Contrast Enhanced Spectral Mammography Technology and Clinical Evidence

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GE Healthcare

Imagination at work

AAPM SPRING CLINICAL MEETING 2020

Disclosures

Grant Stevens

- Employee, GE Healthcare

Outline

CESM Application

CESM Technology

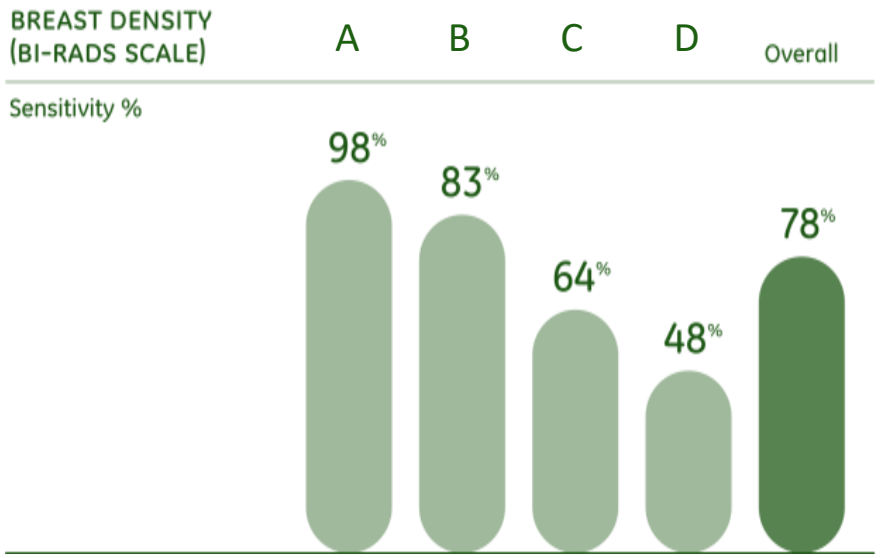
Clinical Evidence

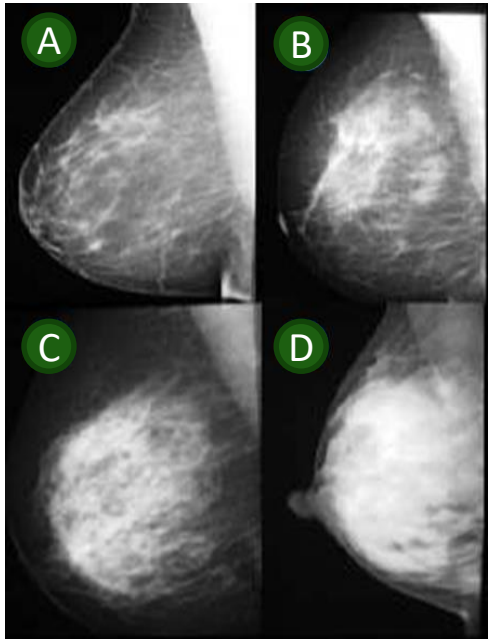
Clinical Examples

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





*Dromain et al. Breast Cancer Research, 2012; 14(3): R94
Kolb et al. *Radiology* 2002; 225:165-175

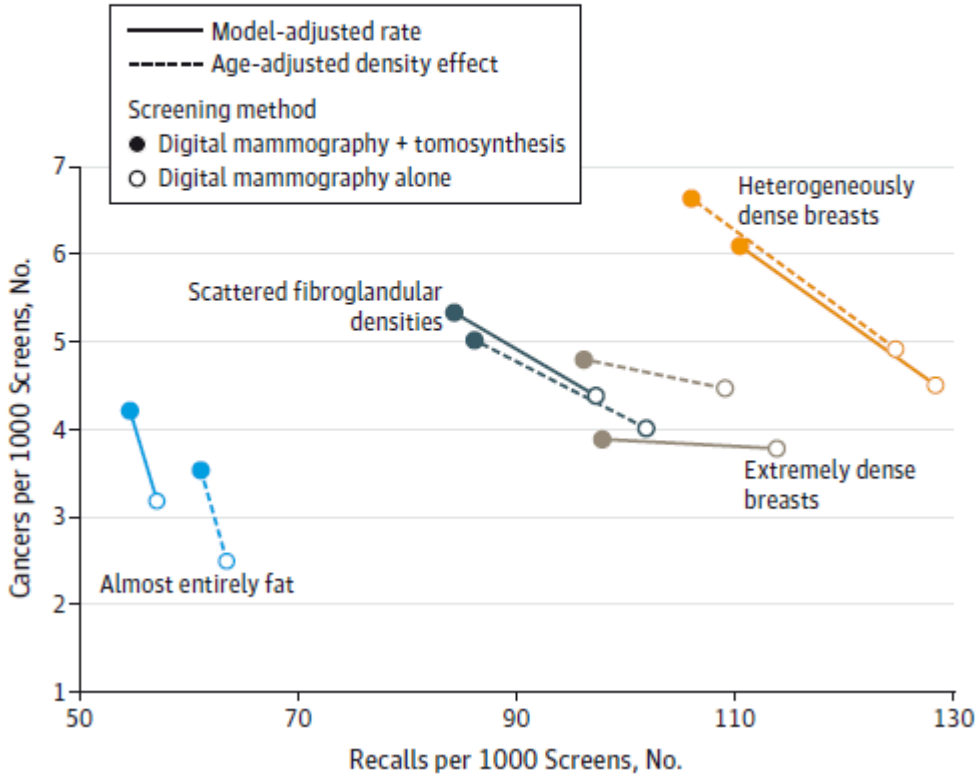
What about DBT performance in dense breasts?

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**."

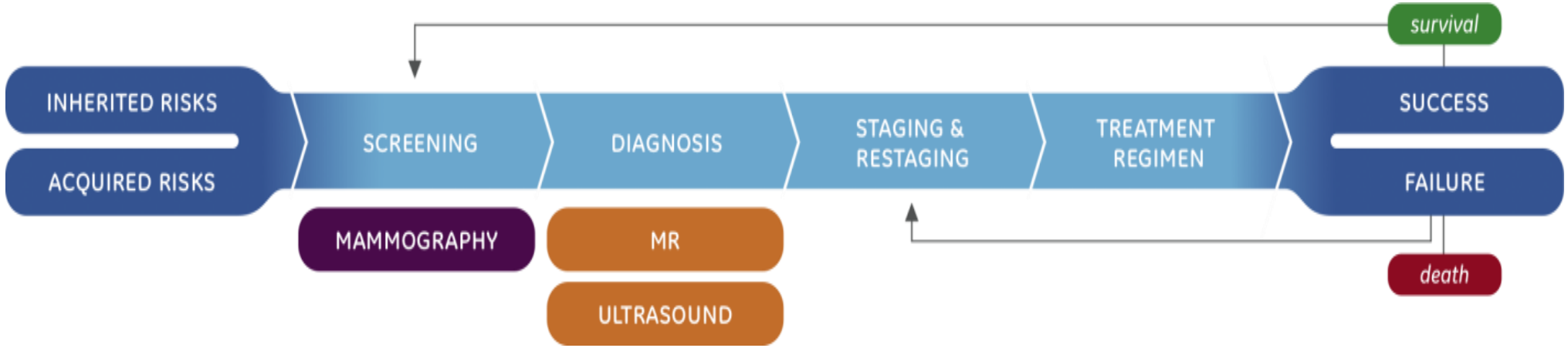
Figure. Combined Change in Recall and Cancer Detection Rates for Digital Mammography vs Digital Mammography Plus Tomosynthesis for Each Breast Density Category



