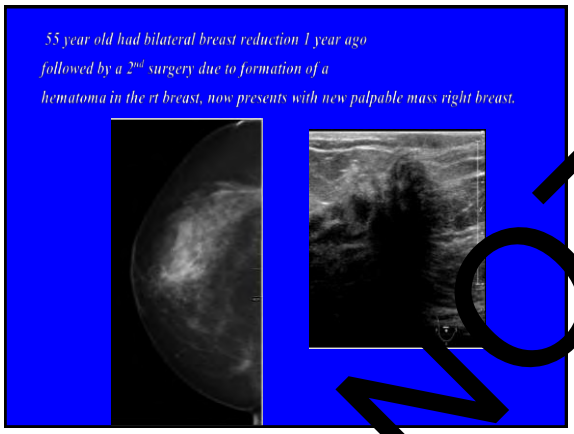
– ***Babuccu I et al. The value of scintimammography in reduction mammoplasty, a preliminary report. Aesth Plast Surg 2003;27:296-300.***

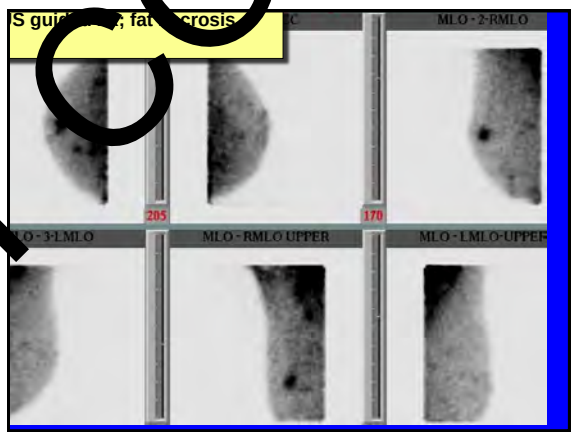
37 year old with bilateral breast reduction 10 years ago presents with a palpable abn in the Rt breast 6 o'clock









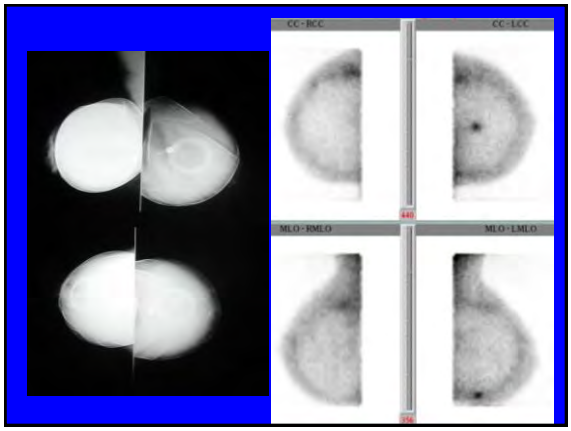


MBI: False Positives

- < 5 %
- Fat necrosis
- Radial scar
- Abscess / inflammatory changes
- Sclerosing adenosis
- Complex fibroadenoma
- Papilloma
- Stromal fibrosis
- High risk marker; ADH, LCIS

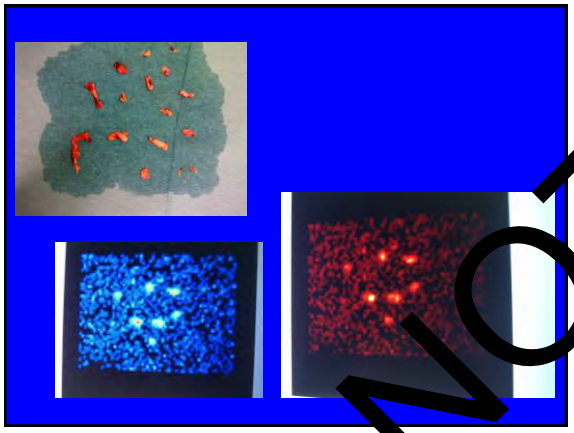
MBI: Implants

- Clearly images breast parenchyma
- Little or no activity over implants due to paucity of tissue
- Can visualize cancer overlying the implant



Guided Biopsy Device

- Easily performed with approach similar to stereotactic biopsy which is mammographically guided.
- Patient is seated.
- Replaces the compression shield.
- FDA approved.



Clinical Role & Cost-Effectiveness of BSGI in the Management of Pts with Negative or Indeterminate MMG, US & Unresolved Dx Concern

- Retrospective analysis 95 pts (102 areas of concern -> BSGI); 7 IDC, 6 DCIS & 2 ILC
- BSGI contributed to pt management by detecting cancers 12/95 (12.6%), high NPV reassured but does not obviate the need for bx when indicated by other imaging modality.
  - San Antonio Breast Meeting 2010

Clinical Role & Cost-Effectiveness of BSGI

- Cost-effectiveness of BSGI compared to MRI is significant, average cost BSGI is $330. MRI is $900.
- MRI has high sensitivity, but high cost & restrictive insurance reimbursement policies prevents use in pts with intermediate & low risk.
- In proper clinical setting, BSGI can improve ability to detect cancers with high sensitivity & NPV.
  - *San Antonio Breast Meeting 2010*

MBI: Conclusion

- MBI when used as an adjunct to MMG & US for the appropriate indications (palpable masses, nipple discharge) provides high sensitivity, specificity & negative predictive value.
- It has less false positives at a lower cost, with less interpretation time needed, not effected by breast density & is better tolerated by patients than MRI.

Thank you!!!

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