Contrast Enhanced Spectral Mammography (CESM) Updates

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Disclosures

- None

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Outline

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- Physics
  Temporal Subtraction
  Dual Energy Subtraction
- CESM Examples
- Current indications/clinical applications
  Dose considerations
- CESM Summary

Background & Motivation

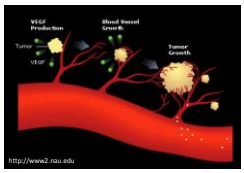
- Mammography (MG) – well established breast imaging technique and the most used for breast cancer detection
  - Contrast based on the differences between atomic numbers & electron densities between normal and malignant tissue
- MG has decreased sensitivity in dense breast tissue and women at high-risk
  - Lesions can be superimposed and hidden under opaque tissue – cancer detection challenging
  - High risk categories need screening at an young age – MRI consistently superior to MG and US and offer a survival benefit

Background & Motivation

Average Risk Population	MG	+3D (Tomosyntesis)	+ US	+ MRI
Cancer Detection Rate (per 1000)	3-5	+1-2	+4	+15

Angiogenesis

- Plays a critical role in the growth and spread of cancer
- Tumors cause the blood supply to form by giving off chemical signals
- Rapid growth of microvasculature that is leaky and poorly differentiates
- Contrast agent will pool in area of unusual blood flow



Angiogenesis & X-ray of the breast

- Contrast-enhanced breast CT
  - Able to differentiate between malignant and benign lesions based on differences in CT numbers

  Chang et al, Am.J. Roentgenol. 1982

- DSA of the breast
  - Showed that benign and malignant lesions could be differentiated based on the strength of enhancement
  - Subtracted images of malignant tumors showed rapid and strong enhancement followed by wash-out, benign tumors showed less or no enhancement

  Ackerman et al. Radiology 1985

  Watt et al, Cancer 1985

  Watt et al. Radiology 1986

Background & Motivation

- Contrast Enhanced Digital Mammography (CEDM)- highlights the iodine uptake in area of unusual blood flow in the breast
- CEDM development started early 2000 following FFDM implementation
  - Currently two commercially available vendors: GE (CESM) and Hologic (CEDM)
- FDA approved for diagnostic breast imaging since 2011

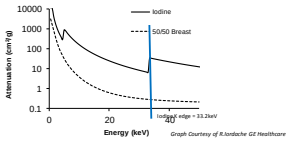
"adjunct following mammography and/or ultrasound exams to localize a known or suspected lesion"

FDA 501(K) Premarket Notification Number: K123873, Hologic, Inc

Physics

- CEDM developmental work done early 2000
  - Modeling and experimental studies to optimize the acquisition and processing of contrast images
  - X-ray energies should be just above the k-edge of iodine 33.2 keV to maximize the iodine contrast associated with areas of unusual flow and leaky vasculature

Skarpathiotakis & Yaffe, Med.Phys. 2002

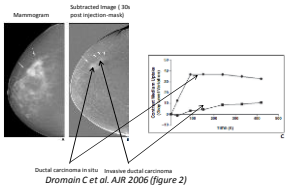


Graph Courtesy of R.Iordache GE Healthcare

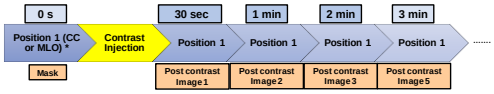
Physics

- Temporal subtraction
  - Similar approach to contrast enhanced MRI
  - Takes a high kV exposure before contrast injection (mask), followed by multiple post-contrast acquisitions
  - Potential for kinetic information
  - Failed to demonstrate clinical relevance
    - Both malignant and benign lesion show progressive uptake of iodine

Jong et al., Radiology, 2003; Diekmann et al., Invest Radiol, 2005; Dromain et al., Am J Roentgenol, 2006; Diekmann et al. Eur J Radiology, 2011;



Dromain C et al. AJR 2006 (figure 2)