*Rafferty et al. JAMA 2016 Apr 26;315(16):1784-6

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

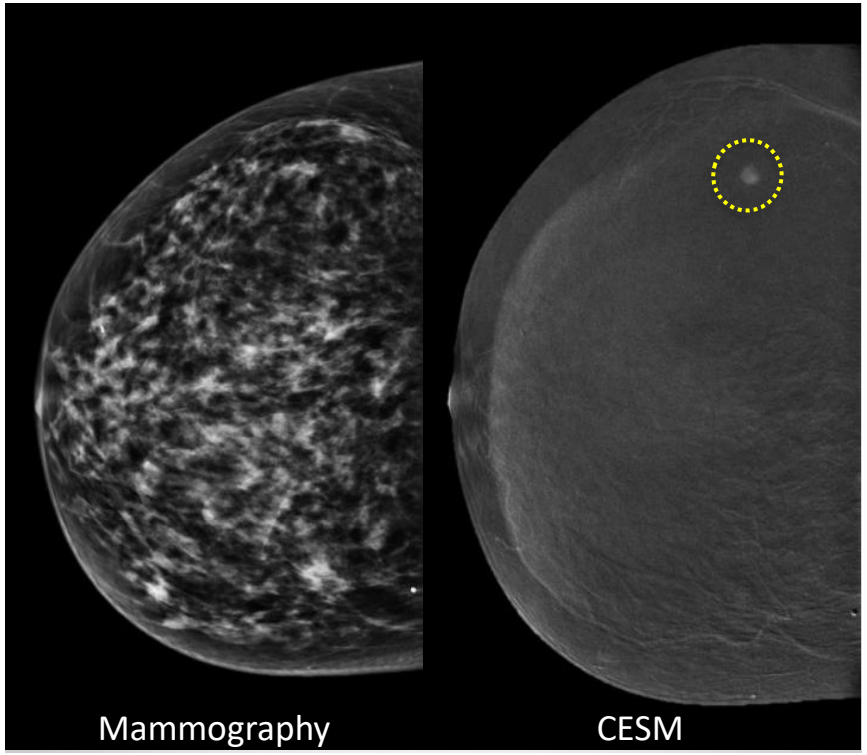
- Helps localize known or suspicious lesions with iodine contrast

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

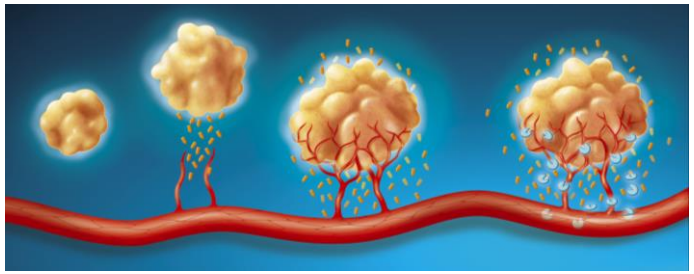


Get a confident diagnosis for your patients faster

Contrast Enhanced Spectral Mammography

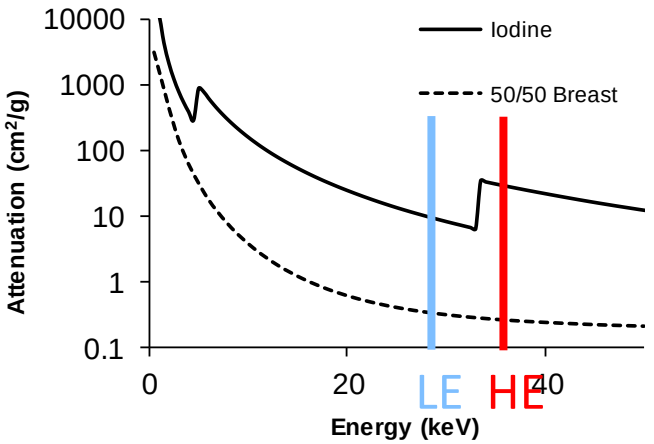
Contrast agent highlights areas of unusual blood flow

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



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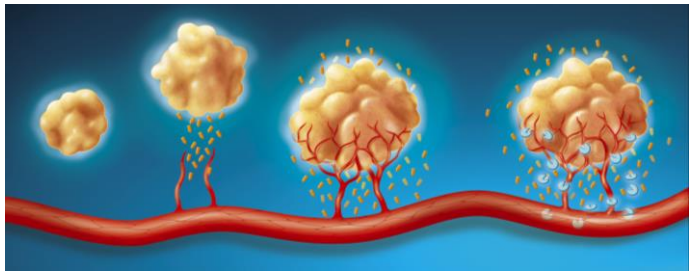
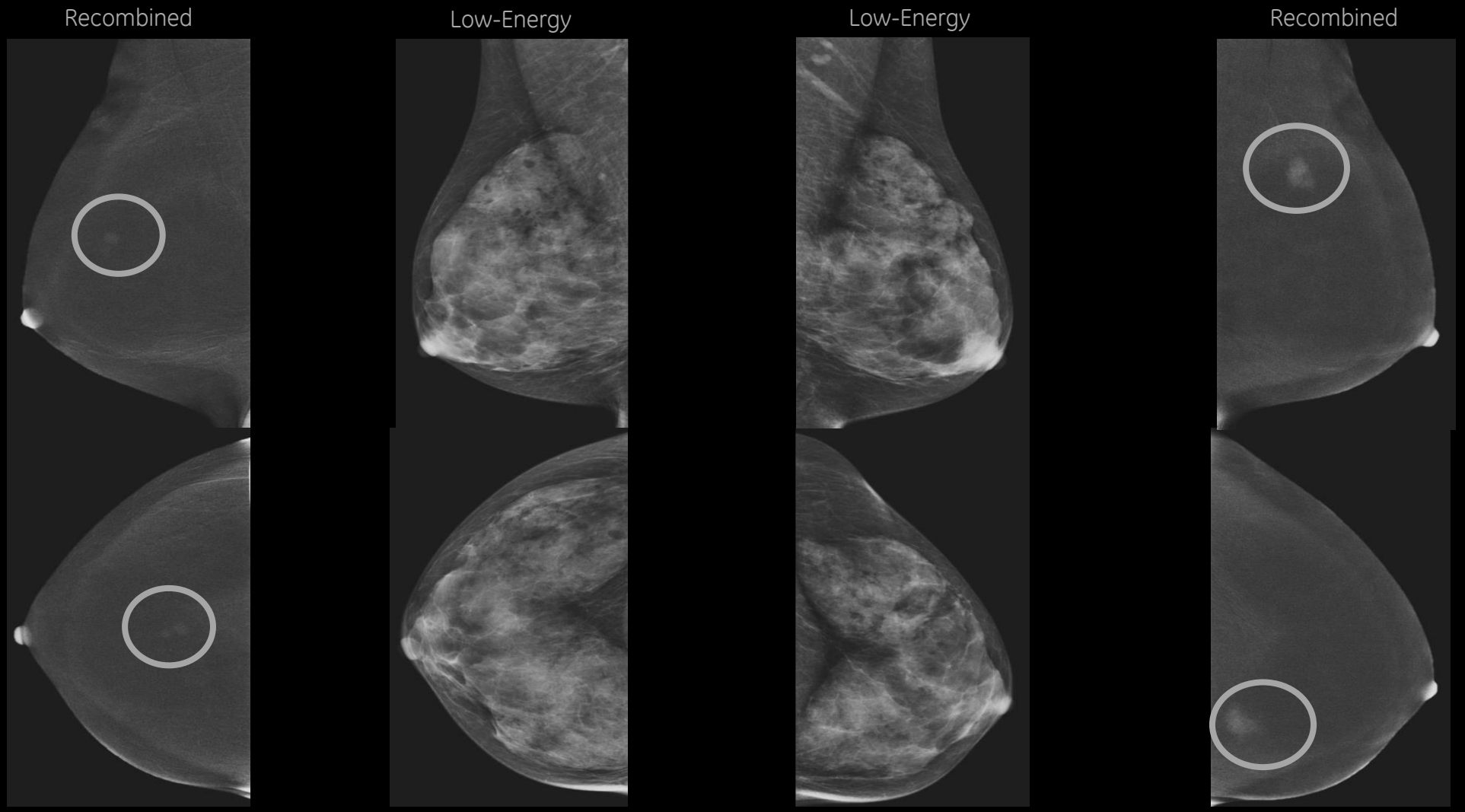


