Advances in Breast Imaging

SCPMG Medical Imaging Technology & Informatics

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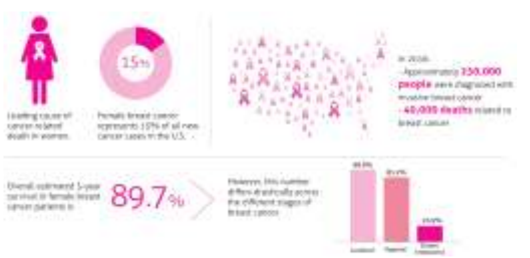
Outline

- History of breast imaging
- Advances in breast imaging
    - a) Full-Field Digital Mammography – DBT and CEDM
    - b) Breast Ultrasound
    - c) Molecular Breast Imaging
    - d) Breast MRI
    - e) Dedicated Breast CT (bCT)

Why Breast Imaging is Important



magellanhealthinsights.com

Why Breast Imaging is Important

Early diagnosis
↓
Early treatment
↓
Reduced mortality

Why Breast Imaging is Important

Two methods of screening for disease:

- Self examination and physical examination
- Mammography

www.sbs.com.au

History of Mammography

1960s: Mammography became a widely used diagnostic tool.

1969: First X-ray units dedicated to breast imaging became available.

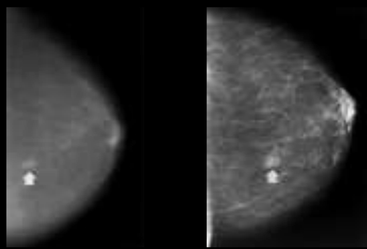
1992: Congress enacts the Mammography Quality Standards Act (MQSA)

2000: FDA approves the first digital mammography system.

2011: FDA approves Hologic's 3D mammography technology.

www.mammoguide.com

Mammograms: 1975 and Current



Breast Imaging: From 1965 to the Present E.Sickles, Radiology 215:1 2000

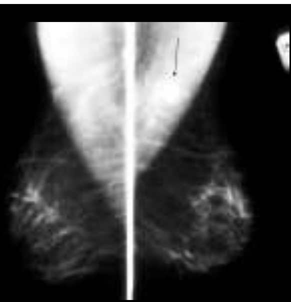
Challenges in Mammography

Mammography is the gold standard for detecting breast cancers.
Challenges:

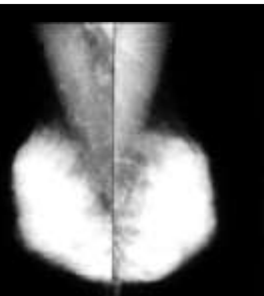
- Low Sensitivity (~85%)
- Less helpful with women:
  - Dense breasts (sensitivity 63%, specificity 89%)
  - Pregnant women
  - Lactating women
  - Breast implants
  - High-risk women

Carney PA. Ann Int Med 2003

"Breast Specific Gamma Imaging" Lillian H Stern, MD, Thomas Jefferson University, Philadelphia, PA



"***Breast Specific Gamma Imaging***" Lillian H Stern, MD, Thomas Jefferson University, Philadelphia, PA



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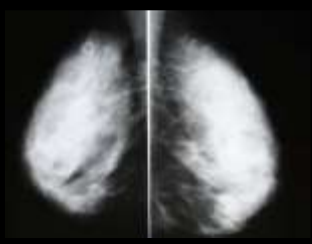


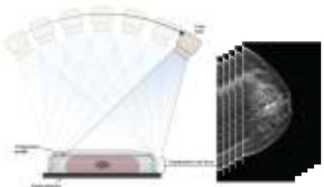
"***Breast Specific Gamma Imaging***" Lillian H Stern, MD, Thomas Jefferson University, Philadelphia, PA

Solid mass with calcifications

"*Breast Specific Gamma Imaging*" Lillian H Stern, MD, Thomas Jefferson University, Philadelphia, PA

DBT – Digital Breast Tomosynthesis

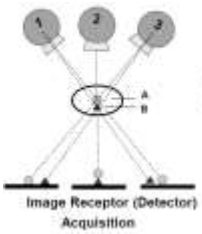
- 2011 Hologic was approved by FDA
- Since then thousands systems been installed in US



