Contrast Enhanced Spectral Mammography Technology and Clinical Evidence

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Disclosures

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Outline

CESM Application
CESM Technology
Clinical Evidence
Clinical Examples
CESM Application
Mammography is a reliable tool, but has limitations*

- Dense breast tissue can overlap with lesions
- Lesions are not always visible with x-ray
- Interpretation of images can vary among radiologists

  Kolb et al. Radiology 2002; 225:165-175
What about DBT performance in dense breasts?

Breast Cancer Screening Using Tomosynthesis and Digital Mammography in Dense and Nondense Breasts
Rafferty et al. JAMA 2016 Apr 26;315(16):1784-6

452 320 exams: 278 906 DM, 173 414 DM + DBT
2157 cancers diagnosed

“Addition of tomosynthesis to digital mammography for screening was associated with an increase in cancer detection rate and a reduction in recall rate for women with both dense and nondense breast tissue. These combined gains were largest for women with heterogeneously dense breasts, potentially addressing limitations in cancer detection seen with digital mammography alone in this group, but were not significant in women with extremely dense breasts.”
Complementary techniques are therefore required

- Limited availability of other exams can increase time to diagnosis
- Delays can increase patient anxiety
- Other imaging modalities can be cost-prohibitive, take a long time to access, and require long exam times, or have highly operator dependent results
Contrast Enhanced Spectral Mammography

Remove the doubt in suspicious cases

• Helps localize known or suspicious lesions with iodine contrast

Follow up faster

• Quick 10-minute study after an inconclusive mammography plus ultrasound

Stay in context

• Get easily the standard mammography views for a confident diagnosis

Get a confident diagnosis for your patients faster
Contrast Enhanced Spectral Mammography

**Contrast agent** highlights areas of unusual blood flow

**CESM** uses multiple x-ray exposures to reduce background signal, effectively highlighting contrast enhanced areas

Two images per view are *acquired*:

- **Low Energy** image uses standard mammographic techniques and represents tissue density
- **High Energy** image uses higher kVp techniques and spectral filtration
Contrast Enhanced Spectral Mammography

**Contrast agent** highlights areas of unusual blood flow

**CESM** uses multiple x-ray exposures to reduce background signal, effectively highlighting contrast enhanced areas

Two images per view are *provided*:

- **Low Energy** image uses standard mammographic techniques and represents tissue density
- **Recombined image** is a contrast-enhanced image in exactly the same position
Correlated morphologic and functional information

Recombined
Low-Energy
Low-Energy
Recombined

Functional
Morphologic
Morphologic
Functional

AAPM Spring Clinical Meeting 2020 | 7 April 2020
CESM - Remove the doubt

Perform additional test right away
Same equipment, Same staff, Same day

Clinically proven results
Leverage a new problem-solving exam for inconclusive mammography
High sensitivity and high specificity exam for a confident diagnosis

Help reduce patient anxiety
By performing follow-up tests quickly
Good patient experience and low anxiety with CESM*

CESM - Follow up faster

**Quick 10-minute study** for inconclusive mammography plus ultrasound

A standard intravenous iodine injection is done in your radiology department

After a 2 minute wait, you can perform the usual 4 mammographic views in 5 minutes
CESM - Stay in context

**Quick learning curve**
CESM images are acquired in standard views

**Easy correlation**
With standard mammography results

**Easy Communication**
Surgeons and specialists can get what they need in familiar mammography views

The information you need, in the context you know
CESM – Average glandular dose (AGD)

*Mihai et al. Phantom Estimated Dose Comparison between Contrast Enhanced Spectral Mammography (CESM) and Established X-ray Breast Screening Modalities, RSNA 2016

“Our phantom study demonstrates that GE CESM has an estimated AGD that is comparable to other commonly used x-ray breast cancer screening tools.”*
CESM – Adverse effects related to iodinated contrast agent


“Both iodinated& and gadolinium contrast agents are associated with a very low rate of adverse effects. Most adverse effects are mild and can be managed in the radiology department. Transfer for additional treatment or observation is rarely needed“*
CESM – Future screening?