CESM uses multiple x-ray exposures to reduce background signal, effectively highlighting contrast enhanced areas

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



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*

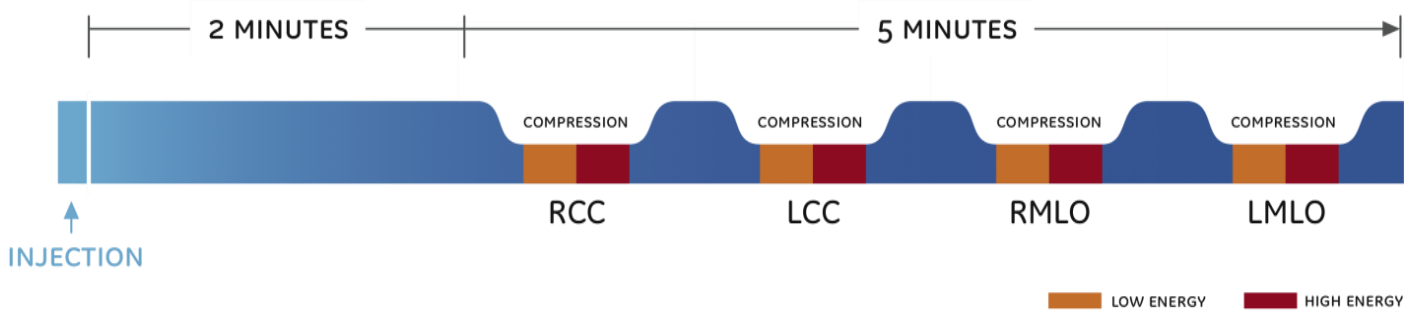
*Hobbs et al. *Journal of Medical Imaging and Radiation Oncology 59 (2015) 300–305*

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

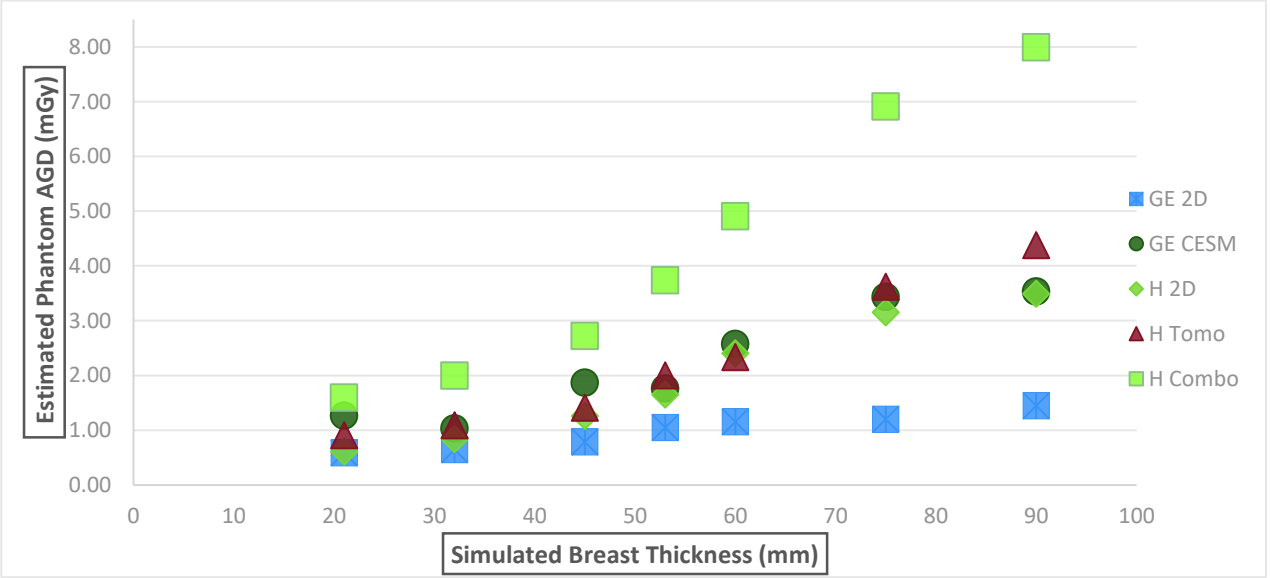
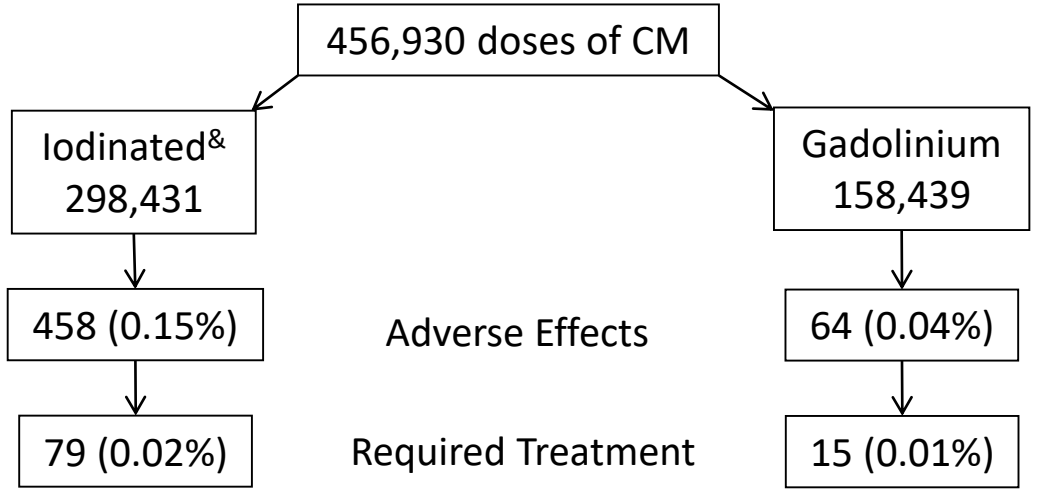