DBT – Digital Breast Tomosynthesis

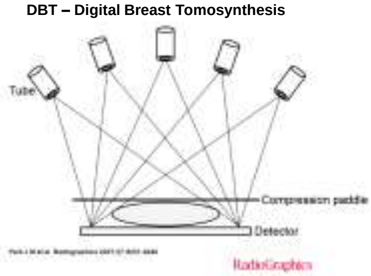
- Is a refinement of conventional tomography, can be considered "limited angle" CT
- Generate an arbitrary number of in-focus planes from a series projection radiographs taken during a single motion (sweep) of x-ray tube
- The various in-focus planes are produced without additional exposure

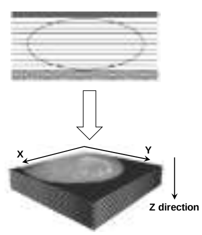
DBT – Digital Breast Tomosynthesis



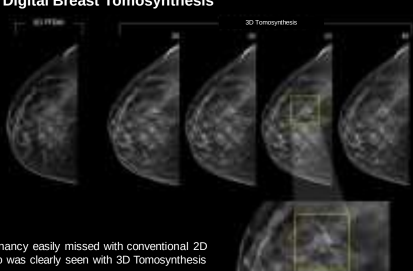
"Shift and Add Tomosynthesis Reconstruction", Dobbins & Godfrey - Phy Med Biol 2003; 48: R65-R106

DBT – Digital Breast Tomosynthesis





DBT – Digital Breast Tomosynthesis



A malignancy easily missed with conventional 2D mammo was clearly seen with 3D Tomosynthesis

by Radiological Society of North America

DBT Performance

- Resolution:
  x-y plane: <= FFDM (< 0.1mm)
  z direction: 1 mm
- Calcification detection:
  Conflicting reports (DBT better if no detector pixel binning)
- Mass detection:
  Sensitivity and specificity improved
  Recall rate dropped

"Breast Tomosynthesis", Bob Liu, 2014 AAPM Annual Meeting

DBT Performance

- Artifacts:
  High density objects in multiple slices (due to limited sampling)
- Radiation Dose:
  Combo (DBT + 2D) acquisition: ~2.2 x FFDM
  DBT acquisition with synthetic 2D: ~1.2 x FFDM
- Workflow:
  Reading time longer
- Cost:
  ~2 x FFDM + cost for more storage

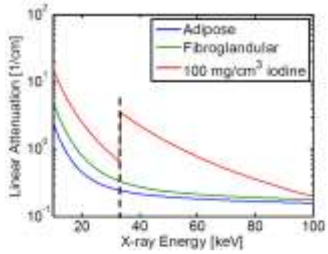
"Breast Tomosynthesis", Bob Liu, 2014 AAPM Annual Meeting

Contrast Enhanced Digital Mammography (CEDM)

- CEDM uses the intra-venous injection of iodinated contrast agent together with mammo exam
- Based on the principle that rapidly growing tumors require increased blood supply
- Contrast agent accumulates in tumor and CEDM offers a method of imaging contrast distribution in breast tissue
- Two techniques have been developed:
  1. Temporal Subtraction
  2. Dual Energy Subtraction

"Contrast enhanced digital mammography (CEDM): From morphological to functional mammography", by S. Muller, etc.

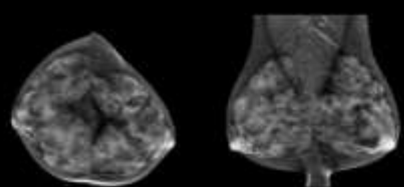
Contrast Enhanced Digital Mammography (CEDM)



"Innovations in Clinical Breast Imaging: Novel Mammography Applications – Contrast Imaging", Martin Y., etc.

CESM: Clarification of mammographically equivocal lesion

79 yo w palpable mass on left breast, original mammography images



Images courtesy of Mikawa Breast Center, Mikawa, Japan and GE Healthcare

CESM: Clarification of mammographically equivocal lesion

79 yo w palpable mass on left breast

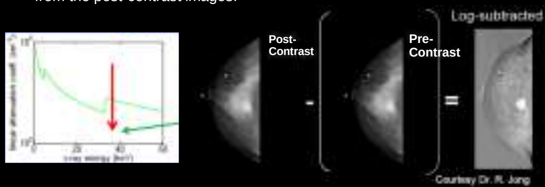
Contrast-enhanced images clearly localize the lesion

CC @ 2 min MLO @ 4 min

Images courtesy of Mikawa Breast Center, Mikawa, Japan and GE Healthcare

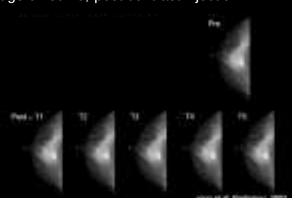
CEDM - Temporal Subtraction

- This technique produces high-energy mammo images before and after contrast injection.
- To enhance visualization of contrast, the pre-contrast image is subtracted from the post-contrast images.