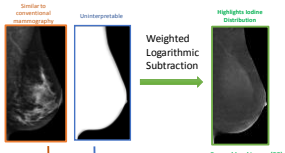


Physics

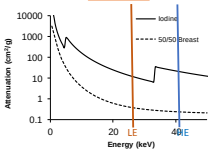
- Dual Energy Technique

Lewin et al., Radiology 2003

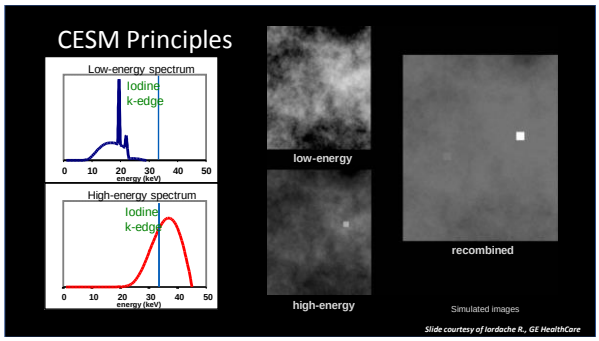
Further developed by GE under CESM acronym



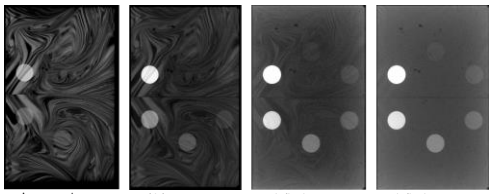
Low Energy Image (LE)
26-33 kV
Mo, Rh or Ag filter
Conventional Mammogram Image



High Energy Image (HE)
45-49 kV
Cu filter
Uninterpretable, but optimized to detect iodine uptake

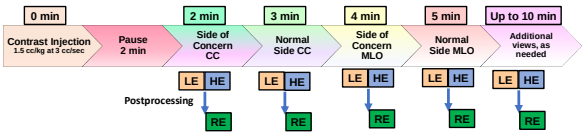


Dual-energy image recombination

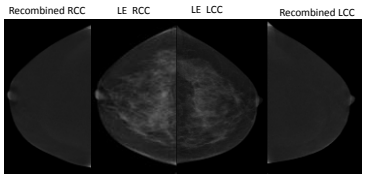


CESM Acquisition

- Contrast injected before the breast is placed in compression
  - 2 minutes delay prior to compression/image acquisition
- No clear consensus exists on the order of the image acquisition
  - Imaging can be performed up to 10 min post contrast
  - Results in 2 images per view, for a total of minimum 8 interpretable images



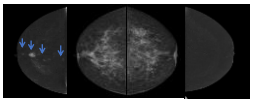
CESM Example 1 –Normal

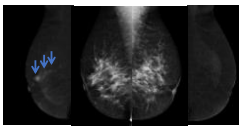


CC views of a normal heterogeneously dense breast

Courtesy of Dr. J. Phillips, BIDMC, Harvard Medical School

CESM Example 2-Abnormal

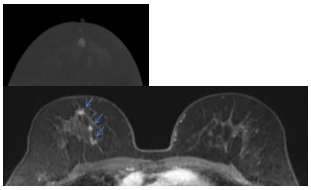




- 57 years old, with heterogenous dense (HD) breast tissue
- Recalled from screening for right retroareolar asymmetry
- Contrast enhancement shows right retroareolar mass with extension posteriorly by 8 cm

Courtesy of Dr. J. Phillips, BIDMC, Harvard Medical School

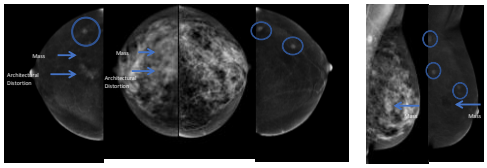
CESM Example 2-Abnormal



- Contrast enhancement shows right retroareolar mass with extension posteriorly by 8 cm
- Malignant breast lesions presence and location confirmed by MRI

Courtesy of Dr. J. Phillips, BIDMC, Harvard Medical School

CESM Example 3-Abnormal



- 49 years old with HD breast tissue with suspicious mass and architectural distortion
- Initially identified masses – no contrast uptake – benign lesions, architectural distortion associated with a malignant lesion, additional malignant lesions identified in the right and left breast
- Example of benefit of contrast enhancement information, both in identifying malignancy and also in identifying benign cysts

Courtesy of Dr. J. Phillips, BIDMC, Harvard Medical School

CESM Current Clinical Indications

- Recall from screening
- Cancer evaluation in the dense breast
- Symptomatic breast evaluation
- Disease extent/intramammary cancer staging
- Evaluation of suspicious microcalcifications