Figure courtesy of Georgeta Mihai, PhD, Beth Israel Deaconess Medical Center – Boston, USA

"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

*Hunt et al. *Frequency and Severity of Adverse Effects of Iodinated and Gadolinium Contrast Materials: Retrospective Review of 456,930 Doses*; AJR 2009; 193:1124–1127

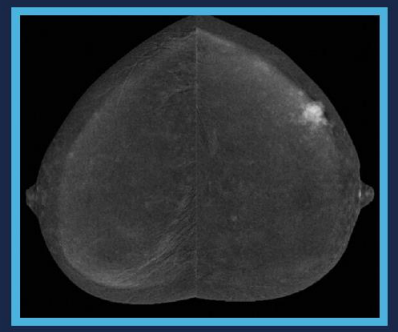


"Both iodinated& and gadolinium contrast agents are associated with a very low rate of adverse effects. Most adverse effects are mild and can be managed in the radiology department. Transfer for additional treatment or observation is rarely needed"*

&low-osmolar

CESM – Future screening?

CMIST Study



CMIST Is Coming in Spring 2020!

Evaluate 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).

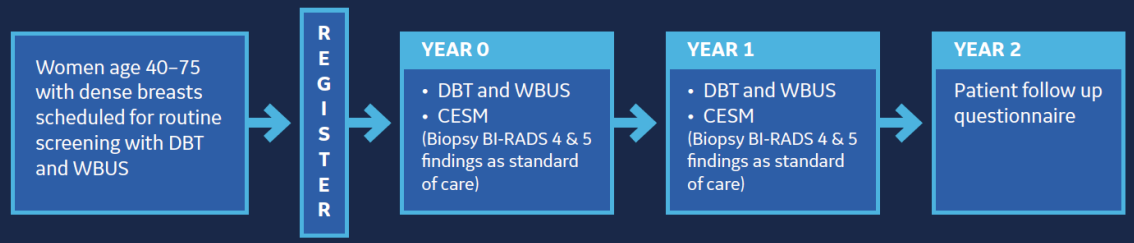
CESM combines mammography and vascular-based screening methods that may offer an efficient screening approach in women with dense breasts.

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



GE Healthcare

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

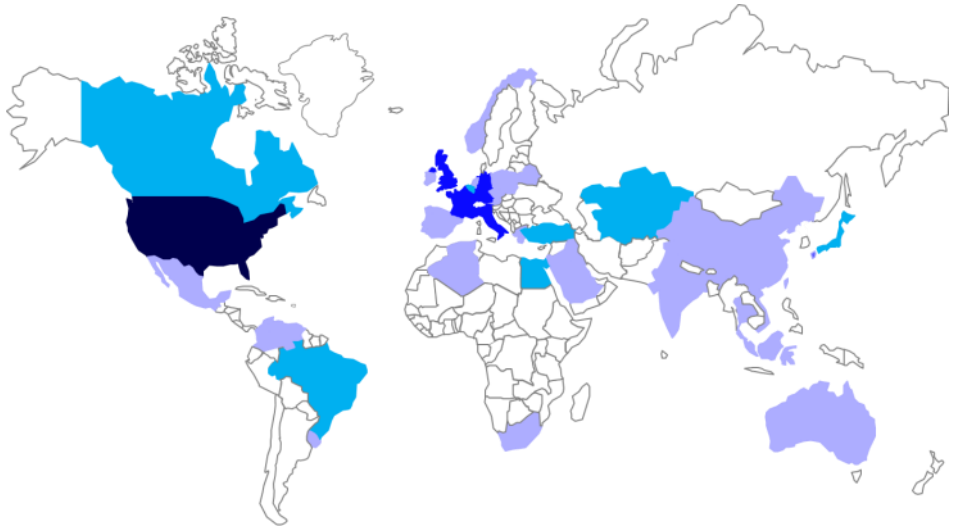
Serena Bright is 510k Pending

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

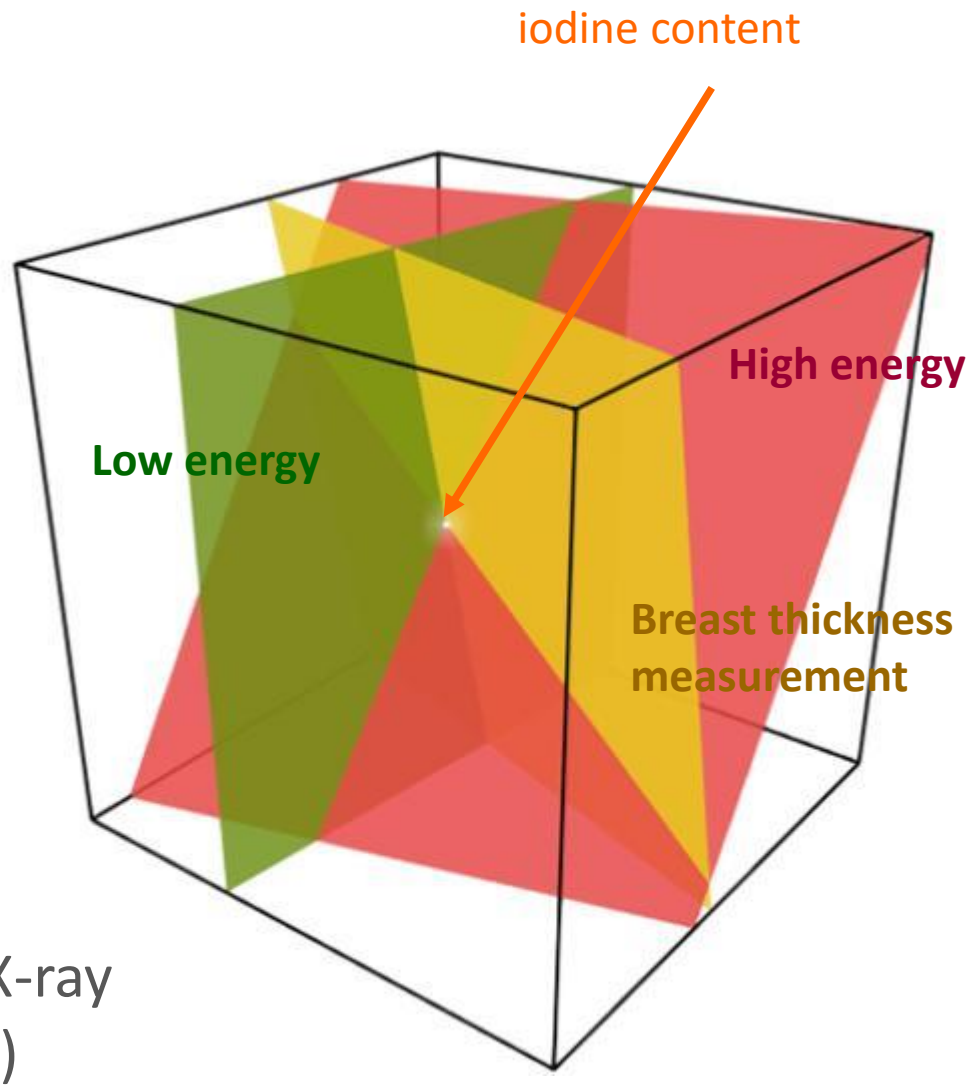
Obtain an iodine content image which demonstrates iodine uptake with the anatomical texture canceled