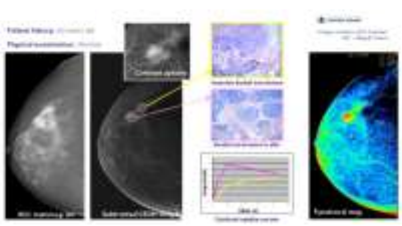


CEDM - Temporal Subtraction

- Temporal subtraction technique offers the possibility to analyze the kinetic curve of enhancement of breast lesions.
- A finite number of sequential images are obtained at a high energy, above the K-edge of Iodine, post contrast injection.



CEDM - Temporal Subtraction



"Contrast enhanced digital mammography (CEDM): From morphological to functional mammography", by S. Muller, etc.

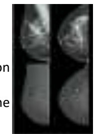
CEDM - Temporal Subtraction

Light breast compression is applied, strong enough to limit motion but limited to avoid reducing the blood flow.

Exam begins with the acquisition of a single mask mammogram. IV contrast injection is then performed and several post-injection images are taken.

Total time: 15 min

Total dose: Similar to a conventional mammo

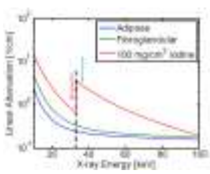


Disadvantages

- Only a single breast can be imaged, patients have to maintain a particular position (usually MLO) for a long period.
- More motion artifacts as breast is under compression when contrast arrives in the blood stream, light breast compression, long acquisition.

CEDM – Dual Energy Subtraction

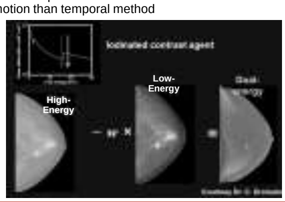
- Dual-energy acquisitions, two images are acquired using distinct low-energy (standard mammo kV and filtration) and high-energy X-ray.
- The differences between X-ray attenuation of iodine and breast tissues at these two energy levels are exploited to suppress the background breast tissue.



"Innovations in Clinical Breast Imaging: Novel Mammography Applications – Contrast Imaging", Martin Y., etc.

CEDM – Dual Energy Subtraction

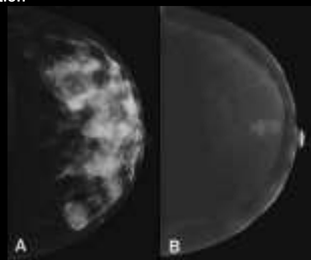
- The procedure takes approximately 10 min and could be followed by either a stereotactic or an US-guided biopsy in the same sitting.
- Dual Energy technique does not provide kinetic information of tumor enhancement but allows the acquisition of multiples views of the same breast or bilateral examination, less sensitive to patient motion than temporal method



CEDM – Dual Energy Subtraction

(a) A benign well-circumscribed lesion shown in in the inner quadrant on FFDM (earlier biopsy proven as fibroadenoma)

(b) On CEDM, no contrast enhancement within fibroadenoma; however, an oblong-shaped enhancing lesion is demonstrated in the retroareolar region, obscured by dense glandular tissue, malignant papillary lesion



"Contrast enhanced dual energy spectral mammogram, an emerging addendum in breast imaging", Br J Radiol. November 2016; 89(1067)

Image Quality Considerations in CEDM

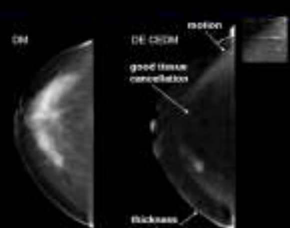
- Background tissue cancellation, haze of image

  Dual Energy mode due to different X-ray spectrum, scatter etc.

  Background uptake fairly common

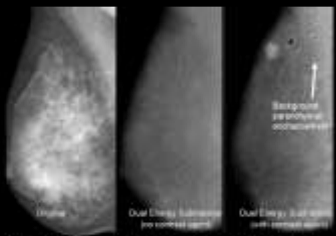
"*Innovations in Clinical Breast Imaging: Novel Mammography Applications – Contrast Imaging*", Martin Y., etc., AAPM 2014

