Contrast-Enhanced Digital Mammography

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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, aka CESM)

• 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
Example: Temporal Subtraction


Courtesy M. Yaffe and R. Jong
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

- 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)
Dual-Energy k-edge Subtraction - Principle

Absorption

33.2 Energy (keV)

I

tissue
Example: Filtered Spectra on a W Mammography Unit
(28 kVp W/Rh ; 45 kVp W/Cu)

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Energy (keV) from 0 to 50 with bins of 5.

- Low Energy line
- High Energy line

Joules per 0.5 keV bin from 0.0005 to 0.0025.

K-edge of Iodine indicated on the graph.
Early Dual Energy Papers

  - 26 subjects (13 cancers)
  - All cancers enhanced

  - 25 lesions (14 cancers)
  - All cancers enhanced
DE CEDM vs Mamma

  - 120, 110 subjects (80, 148 cancers)
  - CEDM > mammo and mammo+U/S by ROC

- Cheung, et al. (Eur Radiol 2014)
  - 89 subjects (72 cancers)
  - CEDM > mammo in both sensitivity (92.7 vs 71.5) and specificity (67.9 vs 51.8)
Two-View Film Mammogram
(wire on excisional biopsy scar)
Lateral … Sagittal Post-contrast MRI … to Medial
Post-Contrast Dual-Energy Digital Subtraction Mammography
CEDM vs MRI: Literature

- Fallenberg, et al. European Radiology 2013; epub 9/19
  - Bilateral CEDM, MRI, mammo
  - 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: 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
Current Research -- CEDM + tomo: 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

Research project funded by Hologic
CEDM/CET Research Study

- Two sites:
  - Rose Breast Center, Denver
    - 30 cases s/p biopsy (all cancers)
  - Kaohsiung Veterans General Hospital, Taiwan
    - 255 cases pre-biopsy (81 cancers)
    - Reader study performed - paper in preparation
CEDM/CET Study Case 1: Unifocal IDCA
Case 1 -- Lessons...

- In some cases, CEDM shows spiculations and general morphology better than MRI.
- With current techniques, no appreciable improvement in morphology depiction with CE Tomo.
- Non-con tomo is best for morphology, esp spiculations.
Case 2: Multifocal IDCA w/ add’l lesions
Case 2 - CC view

Mammo CEDM CET slice

(FA)
Case 2: MRI
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
CEDM /CET Case 3: Invasive Lobular CA

Mammo
CEDM
CE Tomo
MRI MIP
Same case -- CC Views

Mammo
CEDM
CE Tomo
Case 3 -- Lessons...

- CEDM shows lesion extent similar to an MRI MIP
  - More helpful to surgical planning than was the 2D MRI slices (not shown)

- CE Tomo did not add appreciable diagnostic information to the 2-D CEDM
CEDM /CET Case 4: multifocal IDCA

Screening mammo:

? architectural distortion

“very low suspicion”

U/S: mass
Case 4: Mammograms
Case 4: MRI
Case 4: CEDM

Pre-contrast DE sub CEDM - MLO CEDM - CC
Case 4: MRI
Case 4: Low Energy Tomo

Morphology on LE tomosynthesis greatly increases the probability of malignancy.
Case 4: Lessons...

- Low energy tomo images can add useful information on morphology – changing the assessment of the lesion
CEDM – History of Clinical Implementation

- June 2010 – GE CEDM product introduced in Europe (CE mark obtained)
- October 2011 – GE CEDM product receives U.S. FDA 510k approval
- 2012 – Hologic CEDM product receives U.S. FDA 510k approval; also obtains CE mark;
  - 2D CEDM only but can be combined with non-contrast tomo
Dual Energy CEDM Radiation Dose

• Taking dual energy images does not double the radiation dose
  - The high-energy image has less dose than the low-energy image (about 30% - 50% of the dose).
  - The LE beam is equivalent to a standard mammogram, but can be taken at a lower dose if only the subtraction image is important.
  • e.g, you have an unenhanced mammo for seeing calcs
Dual Energy CEDM Radiation Dose (cont.)

• Literature shows variability – These papers both used the GE system:
  – Fallenberg, et al. European Radiology 2013:
    Avg dose of CEDM ~ FFDM (1.72 vs 1.75 mGy)
    Avg dose of CEDM >FFDM by 81% (2.80 vs 1.55 mGy)
M ost of difference is in technique factors for the low energy image
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 M R 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
• Early in life cycle → expect improvements in image quality and interpretation
  - Current results indicate CEDM has similar sensitivity, better specificity
• Addition of tomosynthesis has potential to improve accuracy