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

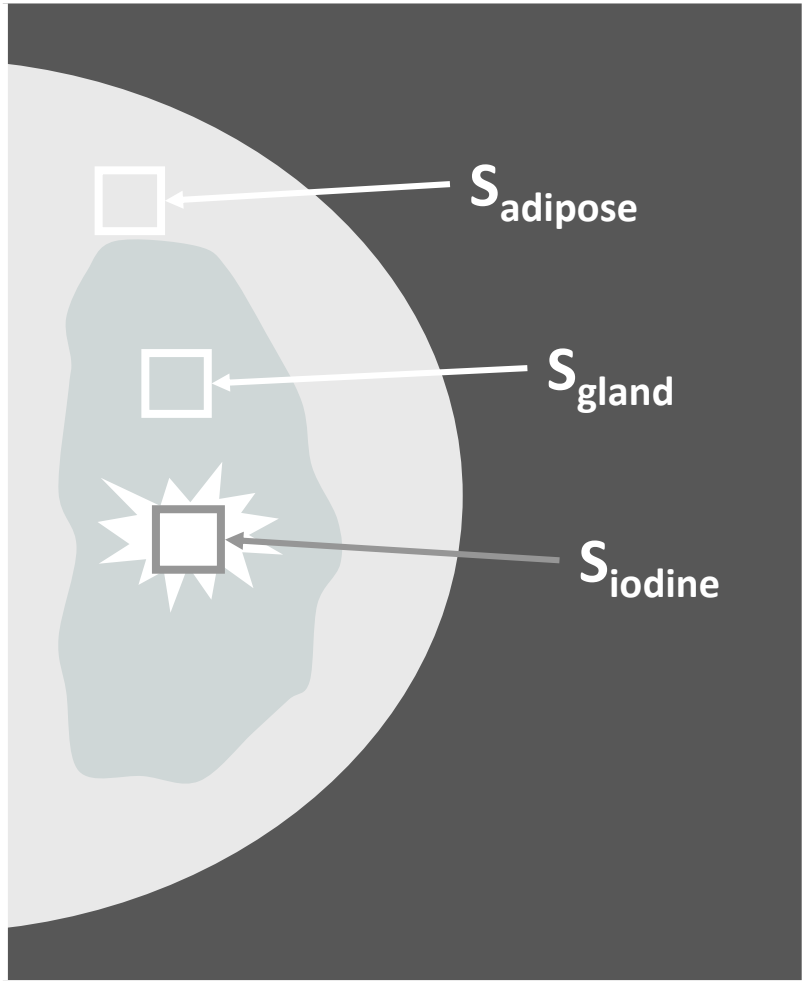
$$C_{texture} = S_{adipose} - S_{gland}$$