Image Quality Considerations in CEDM



Courtesy Dr. C. Dromain

Image Quality Considerations in CEDM



Fat is avascular – little or no uptake in adipose tissue

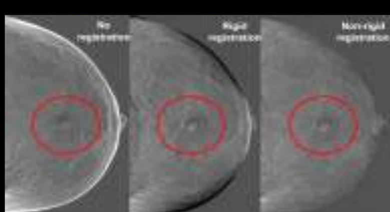
Image Quality Considerations in CEDM

Motion artifacts

- Reduced lesion conspicuity
- Inaccurate iodine quantification
- Strategies for minimized artifacts
  - Breast compression (?)
  - Short exam time
  - Image registration

"Innovations in Clinical Breast Imaging: Novel Mammography Applications – Contrast Imaging", Martin Y., etc., AAPM 2014

Image Quality Considerations in CEDM



"Innovations in Clinical Breast Imaging: Novel Mammography Applications – Contrast Imaging", Martin Y., etc., AAPM 2014

Breast MRI

- A valuable tool to diagnose additional cancer in the same breast in up to 1/3 of patients
- Recommended as a supplemental screening tool to mammo in women considered to be at high risk for developing breast cancer.

Breast MRI

High risk screening - The American Cancer Society recommend yearly screening with mammography plus breast MRI for some women at higher risk of breast cancer including:

- A BRCA1 or BRCA2 mutation
- A strong family history of breast or ovarian cancer
- Radiation treatment to the chest area
- A greater than 20 percent lifetime risk of invasive breast cancer

Breast MRI

- Evaluating in extent of disease in patients recently diagnosed with breast cancer
- Assessing for response to chemotherapy in patients with breast cancer
- Patients with dense breasts
- Evaluate breast implants for rupture

Breast MRI

www.aboutcancer.com

Medical Imaging Technology & Informatics (MITI)
Southern California Permanente Medical Group
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Breast MRI

www.lubbockonline.com

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Southern California Permanente Medical Group
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Breast MRI - Advantage

- Cross-sectional: no overlap of structures
- Ability to include the breast, chest wall and axillary region
- Not influenced by breast tissue density and complexity of fibroglandular pattern
- No compression, no radiation

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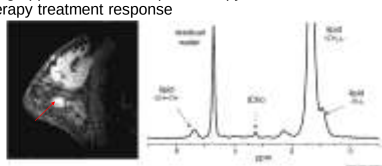
Breast MRI

- Shorter scanning time and higher spatial resolution
  - Parallel Imaging
  - 3 Tesla or higher field strength
- Additional “functional” contrast mechanism
  - Spectroscopy
  - Diffusion

Breast MRI Spectroscopy

- Information on intra-cellular metabolites
- Increased Choline peak in cancer cells
- Showed high sensitivity (83%) and specificity (85%)
- A promising application of MRI spectroscopy is the assessment of chemotherapy treatment response



“Imaging in breast cancer: Magnetic resonance spectroscopy”, Patrick J B, etc., *Breast Cancer Research*, 2005 7:149

Breast MRI - Challenges

- A major disadvantage is that breast MRI screening results in more false positives. If breast MRI were used as a screening tool for everyone, many women would end up having unnecessary biopsies and other tests, not to mention the anxiety and distress.
- More expensive than mammo
- Takes longer time to perform and interpret
- Contraindications: claustrophobia, pacemakers, some aneurysm clips, etc.
- Dedicated breast MRI screening equipment is not widely available

Breast Ultrasound

Ultrasound is the most widely used imaging modality in clinical practice

Advantages:
- Non-ionizing
- Real-time
- Large imaging depth
- Cost-effective
- Portable and widely available

Screening with Conventional Ultrasound

- Whole breast ultrasound
- Labor-intensive with long acquisition times
- Impractical for broad-scale breast cancer
- Lots of user adjustment
  - Focal zones, Transducer frequency, Gain and dynamic range, TGC, on/off harmonics, speckle, compounding
  - Annotates each image capture with clock position, location

Screening Ultrasound

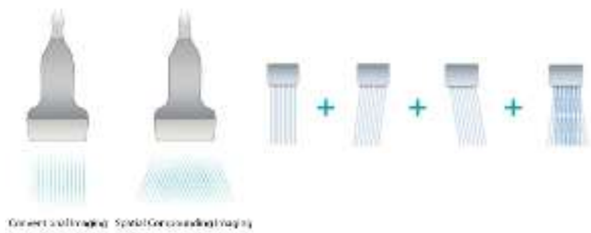
Technologist
- Automated imaging acquisition to minimize the operator dependency
- Standardized procedure for reproducibility and workflow efficiency
- High image quality and good tissue coverage for clinical confidence

Patient
- Quick and comfortable procedure
- No radiation and contrast
- Low cost procedure

