Emerging Technologies in Breast Imaging

June 30, 2016

Jay A. Baker, M.D.
Division of Breast Imaging
New Technologies in Breast Imaging

- **X-ray/Mammography**
  - Full Field Digital Mammography (FFDM)
  - Computer-Aided Detection (CAD)
  - Contrast Enhanced Spectral Mammography
  - Digital Breast Tomosynthesis (DBT)
  - Contrast Enhanced Tomosynthesis
  - Dedicated Breast CT
  - Tissue Harmonic Imaging (THI)
  - Compound Imaging
  - Elastography
  - Extended Field of View Imaging (EFOV)
  - Automated Breast Ultrasound (ABUS)
  - Diffusion Weighted Imaging (DWI)
  - Diffusion Tensor Imaging
  - Gamma Imaging (BSGI/MBI)
  - Positron Emission Mammography (PEM)

- **Ultrasound**
  - Dedicated Breast CT
  - Tissue Harmonic Imaging (THI)
  - Compound Imaging
  - Elastography
  - Extended Field of View Imaging (EFOV)
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  - Diffusion Tensor Imaging
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  - Positron Emission Mammography (PEM)

- **MRI**
  - Dedicated Breast CT
  - Tissue Harmonic Imaging (THI)
  - Compound Imaging
  - Elastography
  - Extended Field of View Imaging (EFOV)
  - Automated Breast Ultrasound (ABUS)
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  - Diffusion Tensor Imaging
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- **Nuclear Medicine**
  - Dedicated Breast CT
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  - Compound Imaging
  - Elastography
  - Extended Field of View Imaging (EFOV)
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- **Other**
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  - Gamma Imaging (BSGI/MBI)
  - Positron Emission Mammography (PEM)
  - Radioactive Seed Localization
  - Optical Imaging

- Ultrasound

- MRI

- Nuclear Medicine

- Other
Lecture Outline

- Contrast Enhanced Mammography
- Gamma Imaging
- Radionuclide seed localization

(courtesy of Dr. Andrew Maidment)
Lecture Outline

- Contrast Enhanced Mammography
- Gamma Imaging
- Radionuclide seed localization
Contrast Enhanced Digital Mammography

- CEDM
- General approach:
  - modified digital mammography system
  - iodinated contrast material
Contrast Enhanced Digital Mammography

- CEDM
- General approach:
  - modified digital mammography system
  - iodinated contrast material
  - two images
  - subtract one image from another
  - iodine-only image

\[ + \text{Iodine} - \text{Iodine} = \text{Sub} \]
Contrast Enhanced Digital Mammography

Modifications
- 45 – 49 kVp
- copper filter
- rapid filter change

k-edge of iodine
Contrast Enhanced Digital Mammography
Contrast Enhanced Digital Mammography

- Temporal Subtraction
- Dual Energy
Temporal Subtraction

- Before & After inject contrast
- position patient and light compress
- baseline image (mask) at 45 – 49 kVp
- inject iodine contrast
  - 1.5 ml/kg @ 3 ml/sec
- repeat images q1 minute over 3-5 min
- subtract mask from subsequent images
- all images high energy: 45 – 49 kVp
Temporal Subtraction

post

pre-con (mask)

subtract
Temporal Subtraction

**Advantages**
- high energy = low dose
- kinetic curves (MRI)
- low cost vs MRI

**Disadvantages**
- long exam time
- motion misregistration
- one projection only (can’t move)
- kinetics not robust
  - compressed breast
  - longer time to inject
  - miss 90-120sec window
Contrast Enhanced Digital Mammography

- Temporal Subtraction
- Dual Energy
Contrast Enhanced Digital Mammography

- Temporal Subtraction
- Dual Energy
Dual Energy Subtraction

- CESM = Contrast Enhanced Spectral Mammography

- dual energy technique
  - both images after contrast
  - one “sees” contrast; other doesn’t
x-ray absorption of iodine at dif energies

- high absorption at high energy (45-49 kVp)
- low absorption at low energy (26-32 kVp)
Dual Energy Subtraction

- x-ray absorption of iodine at different energies
  - high absorption at high energy
  - low absorption at low energy