Iodine contrast in recombined image

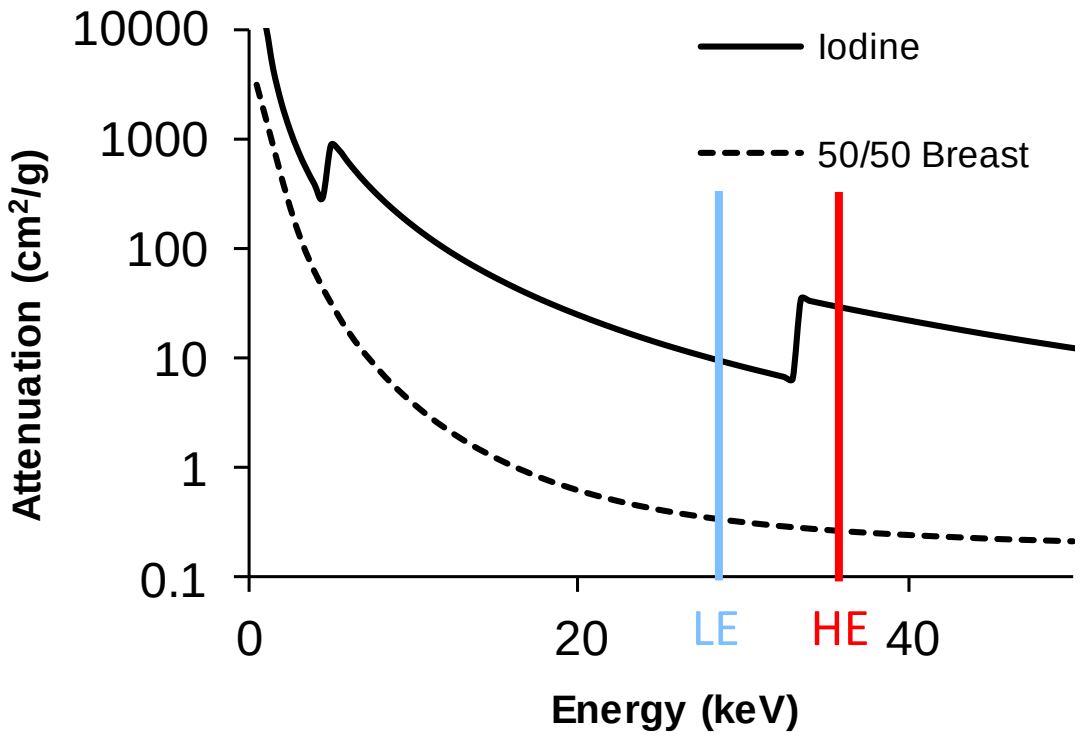
$$C_{iodine} = S_{iodine} - S_{gland}$$

Ratio between residual texture and iodine contrast

$$R_{iodine} = C_{texture} / C_{iodine}$$

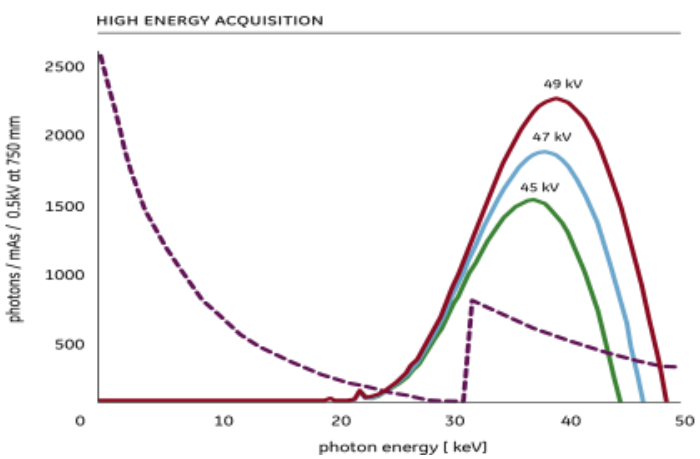


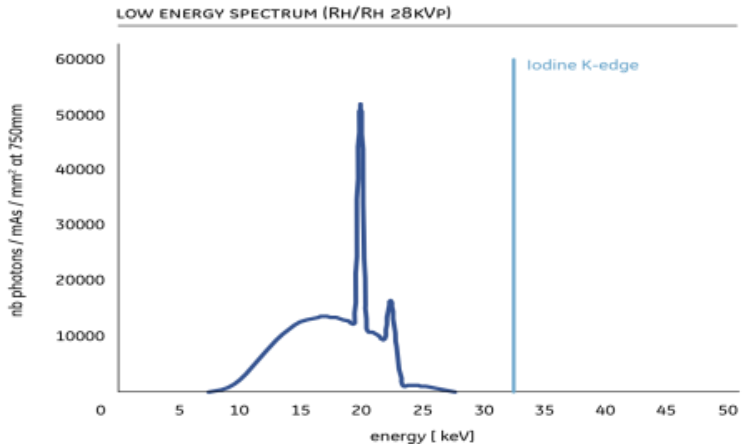
Spectral considerations

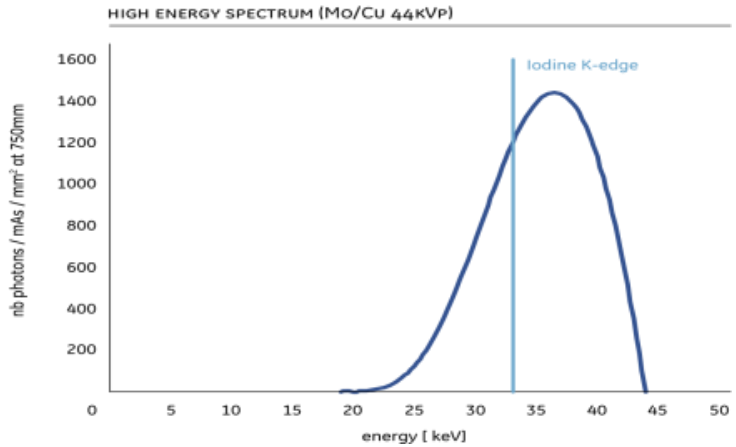


High energy and low energy should be on each side of the iodine k-edge to maximize iodine contrast

Implementation





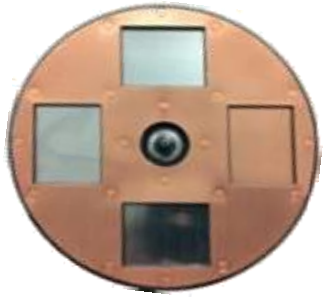


Iodine attenuation vs. energy

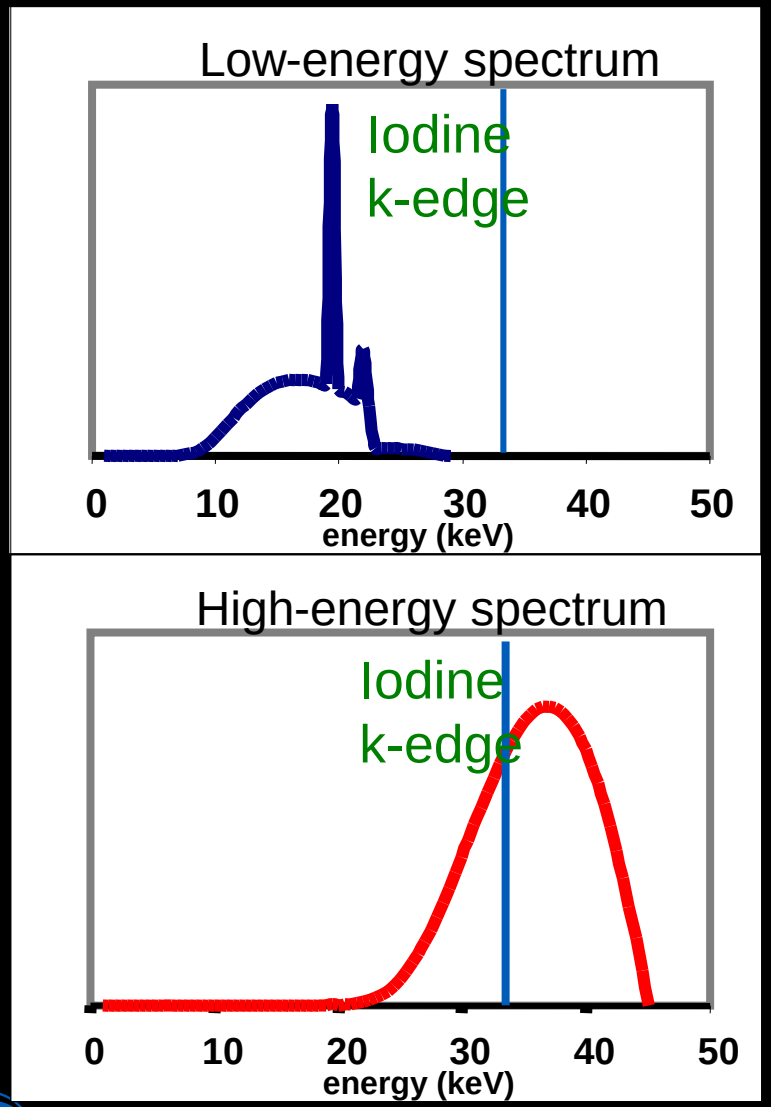
- Iodine attenuation has a k-edge at 33KeV (dashed line in the above graph)
- Take exposures below and above that edge
- Process to suppress background tissue/highlight contrast uptake
- Recombined image represents iodine

Spectral Shaping of X-rays

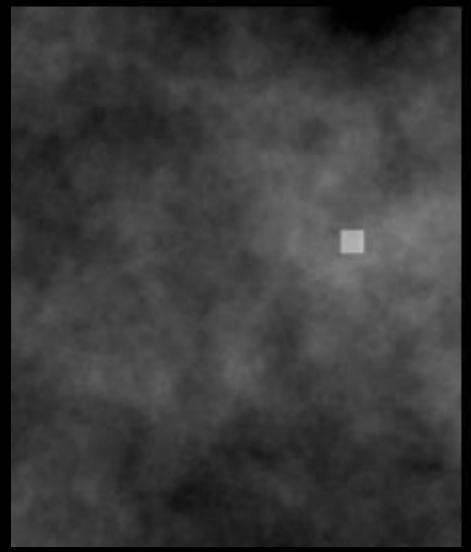
- Generator/Tube capable of 49KV
- Fast KV switching to avoid motion artifacts
- Cu high energy filter