CMIST Study

CMIST Is Coming in Spring 2020!
Evaluates Potential Improvements in Breast Cancer Screening for Women with Dense Breasts

The Contrast Enhanced Mammography Imaging Screening Trial (CMIST) is a planned clinical evaluation designed to determine if using Contrast Enhanced Mammography in breast cancer screening can improve breast cancer detection for women with dense breasts.

The CMIST study will assess whether contrast enhanced spectral mammography (CESM) screening is more accurate in women with dense breasts compared to the combination of digital breast tomosynthesis (DBT) and whole breast ultrasound (WBUS).

CESM combines mammography and vascular-based screening methods that may offer an efficient screening approach in women with dense breasts.

Women with mammographically dense breasts (BI-RADS density categories c and d), ages 40-75, who are at average-to-intermediate risk for breast cancer will be enrolled at select sites using Senographe Pristina™ mammography system, SenoBright HD™ CESM technology, and contrast media from GE Healthcare.

The planned study will be managed by the American College of Radiology Center for Research and Innovation, with support from the Breast Cancer Research Foundation and GE Healthcare.

Please see CMIST schema on other side.

CMIST SCHEMA

YEAR 0
- DBT and WBUS
- CESM (Biopsy BI-RADS 4 & 5 findings as standard of care)

YEAR 1
- DBT and WBUS
- CESM (Biopsy BI-RADS 4 & 5 findings as standard of care)

YEAR 2
Patient follow up questionnaire

Visit https://www.acr.org/Research/Clinical-Research/CMIST or email CMIST@acr.org for more information.
CESM – Biopsy

Biopsy Option

Handle lesions not seen with mammography and ultrasound

Perform in Same room with Same equipment, Same staff
SenoBright™ - in the world

Launched by GE Healthcare
in 2010 in Europe, 2011 in USA, 2013 Canada

400+ SenoBright™ sites in the World

... estimated more than 400,000 CESM exams
CESM Technology
How does it work?

**Objective**
Obtain an iodine content image which demonstrates iodine uptake with the anatomical texture canceled.

**Assumption**
Three compartment model of the breast: fibro-glandular, adipose, and iodine.

**Solution**
Solve a 3 equation system: 2 acquisitions at 2 different X-ray spectra and compressed breast thickness measurement) to obtain the iodine content.
Optimization criteria: iodine visibility

Texture cancellation in recombined image

\[ C_{\text{texture}} = S_{\text{adipose}} - S_{\text{gland}} \]

Iodine contrast in recombined image

\[ C_{\text{iodine}} = S_{\text{iodine}} - S_{\text{gland}} \]

Ratio between residual texture and iodine contrast

\[ R_{\text{iodine}} = \frac{C_{\text{texture}}}{C_{\text{iodine}}} \]
Spectral considerations

High energy and low energy should be on each side of the iodine k-edge to maximize iodine contrast.
Iodine attenuation vs. energy

- Iodine attenuation has a k-edge at 33KeV (dashed line in the above graph)
- Take exposures below and above that edge
- Process to suppress background tissue/highlight contrast uptake
- Recombined image represents iodine

Spectral Shaping of X-rays

- Generator/Tube capable of 49KV
- Fast KV switching to avoid motion artifacts
- Cu high energy filter
Expected results

Low-energy spectrum

High-energy spectrum

Iodine k-edge

Simulated images

low-energy

high-energy

recombined
Dual-energy image recombination

low-energy image (Rh/Rh, 28kV)

high-energy image (Rh/Cu, 44kV)

iodine image recombined with log-subtraction

iodine image recombined with quadratic algorithm*

*S. Puong et al. SPIE, Medical Imaging, San Diego, USA, 17-22 February 2007
Calibration of the recombination algorithm

The calibration ensures that the recombination algorithm is tuned for each individual system

*Simulated data

0.5 mg/cm² corresponds to a lower bound of concentration clinically expected
QC for SenoBright™ HD

Adds specific tests to be executed in addition to those from Senographe Pristina™ QC for both medical physicist and radiologic technologist
Clinical Evidence
CESM Clinical Performance

Comparison to mammography
Comparison to mammography + ultrasound
Comparison to MRI