- inject 1.5 ml/kg contrast @ 3cc/sec

- wait 2 min

- position & compress in MLO; hi/lo \( E \) images

- hi/lo \( E \) images in all 4 projections (5 min)
Dual Energy Subtraction

- Advantages
  - no motion issues
  - shorter compression
  - multiple projections

- Disadvantages
  - Dual Energy Subtraction
Case 1 – 79 yo w palpable mass, left breast standard mammogram

GE Healthcare, Inc
images courtesy of Mikawa Breast Center, Mikawa, Japan
Invasive Ductal Carcinoma
Case 2 – Invasive Ductal Carcinoma

CC @ 2min Low Energy Subtraction

MLO @ 4min Low Energy Subtraction

GE Healthcare, Inc
images courtesy of Mikawa Breast Center, Mikawa, Japan
Case 3 – Invasive Lobular Carcinoma

CC @ 2min  Low Energy  Subtraction

MLO @ 4min  Low Energy  Subtraction

GE Healthcare, Inc
images courtesy of Mikawa Breast Center, Mikawa, Japan
Dual Energy Subtraction

**Advantages**
- no motion issues
- shorter compression
- multiple projections

**Disadvantages**
- dose
Dose
- dual energy $\approx 1.2x$ routine mammo
  - high energy = 0.2x mmg
  - low energy = 1.0 mmg
  - 4 views $\approx 4.8x$ mmg
- temporal subtraction $\approx 0.2x$ mmg
  - pre + 3-5 post images
  - total $\approx 1.0$ mmg
Methods

- prototype dual energy (spectral)
- n=142 lesions (80 malignant)
- compare:
  - mammo alone
  - mammo + US
  - mammo + CESM
### CEDM – Clinical Studies

- Thibault *Eur Radiol* 2011

### Methods
- prototype dual energy (spectral)
- n=142 lesions (80 malignant)

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>ROC</th>
<th>Multifocal lesions detected</th>
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</thead>
<tbody>
<tr>
<td>mammo</td>
<td>0.78</td>
<td>0.50</td>
<td>0.75</td>
<td>16</td>
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<tr>
<td>mammo + US</td>
<td>0.94</td>
<td>0.39</td>
<td>0.85</td>
<td>15</td>
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<tr>
<td>mammo + CEDM</td>
<td>0.93*</td>
<td>0.56*</td>
<td>0.88*</td>
<td>23</td>
</tr>
</tbody>
</table>
CEDM – Clinical Studies

- Jochelson MS (MSK) *Radiology* 2013

**Methods**
- prototype dual energy (spectral)
- n=52 women; bx-proven malignancy
- MRI vs dual energy CESM
Jochelson MS (MSK) *Radiology* 2013

### Methods
- prototype dual energy (spectral)
- n=52 women; bx-proven malignancy

<table>
<thead>
<tr>
<th></th>
<th>mammo</th>
<th>MRI</th>
<th>CESM</th>
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</thead>
<tbody>
<tr>
<td>Index lesion (n=52)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Multifocal/centric (n=25)</td>
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<td></td>
<td></td>
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<tr>
<td>Contralateral CA (n=1)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>False positives</td>
<td></td>
<td></td>
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</table>
Pros/Cons CEDM

**Advantages**
- cost
- accessibility
- ↓ false positives

**Disadvantages**
- contrast reaction
- contrast nephropathy
- patient acceptibility
- lack of image-guided bx
CEDM – State of the Art

- Imaging system
  - Health Canada and FDA-approved (GE)
  - Software upgrade to existing units (2010)
  - Generator already capable of 45 – 49 kVp
  - Copper filter

- Billing
  - HCPCS G0204 – Bilat digit mammo
  - CPT 96374 – Diagnostic injection
  - Contrast material
Lecture Outline

- Contrast Enhanced Mammography
- *Gamma Imaging*
- Radionuclide seed localization
In the beginning . . .

1990

Cardiolite

- Tc-99m sestamibi (20 mCi)
- (2-methoxy isobutyl isonitrile)
- cardiac perfusion
In the beginning . . .

- **1990**
- **Cardiolite**
  - Tc-99m sestamibi (20 mCi)
  - (2-methoxy isobutyl isonitrile)
  - cardiac perfusion
    - heart
    - thyroid
    - submandibular glands
    - liver
  - *breast cancer*
Why does sestamibi concentrate in breast cancer?
Why does sestamibi concentrate in breast cancer?