Automated breast ultrasound (ABUS)

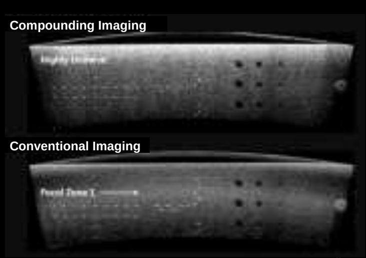
www.itnonline.com

Ultrasound – Coherent Compounding



www.mindray.com

Phantom Image Comparison



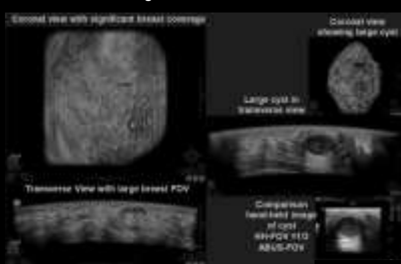
"Automated Breast Ultrasound (ABUS)", by Mallika K.

ABUS Workflow

Technologist:
- Position patient
- Acquire 3D image data in a automated manner from both breasts (multiple view if needed)
- Complete exam and push to reading workstation

Radiologist:
- Review 3D image sets on workstation
- Read entire case in 3-5 minutes

Example ABUS Clinical Images



"Automated Breast Ultrasound (ABUS)", by Mallika K.

Benefits of ABUS

ABUS Clinical Trial Results (Mammography vs. Mammography + ABUS)
- The majority of mammographically occult cancers detected were invasive, small and node negative
- Doubles cancer detection from 3.6 to 7.2 per 1,000 compared with mammo alone in dense breasts and triples detected invasive cancers < 10 mm

Study results compiled from USI 20082002, clinicaltrial.gov NCT00816530 data

Median 10 mm, mean 15.2 mm

"Automated Breast Ultrasound (ABUS)", by Mallika K.

Benefits of ABUS

- ABUS enhances image reproducibility and reduces variability in scanning
- Uncouple image acquisition from interpretation
  radiologist review image
  technologist only positions for auto-scan
- No image adjustments, quick workflow
- Large FOV compared to hand-held ultrasound
- Designed for patient comfort
- Increase sensitivity in dense breast

"Automated Breast Ultrasound (ABUS)", by Mallika K.

Challenges of ABUS

- Lymph node stations not reliably evaluable
- Doppler and elastography not possible
- Imaging artifacts
  - Suboptimal contact
  - Transducer movement due to breathing
  - Skin artifact for superficially located tumors
- New clinical workflow requires an intensive training for both technologist and radiologist (volumetric 3D images)

"Automated Breast Ultrasound (ABUS)", by Mallika K.

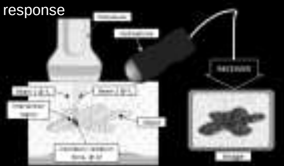
Vibro-acoustography (VA) in Breast Cancer Detection

- VA and ultrasound elastography techniques: use palpation like information
- Tissue stiffness is closely related to pathology of tissue
- A new imaging method that is sensitive to tissue stiffness

"Innovations in Ultrasound and Breast Cancer Imaging", Azra Alizad, Mayo Clinic of Medicine

Vibro-acoustography (VA) in Breast Cancer Detection

- VA and ultrasound elastography uses the force of ultrasound to produce images at low frequencies
- Main step:
  - Vibrate object by "force" of ultrasound
  - Record the sound from the object response
  - Image object by scanning



"Innovations in Ultrasound and Breast Cancer Imaging", Azra Alizad, Mayo Clinic of Medicine

Vibro-acoustography (VA) in Breast Cancer Detection

Breast Fibroadenoma

42 yr old woman with palpable abnormality
Mammography: dense but unremarkable
VA: Round mass with defined border and some lobulations

Alizad et. al., *Breast Cancer Research*, 2012

Vibro-acoustography (VA) in Breast Cancer Detection

Invasive ductal carcinoma

64 yr old woman
Mammography: Minimal architectural distortion, increased density
US: 5x7 mm hypoechoic lesion with posterior shadowing
VA: mass with higher contrast fine spiculations

Alizad et. al., *Breast Cancer Research*, 2012

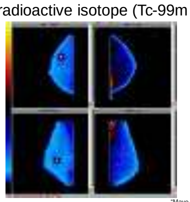
Vibro-acoustography (VA) in Breast Cancer Detection

- VA can be used breast cancer diagnostic tool as a complementary to conventional US
- VA is sensitive to tissue stiffness, detect micro-calcifications, a sensitive tool for early diagnosis and in patients with dense breast where mammography fails

