AAPM Spring Clinical Meeting
Advanced Mammography Applications
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Disclosures
• Research Contract from Hologic
• Hologic Scientific Advisory Board
• Philips Women’s Healthcare Medical Advisory Board

The use of iodinated contrast agent with digital mammography has not been evaluated by the FDA and is an “off-label” use.

Off-label Use
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Non-FDA approved devices
Some devices discussed in this presentation have not been approved by the FDA for clinical use in the United States.

Learning Objectives
• Understand the basic principles of digital breast tomosynthesis
• Understand the clinical strengths and limitations of digital breast tomosynthesis
• Understand the basic principles of contrast enhanced digital mammography
• Understand the clinical strengths and limitations of contrast enhanced digital mammography

Part I - Tomosynthesis

Primer/Refresher: Breast Tomosynthesis
• Mammography is only about 70% sensitive
• One reason cancers are not seen on mammography is that they are obscured by surrounding dense tissue
• Tomosynthesis is a way to separate the cancer from the surrounding dense tissue
Multiple (10-25) digital images taken at different angles are combined to give an image at a single plane.

- Total sweep is typically 15–50 degrees.
- Each image is acquired at low dose so total ~ standard mammogram.

Design Issues

- **Arc size**
  - Wider arc → better z resolution
  - But... increased dose
- **# of images**
  - More images → fewer artifacts
  - But... longer acquisition time, more dose or more noise
- **Stationary vs moving detector**
- **Stop and shoot vs continuous imaging**

Current Tomo Systems - design

- **Hologic** – 15° arc / 15 images / 3.7s
- **GE** – 25° arc / 9 images / 7s
- **Siemens** – 50° arc / 25 images / 25s
- **IMS Giotto** – 40° arc / 13 images / 12s
- **Planmed** – 30° arc / 15 images / 20s
- **Philips** – 11° arc / 21 images / 3-10s

Source: Sechopoulos. A review of breast tomosynthesis. Medical Physics 2013, 40(1)

Current Tomo Systems - Regulatory

- **Hologic** – FDA approved
- **GE** – commercial use outside U.S.
- **Siemens** – commercial use outside U.S.
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Example: Hologic Selenia Dimensions

- Digital Mammography and Tomosynthesis System
- 15 degree tomosynthesis sweep, 15 images, ~5 second tomosynthesis acquisition
- Continuous x-ray tube movement
- 24 x 29 cm detector
- 2D and 3D Imaging under same compression
  - 2D (mammo), 3D (tomo) or Combo modes
Literature Review

Hologic FDA Study
- Multi-reader study with enriched screening case set
- 7% increase in accuracy (area under ROC curve)
- 15-20% increase in sensitivity for invasive cancers


Oslo Tomosynthesis Trial
- 12,631 screening exams in combo mode (2D mammography + tomosynthesis)
- 4 readers – 2 for each arm (mammo alone, mammo+tomo)
- RESULTS:
  - Cancer Detection Rate: 6.1/1000 vs. 8.0/1000
  - 27% increase in cancer detection with combo (p=.001)
  - 40% increase for invasive cancers (p=.001)
  - False Positive Rate (recall rate) before arbitration: 8.0% vs. 6.1%
  - 15% decrease in FP rate with combo mode (p<.001)
  - PPV after arbitration similar for mammography and combo, however
    - 29.1% vs 28.5% (p=.72)


Italian Tomosynthesis Screening Trial
Screening with Tomosynthesis OR Standard Mammography (STORM)
- 7292 screening exams in combo mode (2D mammography + tomosynthesis)
- RESULTS:
  - 39 cancers detected on 2D reading; 59 cancers using 2D + tomo
  - Cancer Detection Rate: 5.3/1000 vs. 8.1/1000
  - False Positive Rate: 4.4% vs 3.5%
  - 17.2% decrease in recalls with 2D + tomo


Cases

Case 1: Invasive Ductal Carcinoma - Mammography
Case 1: Mammo vs Tomo (CC)

Case 1: Mammo vs Tomo (spot CC)

Case 2: Invasive Lobular Carcinoma
Decreased Recalls from Overlap with Tomo

Mamm: callback

Tomo: no callback

Calcifications - DCIS

Tomo only lesion - ? U/S correlate

Path: Radial Scar

Marker placed under U/S

Inp vacuum bx new marker placed

Tomo-only Finding

Upright vacuum-assisted biopsy using tomo is available (and would be good for cases like these)

My experience with screening tomo:

- Year 1 (prevalence year):
  - 3 tomo-only cancers in ~ 2200 exams
  - Better than expected - stopped counting after that
  - All were low grade
  - Also - lots of radial scars
- Year 2 (i.e., year after pt’s 1st tomo):
  - All new cancers have been high grade
  - Some have been tomo-only
My experience with diagnostic tomo:

- All spot compression views are now done in combo mode
- Much more reassuring than standard spots
- Replaces straight lateral view, off-angle views, rolled views, etc.
- Several cases where cancers seemed to spot out on 2D but shown on tomo to be true masses

Radiation and Tomosynthesis

- The radiation dose from the Hologic tomo is about 10% higher than a comparable Hologic 2D image
  - So combo mode is more than double a 2D mammogram
- Key tradeoffs:
  - # of images
    - More images = fewer artifacts
    - More images not as dose efficient (more noise/dose)
  - Tomo acquisitions are basically dose-limited

2D Synthetic View

- Uses the tomosynthesis data to create a view that simulates a 2D mammogram
  - Allows one to see calcification distributions that might be difficult to perceive on tomo slices
- Basically a type of MIP image
- Can be made to simulate a 2D image, or improve on it
- Idea is to eliminate requirement for 2D mammo to be done with tomo (Hologic)
Example (courtesy Hologic): Tomosynthesis Reconstruction Slices (showing one slice)

Example (courtesy Hologic): Synthetic 2D

Example (courtesy Hologic): Spiculated mass lesion side-by-side

Oslo Trial Synthetic View Study

- 24,901 screening exams (continuation of above trial)
- Combo mode; double reading
- Compared 2D + tomo to tomo with syn. view
- Results (cancer detection rate):
  - A little complicated because syn. view algorithm changed in middle of study
  - Before change: 2D + tomo > tomo with syn. View
  - After change: no difference


Breaking News

- AMA approved 3 CPT codes for tomosynthesis last week (3/5/14).
  - Doesn’t mean we will actually get paid extra for doing tomo, however (but it is a first step)

Tomosynthesis - summary

- Currently in routine clinical use
- Shown in clinical settings to give both improved sensitivity and improved specificity compared to 2D mammography
- Can be used as an addition to 2D or with a synthetic view
- Additional systems in FDA approval process
- Payment and use of CAD are issues
Part II - Contrast-Enhanced Digital Mammography

CEDM - Outline
- History
- Technique
- Literature Review / Cases
- Clinical Status

Mammography
- Inexpensive, fast
- But...
  - Only about 75% sensitive
    - ~60% in dense breasts; 90% in fatty breasts

MRI
- Very high sensitivity
- But...
  - Expensive
  - Inconvenient – long, noisy, claustrophobic
  - Limited specificity

Question: What makes MRI so good at showing cancers?
Answer: The contrast agent
- Despite 3-D capability and excellent contrast sensitivity, non-contrast MRI has not been shown to work for cancer detection

To get the best of both mammography and MRI...

Contrast-Enhanced Digital Mammography (CEDM)
- Hypothesis
  - By using intravenous iodinated contrast with digital mammography, occult cancers can be made visible
  - Rationale: Breast cancers have been shown to enhance on MRI and CT

CEDM - Hurdles
- Contrast resolution of digital mammography is far lower than CT and MRI
- Breast compression inhibits blood flow
CEDM – Subtraction Techniques

• Temporal Subtraction: post-contrast - pre-contrast
  • Dual-Energy Subtraction: high-energy - k*low-energy

Temporal Subtraction - Limitations

• Breast must be immobilized during contrast administration
  – Limited to one view of one breast
    • Bilateral exam requires 2nd injection
  – Only light compression can be used
    • Increases motion (misregistration), scatter

Dual-Energy Subtraction - Principle

Dual-Energy Subtraction

• Images are acquired at two X-ray energies after contrast injection
  – Iodine absorbs high-energy beam better than low energy beam
  – Breast tissue absorbs low-energy beam better than high-energy beam
  – In practice, energies straddle the k-edge of iodine
  – Final image is weighted logarithmic subtraction

Dual-Energy Subtraction

• Advantages
  – Image both breasts in multiple projections
  – Can image with full compression
  – Images obtained only seconds apart
    • Minimal misregistration
    • Improved morphology information
• Disadvantage
  – Weighted subtraction is imperfect (magnitude of effect depends on beam quality)
Example: Filtered Spectra on a Mo/Rh Mammo Unit