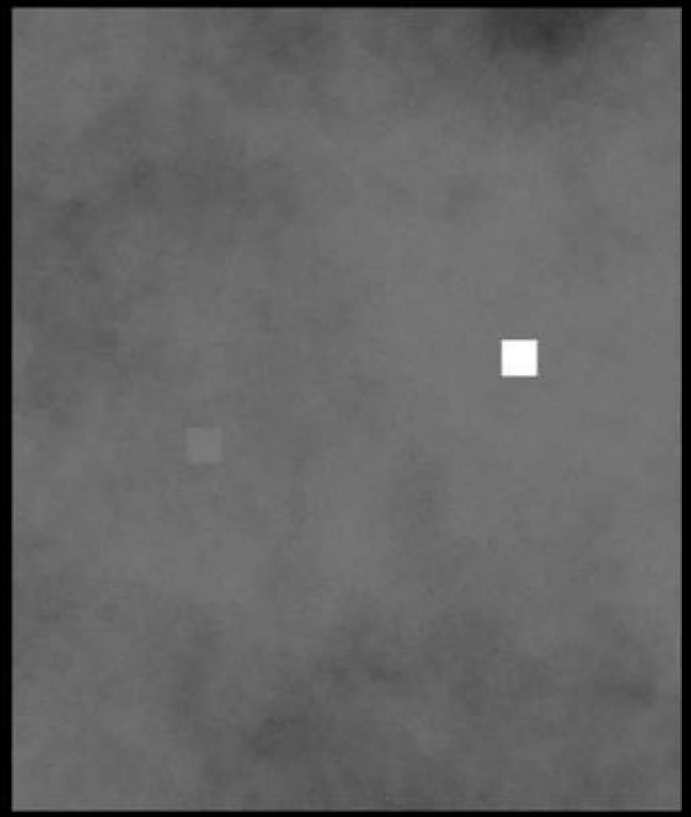
Expected results



low-energy



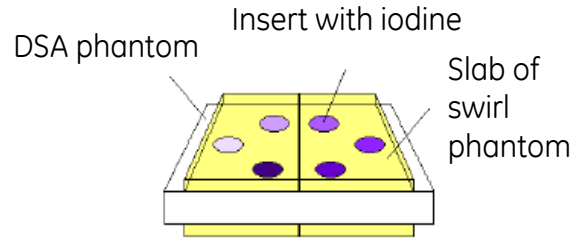
high-energy

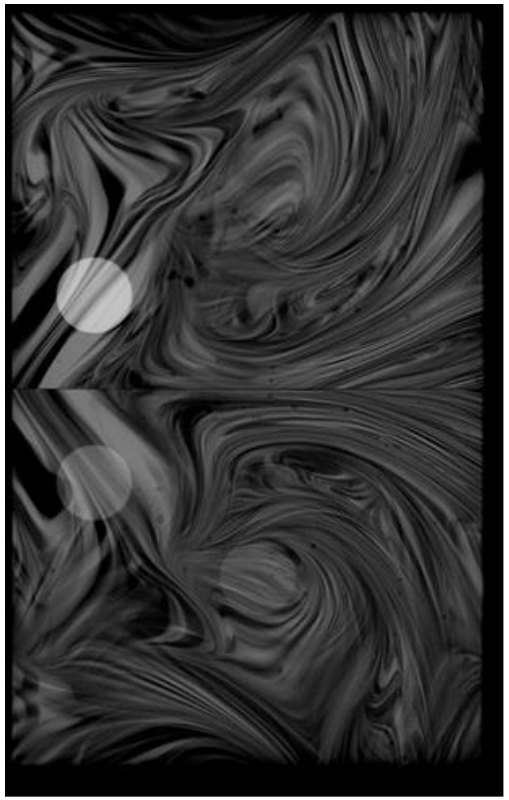


recombined

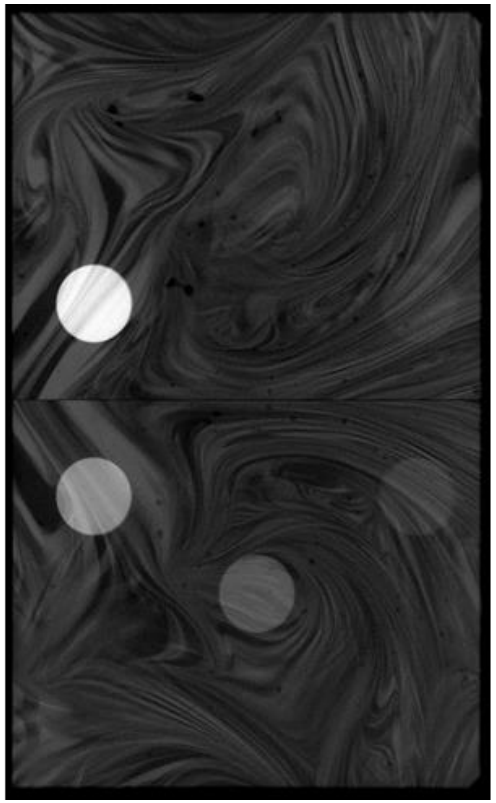
Simulated images

Dual-energy image recombination

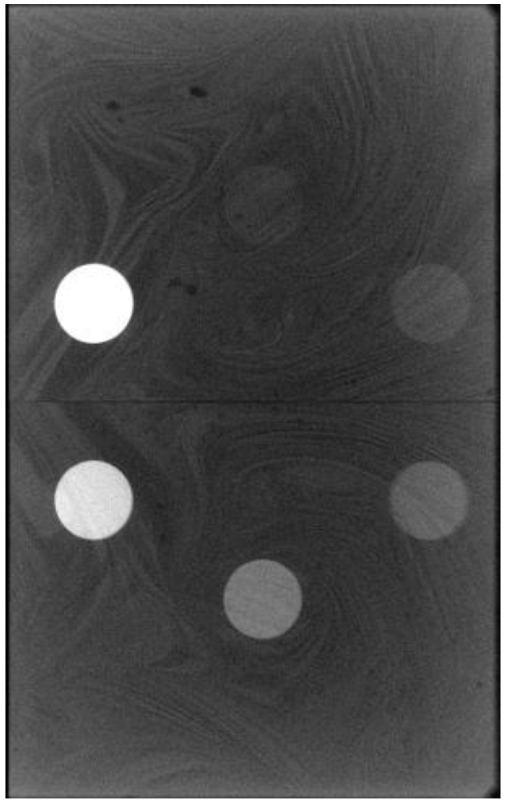




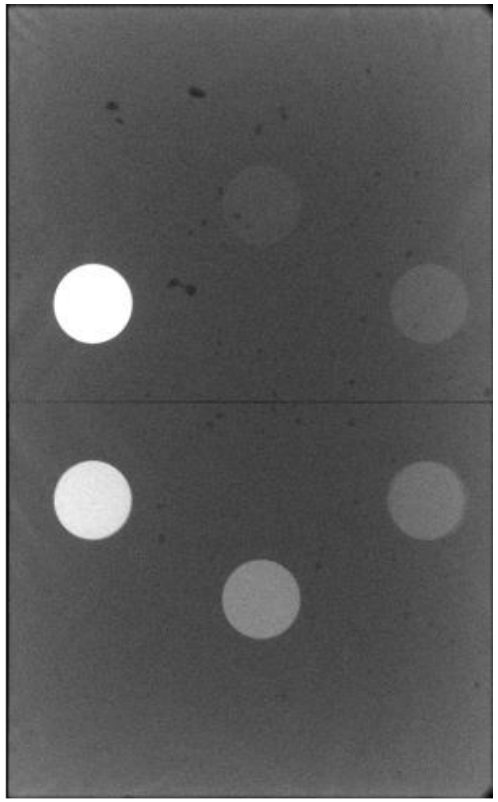
low-energy image (Rh/Rh, 28kV)



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



iodine image recombined with log-subtraction

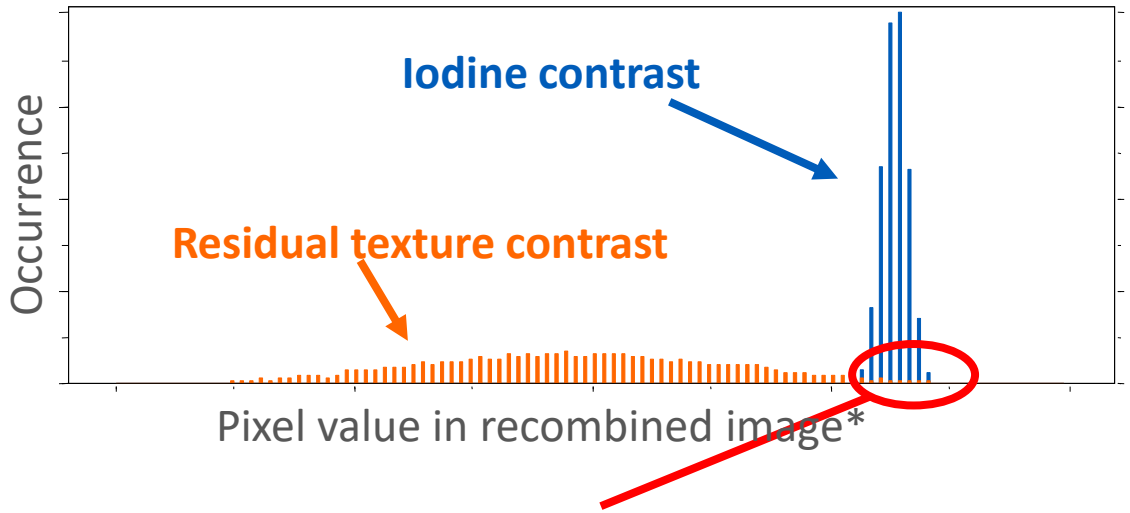


iodine image recombined with quadratic algorithm*

*S. Puong et al. SPIE, Medical Imaging, San Diego, USA, 17-22 February 2007

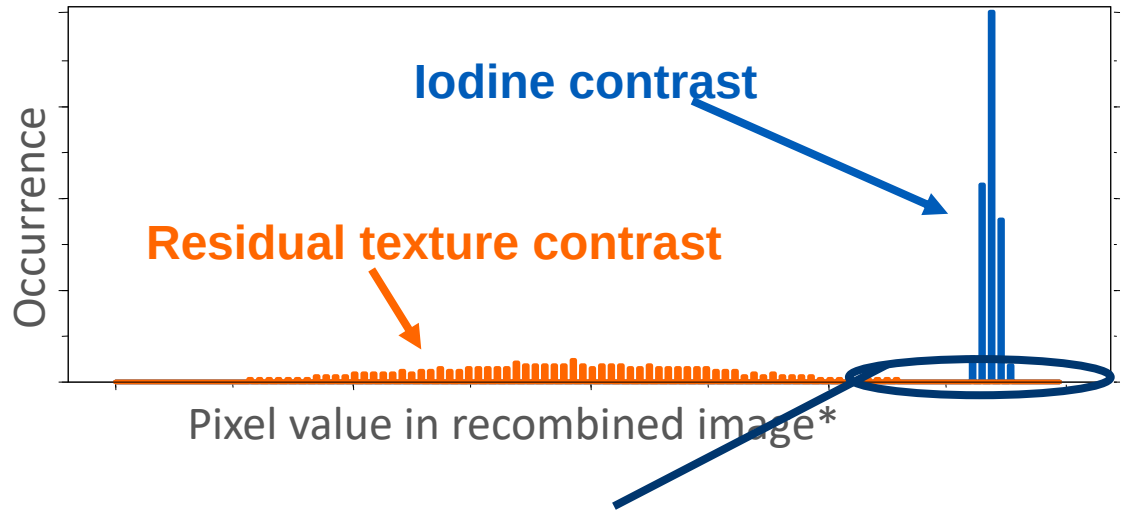
Calibration of the recombination algorithm