- Backed-up by published research data on CESM performance versus MG, US and MRI

CESM Clinical Indications

BREAST

Contrast-enhanced spectral mammography vs. mammography and MRI – clinical performance in a multi-reader evaluation

Eva M. Fallenberg[1] · Florian F. Schmitzberger[1] · Heba Amer[1] · Barbara Ingold-Heppner[1] · Corinne Balleyguier[2] · Felix Diekmann[3] · Florian Engelken[1] · Rüne M. Mann[4] · Diane M. Renz[4] · Ulrich Bick[1] · Bernd Hamm[1] · Clarisse Dromain[5]

NON DENSE	MG	CESM	MRI
Sensitivity	0.62	0.72	0.73
Specificity	0.94	0.95	0.90

DENSE	MG	CESM	MRI
Sensitivity	0.49	0.71	0.78
Specificity	0.96	0.93	0.86

- "….CESM, alone or in combination with MG, is as accurate as MRI but is superior to MG for lesion detection"

CESM Breast Radiation Dose

- CESM superior breast cancer detection ability comes at increased radiation dose to the breast
  - Dromain et al., Breat Cancer Res, 2012
    - AGD CESM 20% higher than AGD MG
  - Fallenberg et al., Breast Cancer Res Treat, 2014
    - Average AGD of CESM (LE+HE) compared to the average AGD of MG: 6.2% higher
  - Jeukens et al., Investigative Radiology, 2014
    - Average AGD of CESM (LE+HE) compared to the average AGD of MG: 81% higher
  - James et al., AJR, 2017
    - AGD of CESM (LE+HE) compared to AGD of MG: 81%, compared to AGD 3D tomosyntesis 33% higher

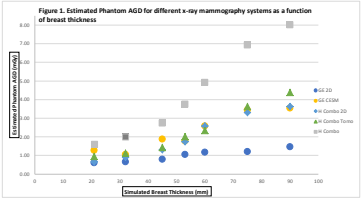
CESM Breast Radiation Dose

- Displayed AGD can not be used to compare dose between vendors
  - Phantom experiment (PMMA) to estimate/calculate AGD using the method of Dance et al.(2000-2016) (the accepted European standard protocol for dosimetry in projection mammography)
    - **AGD = ESAK × g × c × s × t**
      - *ESAK* represents the incident air kerma at the upper surface of the breast or phantom
      - *g* is a conversion factor for incident air kerma to glandular dose for a breast with a glandular fraction by weight of 50%,
      - *c* is the conversion factor for breast thickness, glandularity and half value layers (HVLs),
      - *s* is the conversion factor for x-ray spectrum used
      - *t* is the conversion factor for series of exposures in 3D acquisitions.

G.Mihai et al. RSNA, 2016

CESM Breast Radiation Dose

- Phantom experiment (PMMA) to estimate/calculate AGD using the method of Dance et al.(2000-2016)



- Similar results for dose estimates were observed in patients who underwent all imaging modalities

G.Mihai et al. RSNA, 2016
J. Philips et al. RSNA, 2016

Future CESM applications

- High/moderate risk screening
- Assessing response to neoadjuvant chemotherapy
- Patients with contraindications to breast MRI
- Occult malignancy

- Future development of contrast enhanced guided interventions such as Contrast-Enhanced Digital Breast Tomosyntesis (CE-DBT) with biopsy?
  - Initial clinical experience (temporal subtraction) suggest CE-DBT similar results with CEDM
    Chen et al. Acad Radiol. 2007
  - Increase in radiation dose in CE-DBT as compared with CESM makes is probably unjustified, as breast lesion enhancement in CESM will warrant stereotactic breast lesion biopsy
    Letter to the Editor, European Journal of Radiology 2016, 85; 507-508

CESM Summary

- CESM has become a reliable clinical imaging tool for breast cancer detection
- Combines standard FFDM with iodine injection to produce contrast-enhanced low energy (LE) and high energy (HE) images
- LE image provides details of soft tissue morphology and calcifications similar with standard FFDM
- Recombined image (RE) removes the normal glandular tissue and highlights area of angiography (increased microvascularity and permeability)
- Higher sensitivity than FFDM, especially in dense breasts
- Similar sensitivity and slightly higher specificity than MRI in malignancy detection
- Continued research will fine tune it further…

Thank you!