Original
Dual Energy Subtraction (no contrast agent)
Dual Energy Subtraction (with contrast agent)

Early Dual Energy Papers
  - 26 subjects (13 cancers)
  - All cancers enhanced
  - 25 lesions (14 cancers)
  - All cancers enhanced
  - 120, 110 subjects (80, 148 cancers)
  - CEDM > mammo and mammo+U/S by ROC
- Schmitzberger, et al (Radiology 2011)
  - 80 subjects (9 cancers) with photon counting tomosynthesis

Two-View Film Mammogram
(wire on excisional biopsy scar)

Sagittal Post-contrast MRI
Post-Contrast Dual-Energy Digital Subtraction Mammography

CEDM vs MRI: Recent Literature

- Fallenberg, et al. European Radiology 2013; epub 9/19
  - Bilateral CEDM, MRI, mammo
  - Note: Average rad dose of CEDM sl. < mammo (1.72 vs 1.75 mGy)
  - 80 subjects with new CA at 1 site
  - Single reader of CEDM, clinical read of MRI
  - CEDM > MRI sensitivity for index lesion (100% vs. 97%)
    - 80/80 vs 78/80
  - CEDM correlated best with path in terms of size of lesion
    - MRI and mammo both underestimated size

CEDM vs MRI: Recent Literature (cont.)

  - Bilateral CEDM vs MRI
  - 52 subjects with new cancer
  - CEDM = MRI sensitivity for index lesion (96%)
    - 50/52
  - MRI > CEDM in detection rate for additional foci
    - 22/25 (88%) vs 14/25 (56%)
  - CEDM had fewer false positives than MRI
    - 2 vs 13

Additional CEDM Papers of Note

Clinical Papers:

Physics Papers:

CEDM - Current Clinical Status

- June 2010 – CEDM product introduced in Europe
- October 2011 – CEDM product receives U.S. FDA 510k approval
- Currently – being incorporated into routine practice, esp. outside U.S.
- At least one additional company has attained 510k approval for a CEDM product
What is next?

✓ Compare CEDM to MRI
• Optimize the technique
  – Beam energies (target, filter, kVp)
  – Image processing
  – ???
• Combine CEDM with tomosynthesis

CEDM/CET Research Study

• CEDM and CE Tomosynthesis vs MRI
  – Subjects with newly diagnosed cancers
• CEDM and CET performed in single compression
  – Prototype device allowing dual energy combo-mode imaging (2D and tomo)
  – < 1 sec between LE and HE images
  – Tomo with 22 source images (alt HE and LE)
  – Affected breast only

CEDM / CET Case 1: 65 yo with invasive ductal CA

Case 1 – CC view

Lessons...

• Benign masses that light up on MRI also light up on CEDM (e.g. FAs, LNs)
• Sometimes you see things better on CEDM and other times on CET
Case 2:
53 yo woman with IDCA

Screening mammo:
? architectural distortion
"very low suspicion"
U/S: mass

Case 2: Mammograms

Case 2: MRI

Case 2 - CEDM

Pre-contrast DEl sub
CEDM - MLO
CEDM - CC

Case 2: Low Energy Tomo

Morphology on LE tomosynthesis greatly increases the probability of malignancy
Case 2: Lesson

• Low energy tomo images can add useful information on morphology – changing the assessment of the lesion

CEDM vs MRI

• CEDM
  – Lower cost
  – Easier on patient (noise, claustrophobia)
  – Faster
  – More specific (esp. with tomo)
  – Single exam for high risk screening (shows calcs)
  – Upright stereo biopsy easier than MR biopsy

• MRI
  – Includes all of breast and chest wall
  – Signal to noise for enhancement very good / more sensitive
  – Gad safer than iodinated contrast
  – No radiation

Where will CEDM/CET fit in?

• Possible indications:
  – Cancer Staging
  – High Risk Screening
  – Moderate Risk Screening

• Must compete against MRI, nuc med, unenhanced tomo
  – Cheaper, easier and faster than MRI
  – Faster than Nucs – no systemic radiation
  – Shows lesions that tomo misses

Summary

• CEDM has gone from research to clinical use
  – Cancers reliably enhance with this technique
  – Morphology helps with specificity

• Potential to reduce costs by decreasing need for MRI
• Very early in life cycle → expect improvements in image quality and interpretation
  – Early results indicate MRI is more sensitive, less specific

• Addition of tomo has potential to further improve results
• Continued research is needed…