Alizad et. al., *Breast Cancer Research*, 2012

Molecular Breast Imaging

- Instead of looking at structures (anatomy) or angiogenesis, these tests analyze cellular activity
- Cancer cells are more active than normal cells and will therefore absorb more of the injected radioactive isotope (Tc-99m Sestamibi or FDG-18)



"Mayo Clinic Minute: Molecular breast imaging finds breast cancer" by Vivien W

Molecular Breast Imaging

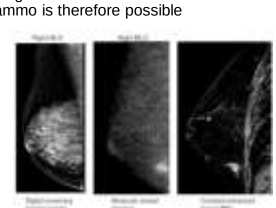
- Involves an injection of a tracer dose of radioactive material
- Breast images are obtained using the same views as mammo. Direct comparison with the mammo is therefore possible

Screening mammo was interpreted negative

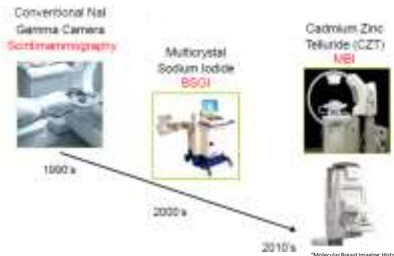
MBI indicates a small lesion in the lower quadrant

Also visible in MRI and confirmed at surgery

(O'Connor, Ex Rev 2009)



Molecular Breast Imaging - Evolution



"Molecular Breast Imaging: History and Recent Developments", by S. Cheenu K

Breast Specific Gamma Imaging (BSGI)

- Dilon Technologies Inc. (Newport News, VA)
- Dilon 6800 system
  - [illegible]
- Dilon 6800 Acella model
  - [illegible]

"Molecular Breast Imaging: History and Recent Developments", by S. Cheenu K

Molecular Breast Imaging

GE Discovery NM 750b

System sensitivity: 550 cpm / µCi
Energy resolution (NEMA): 6.5 %
Field of View: 160 x 240 mm

Highlights
- CZT based gamma camera dedicated to imaging of breast cancer as adjunct to mammography
- High-resolution, direct conversion, **solid-state CZT semiconductor detectors**
- For dense breast, MBI technology outperformed - mammography in early detection and in finding more cancers

"Molecular Breast Imaging: History and Recent Developments", by S. Cheenu K

Molecular Breast Imaging

Detector Configuration	Dual head
Detectors	Cadmium Zinc Telluride (CZT)
Typical Clinical Dose	8 mCi (99mTc-Sestamibi)
Whole-Body Dose	2.4mSv (at 8 mCi)
Intrinsic Spatial Resolution	1.6mm
Energy Resolution: Full-Width Half-Maximum (FWHM)	<5% (at 140 keV)
Sensitivity	91% (with mammo)
Specificity	93%
Collimator	Registered tungsten
Field-of-View	16×20 cm

www.cmr-naviscan.com

Molecular Breast Imaging

Can we decrease the activity? Yes

- Dual-headed MBI system has improved sensitivity
- Matched-hole collimator design
- Wide-energy window for imaging

20-25 mCi (BSGI) -> 8 mCi (MBI)

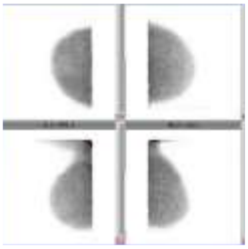
"Molecular Breast Imaging: History and Recent Developments", by S. Cheenu K

MBI – Clinical Workflow

- 8 mCi Tc-99m Sestamibi administered intravenously
- 5 min uptake time
- 2 views of each breast similar to mammo – CC and MLO views
- Planar images in each view for 10 min/view
- Total exam time completed in 1 hour time slot – time for prep, dose injection, uptake, data acquisition, etc.

"Molecular Breast Imaging: History and Recent Developments", by S. Cheenu K

MBI – Typical Normal Study



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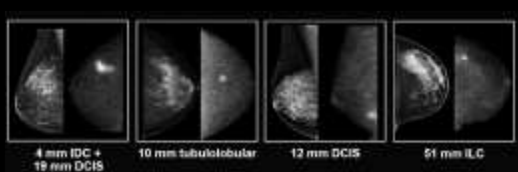
Examples of Mammogram Occult Cancers Detected on MBI



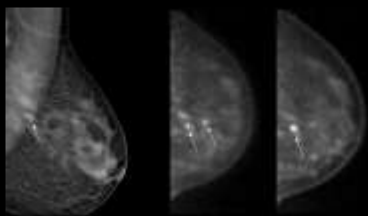
Rhodes et al. *Radiology* 2011.