- unclear
- 90% concentrates in mitochondria
- depends on
  - regional blood flow
  - angiogenesis
  - tissue metabolism
Small Field of View
Gamma Cameras
Dedicated Breast Gamma Cameras

BSGI = Breast Specific Gamma Imaging (analog)
MBI = Molecular Breast Imaging (digital, CZT detector)
Small FOV Camera

- high resolution (<2mm)
- ↓ scatter from liver, heart
- mild compression
- ↓ detector-to-breast
- narrow dead zone at edge
- ↑ visibility medially
- ↑ visibility posteriorly
- same projections as mammo

Courtesy of GE Healthcare
Imaging Technique

- Tc-99m sestamibi
  - dose = 20-30 mCi
  - <20 mCi is off-label
- wait 5-15 min
- 10 min per projection (4 total ≈ 60min)
- light compression
- CC and MLO positions match mammo
invasive ductal carcinoma
Clinical Trials

- retrospective review of BSGI
  - n = 146 women (variety of indications)
  - n = 167 lesions (83 malignant)
  - 30 mCi Tc-99m-sestamibi (CC and MLO)

### Results

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
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<tbody>
<tr>
<td>BSGI</td>
<td></td>
<td></td>
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MBI Screening

Rhodes DJ. *Radiology* 258, 2010 (Mayo)

- MBI for screening
  - n=936 women
  - hetero or extremely dense tissue
MBI Screening

Rhodes DJ. *Radiology* 258, 2010 (Mayo)

- MBI for screening
  - n=936 women
  - hetero or extremely dense tissue
  - moderate-high risk
  - 20 mCi Tc-99m sestamibi

**Risk Factors**

- BRCA1 or BRCA2
- Lifetime risk ≥ 20%
- 5-yr risk ≥ 1.6-2.5%
- Mantel or axilla radiation
- Personal hx of breast CA
- Hx of ADH, ALH, LCIS, etc
- Family Hx of breast cancer
MBI Screening

Rhodes DJ. *Radiology* 258, 2010 (Mayo)

- MBI for screening
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- Results

<table>
<thead>
<tr>
<th>Cancers</th>
<th>Mammo</th>
<th>MBI</th>
<th>Both</th>
<th>Neither</th>
<th>TOTAL</th>
</tr>
</thead>
</table>

-
MBI Screening

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Results

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<tr>
<th></th>
<th>Mammo</th>
<th>MBI</th>
<th>Both</th>
</tr>
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<tbody>
<tr>
<td>CA/1000</td>
<td></td>
<td></td>
<td></td>
</tr>
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</table>
High risk screening, Normal mammogram

Bx = 5mm invasive ductal CA
Gamma Imaging Limitations

- false positives
- NPV < 98% (ie., cannot rule-out cancer)
- availability
- dose
  - FDA = 20-30 mCi
  - req’d = 2-4 mCi

(courtesy of R. Brem, GWU)
Low Dose MBI Screening

Rhodes DJ. *AJR* 204, 2015 (Mayo)

- MBI for screening
  - n=1585 women
  - hetero or extremely dense tissue
  - improved collimator; wider energy window
  - 8 mCi Tc-99m sestamibi

- Results

<table>
<thead>
<tr>
<th></th>
<th>Mammo</th>
<th>MMG/MBI</th>
</tr>
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<tbody>
<tr>
<td>CA/1000</td>
<td></td>
<td></td>
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Lecture Outline

- Contrast Enhanced Mammography
- Gamma Imaging
- *Radionuclide seed localization*
Disclosure

Off label usage:

• Breast localization with an I-125 radioactive seed is off label use of this FDA-approved product.
Traditional Wire Localization

- Wire placed using mammo or ultrasound guidance
- Wire skewers lesion
- Surgeon uses wire as roadmap to lesion
Traditional Wire Localization

- **Pros**
  - easy placement
  - accurate excision
  - standard-of-care

- **Cons**
  - uncomfortable procedure
  - wire in place
  - lengthens day for patient
  - can’t be first case for O.R.
  - limits surgical approach
  - wire kinks send surgeon in wrong direction
  - localization must be done in same facility as surgery
Radioactive Seed Localization