Many peer-reviewed publications, with 100+ on GE SenoBright™
CESM vs Mammography


152 preoperative patients (114 patients with BC - 101 invasive), 173 findings Diagnosed on MG or CESM. Time interval between MG and CESM < 4 weeks
1 reader, 7-14 days interval btw MG and CESM readings
Truth: histopathology. Per finding analyses. TP threshold: BI-RADS ≥4

“CESM may provide higher sensitivity for breast cancer detection and greater diagnostic accuracy than conventional mammography”

Inclusion criterion was referral after mammography screening due to suspected breast cancer.
CESM vs Mammo for dense breasts


89 women with dense breasts (Bi-RADS class C & D) with 100 lesions (72 malignant) underwent CESM examinations. 4 independent radiologists (2-29 years of experience) blinded on case history assessed CESM low energy 1st, then CESM subtracted images for each case.

Inclusion criterion was density (ACR 3 or 4) and histologically confirmed lesions.

CESM showed superior clinical performance in dense breasts

CESM reduced inter-reader variability

* (# of correct assessments / total # of assessments) x 100
CESM *adjunct to mammography + US*

Dromain et al, BCR 2012
110 women, 148 breast lesions (84 malignant, 64 benign)
6 readers (4 institutions), MG+US -> MG+US+CESM
Truth: histology for 138, follow-up for 12 lesions
Unit of analysis = the finding; TP threshold BI-RADS ≥4

<table>
<thead>
<tr>
<th></th>
<th>MG+US</th>
<th>MG+US+CESM</th>
<th>Difference</th>
<th>95% CI of Δ</th>
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<tbody>
<tr>
<td>ROC AUC (BI-RADS across readers)</td>
<td>0.827</td>
<td>0.871</td>
<td>0.043</td>
<td>(0.001, 0.085)</td>
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<td></td>
<td></td>
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<td></td>
<td><em>p = 0.045</em></td>
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<tr>
<td>Per-Lesion Sensitivity</td>
<td>0.712</td>
<td>0.778</td>
<td>0.065</td>
<td>(0.019, 0.112)</td>
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<td><em>p = 0.006</em></td>
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Inclusion criterion was recall from screening with unresolved findings after mammography and ultrasound.
CESM clinical performance vs MRI


CESM and MRI examinations performed in 102 patients who had suspicious lesions in MG
2 experienced radiologists scored image sets (BI-RADS 1-5) and measured largest dimension of each lesion, independently. BI-RADS ≥4a were considered positive readings
Histopathology available for all lesions detected by the combination CESM+MRI
118 lesions: 81 malignant - 72 invasive (49% IDC)+ 9 in situ

"CESM has the potential to be a valuable diagnostic method that enables accurate detection of malignant breast lesions, has high NPV, and a FPR similar to that of MRI"
Hobbs et al (Royal Pereth Hospital), Jour of Med Im. and Rad. Onc. 59 (2015) 300–305

49 patients with BC underwent both CESM and MRI examinations for staging, with a time interval of min. 24h

Each patient completed a Likert questionnaire rating individual perceptions on
3 criteria for each modality (1=worst, 3=neutral, 5=best),
1 global preference CESM vs. MRI (1=strongly MRI, 2=neutral, 3=strongly CESM)

Wilcoxon sign-ranked and chi-squared tests

"Overall, patients prefer the experience of CESM to CEMRI, adding support for the role of CESM as a possible alternative to CEMRI for breast cancer staging"
Clinical Cases
Case 1

Prior Right Mastectomy - Indication: Palpable area
CESM LE finding: Spiculated mass, Left UOQ
CESM finding: UOQ uptake, satellites
Biopsy Result: Invasive Lobular Carcinoma
Indication: Induration palpation Left UOQ
Fast diagnostic: No FFDM
CESM finding: Left UOQ extensive uptake

Biopsy Result: DCIS Low grade
Case 3  Left Surgical Follow up

59 Yr, Prior surgery left breast. Indication: Nodule palpated in the surgery bed

Fast diagnostic, surgery follow up: No FFDM
CESM finding: No uptake – True Negative
Case 4  
Left Surgical Follow up

53 Yr, Prior Surgery Left breast Indication:  Left  increase density in surgery bed

CESM finding:  No uptake – True Negative
Thank You for your attention