Dedicated Breast PET (Positron Emission Mammography, PEM)

- Breast PET uses an injection of a radioactive sugar (18-FDG) into the body to detect metabolically active lesions
- Imaging takes 10 minutes per view (total of 40 minutes for a standard 4-view examination) and starts at least one hour after injection of the radiotracer.

womens-imaging.com

Dedicated Breast PET (Positron Emission Mammography, PEM)



Courtesy of Dr. Lorraine Tafra

48 yr old woman with heterogeneously dense breasts. Vague asymmetry is seen on mammo. Biopsy showed early breast cancer. PEM shows more extensive disease than was suspected on the mammo.

MBI Challenges – Radiation Doses

- Radiation dose to patient is proportional to the administered activity
- MBI breast dose is ~0.5 mGy for 8 mCi admin. activity, lower than the dose for a screening mammogram (typically 2-3 mGy for 5 cm thick compressed breast)
- However MBI delivers radiation dose to the whole body
- MBI whole body effective dose ~ 2.4 mSv, compared to Mammo effective dose of 0.5 mSv

	MG	MBI	Background Radiation
Dose/Activity	4 mGy	8 – 30 mCi	[illegible]
Effective dose (mSv)	0.5	2.4 – 6	2.5 / 3 / 4.5
Mortality (per $10^{[illegible]}$)	15-20	144 – 360	810 / 1010 / 1460

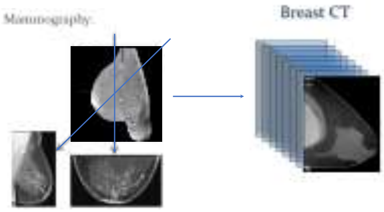
O'Connor, Med Phys [illegible]

MBI Challenges – Variables Affecting Uptake

- Fasting increase uptake by 25%
- Peripheral warming increase uptake by 20%
- Exercise decrease uptake by 35%
- Uptake did not correlate with patient's height, weight or breast thickness

O' Connor et al., JNMT 2015

Dedicated Breast CT (bCT)



"Advances in CBCT for Breast Imaging" by John B

Dedicated Breast CT (bCT)

"Advances in CBCT for Breast Imaging" by John B

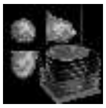
Dedicated Breast CT (bCT)

- UC Davis
- U Mass Worcester
- U Nurnberg
- U Rochester
- MD Anderson
- Duke
- Louisiana State University
- U Naples
- Università di Bologna
- UC Irvine

"Innovations in Clinical Breast Imaging", Kai Yang, AAPM 2014

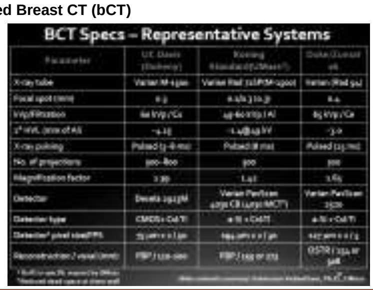
Dedicated Breast CT (bCT)

- Tungsten anode x-ray tube
- Cone beam geometry with flat panel detectors
- 10-20 seconds scanning time
- 300-512 images across the breast in 360 degrees
- FDK or iterative reconstruction
- Prone patient position
- Breast pendant through a hole
- No compression
- Equal radiation dose to 2-view mammography



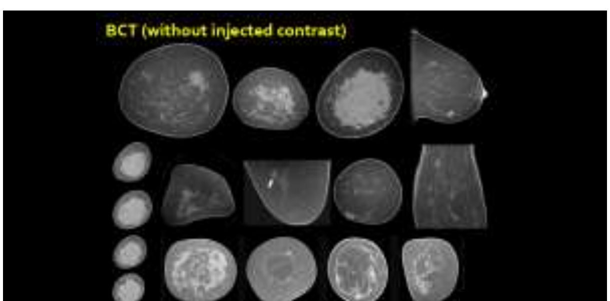
"Innovations in Clinical Breast Imaging", Kai Yang, AAPM 2014

Dedicated Breast CT (bCT)