- I-125 seed, sealed titanium source
- Prostate brachytherapy seed but lower dose
- Seed placed using mammo or ultrasound guidance
- Seed placed within the lesion and/or near biopsy marking clip
- Surgeon uses handheld gamma probe to detect seed and dissect down to seed
Accurancy


- 1000 RSL procedures
- 97% negative margin on 1st excision
- 9% re-excision for close margin

- >300 cases: half RSL / half wire loc

<table>
<thead>
<tr>
<th></th>
<th>WIRE LOC</th>
<th>SEED LOC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive Margins</td>
<td></td>
<td>p=ns</td>
</tr>
<tr>
<td>Operative Time</td>
<td></td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Surgeon Preference</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient Pain</td>
<td></td>
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Radioactive Seed Localization

Pros
- Easy, comfortable procedure
- No wire in place
- Done 1-5 days before O.R.
- Shortens day for patient
- Any surgical approach
- Can be first case of day
- Same or better positive margin rate (seed placed at lesion; seeds don’t migrate)
- Seed placement disconnected from O.R. location

Cons
- Uncomfortable procedure
- Radioactivity
- Bracketing is challenging
- Seed cannot be repositioned
- Billing issues for Radiology
- Losing a seed creates substantial problems
Because of it’s benign physical properties, Iodine-125 is not THIS complicated to deal with...
Proper Handling of Seeds

This Way...

...NOT This Way!
Seed Program Challenges

- Start up
  - cooperation:
    - Radiology
    - Surgery
    - Pathology
    - Radiation Safety

- Learning curve

- Administrative oversight

- Reimbursement issues
“Frankly sir, we’re tired of being on the cutting edge of technology.”
Conclusions

- **Contrast Enhanced Mammography**
  - potential alternative to MRI

- **Gamma Imaging (BSGI or MBI)**
  - limited utility for work-ups
  - screening requires dose reduction

- **Radioactive Seed Localization**
  - advantages for patient, surgeon, radiol
  - requires cooperation and oversight
The Future
NEXT EXIT
THANK YOU
Courtesy of GE Medical Systems, Inc.
now near future
CESM – Case 3

Images courtesy of Dr. Mizutani Mikawa Breast Cancer Clinic – Miakawa-anjo, JAPAN
Fig. 2. Same patient as in Fig. 1. Preoperative bilateral contrast enhanced spectral mammography. Post-contrast low-energy (a-b) and combined images (c-d). Contrast uptake is highlighted in both index lesion and anterior focus (arrows). No significant enhancement of breast tissue is seen otherwise. Note similar lesion visibility on CESM and MRI.
History of Breast Imaging

- 1895 – Wilhelm Roentgen discovers the x-ray
- 1913 – Albert Salomon images mast specimens
- 1930 – Stafford Warren invents mammogram
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- 1950’s – Robert Egan, dedicated mammo film
- 1966 – first dedicated mammogram
- 1970s – xeromammography
- 1980s – plain film analog mammography
- 2000 – first digital mammography
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- 2000 – first digital mammography system (GE)
- 2011 – digital breast tomosynthesis (Hologic)
www.santarosa.edu
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What Will It Take?

- Out-side-the-box concepts and engineering
- Compelling empiric data
  - Screening vs Diagnostic vs Extent of Disease
  - Consecutive case series
  - Multi-institutional data
- Convenience (prone, water bath, etc)
- Cost
- Reimbursement
- Biopsy capability (eg., ARIA)
Review emerging technologies

Discuss potential role in patient care

- Problem solving? What is NPV?

Compare claims to empiric data
The Future
NEXT EXIT

Tomosynthesis
Case 4 – Invasive Ductal Carcinoma

SenoBright contrast-enhanced images

The SenoBright images clearly showed the exact location of the contrast-enhanced lesion on both views, with no suspicions of other foci. Biopsy proved the lesion to be invasive ductal carcinoma.
Contrast Enhanced Digital Mammography

**Equipment**

- modified mammo gantry
  - generator/tube: 45-50 kVp
  - fast kV switching: avoid motion (dual sub)
  - copper filter
- power injector
Disclosure

- Siemens Medical Systems – tomosynthesis grant