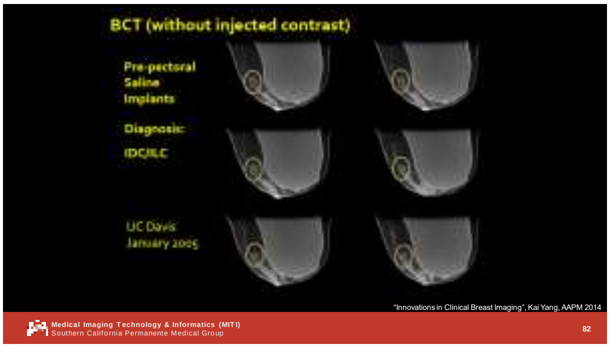


BCT Specs – Representative Systems

[illegible]	[illegible]	[illegible]	[illegible]
X-ray tube	[illegible]	[illegible]	[illegible]
Focal spot (mm)	[illegible]	[illegible]	[illegible]
kVp/Filtration	[illegible]	[illegible]	[illegible]
1st HVL (mm of Al)	[illegible]	[illegible]	[illegible]
X-ray pulsing	[illegible]	[illegible]	[illegible]
No. of projections	[illegible]	[illegible]	[illegible]
Magnification factor	[illegible]	[illegible]	[illegible]
Detector	[illegible]	[illegible]	[illegible]
Detector type	[illegible]	[illegible]	[illegible]
Detector pixel size/FPS	[illegible]	[illegible]	[illegible]
Reconstruction / voxel (mm)	[illegible]	[illegible]	[illegible]



"Innovations in Clinical Breast Imaging", Kai Yang, AAPM 2014


BCT (without injected contrast)
Pre-pectoral
Saline
Implants
Diagnosis:
IDC/ILC
UC Davis
January 2005
"Innovations in Clinical Breast Imaging", Kai Yang, AAPM 2014
Medical Imaging Technology & Informatics (MITI)
Southern California Permanente Medical Group
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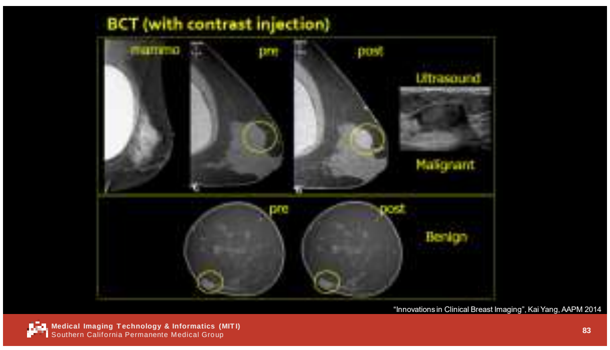
BCT (with contrast injection)
mammo
pre
post
Ultrasound
Malignant
pre
post
Benign
"Innovations in Clinical Breast Imaging", Kai Yang, AAPM 2014
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Southern California Permanente Medical Group
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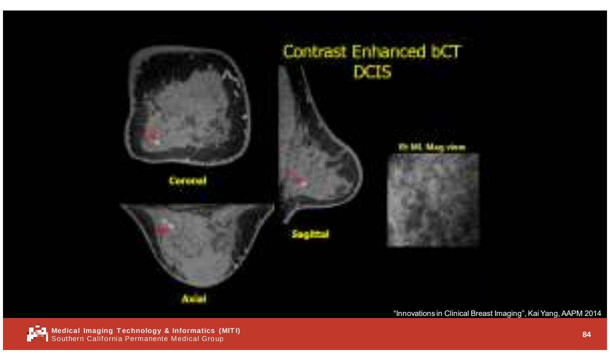
Contrast Enhanced bCT
DCIS
Coronal
Sagittal
Axial
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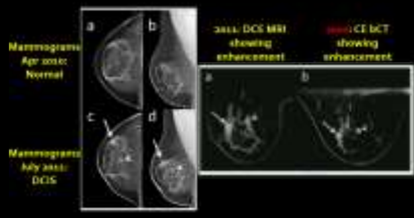

"Innovations in Clinical Breast Imaging", Kai Yang, AAPM 2014

Dedicated Breast CT (bCT) - Benefits

Breast CT (Koning) FDA approved for diagnostic breast imaging Feb 2015

- Full isotropic spatial resolution
- True multi-planar and 3D imaging
- bCT can be performed in a dose efficient manner, equal or less than two-view mammo
- Patient's comfort, no compression
- Almost certainly outperforms mammo for masses

Dedicated Breast CT (bCT) - Challenges

- Improve micro-calcification detection to be equivalent to mammo for bCT screening
- Improve low contrast resolution due to relative high kV (49-80 kV vs. 20-30 kV in mammo)
- Improve Signal-to-Noise (SNR) ratio, noise due to dose limit, potentially low SNR in each projection image
- Improve in chest wall coverage, table top/gantry design

Thank you for your attention!

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