No calibration



Residual texture and 0,5mg/cm²iodine[&] not separated in 7% of cases

With calibration



Separation of iodine from residual texture in more than 99% of cases

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

[&]0.5 mg/cm² corresponds to a lower bound of concentration clinically expected

*Simulated data

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

Senographe Pristina™

Quality Control Manual

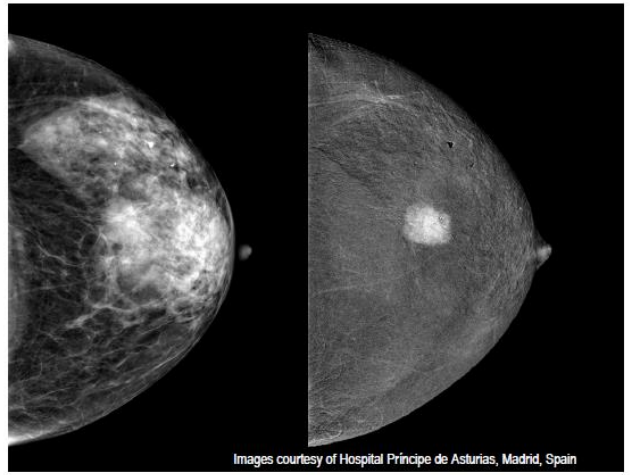
Non-contractual image.

5762778-8EN
Revision 5

SenoBright™ HD

CESM HD

Quality Control Manual



5722116-8EN
Revision 3

Clinical Evidence

CESM Clinical Performance

Comparison to mammography

Comparison to mammography + ultrasound

Comparison to MRI

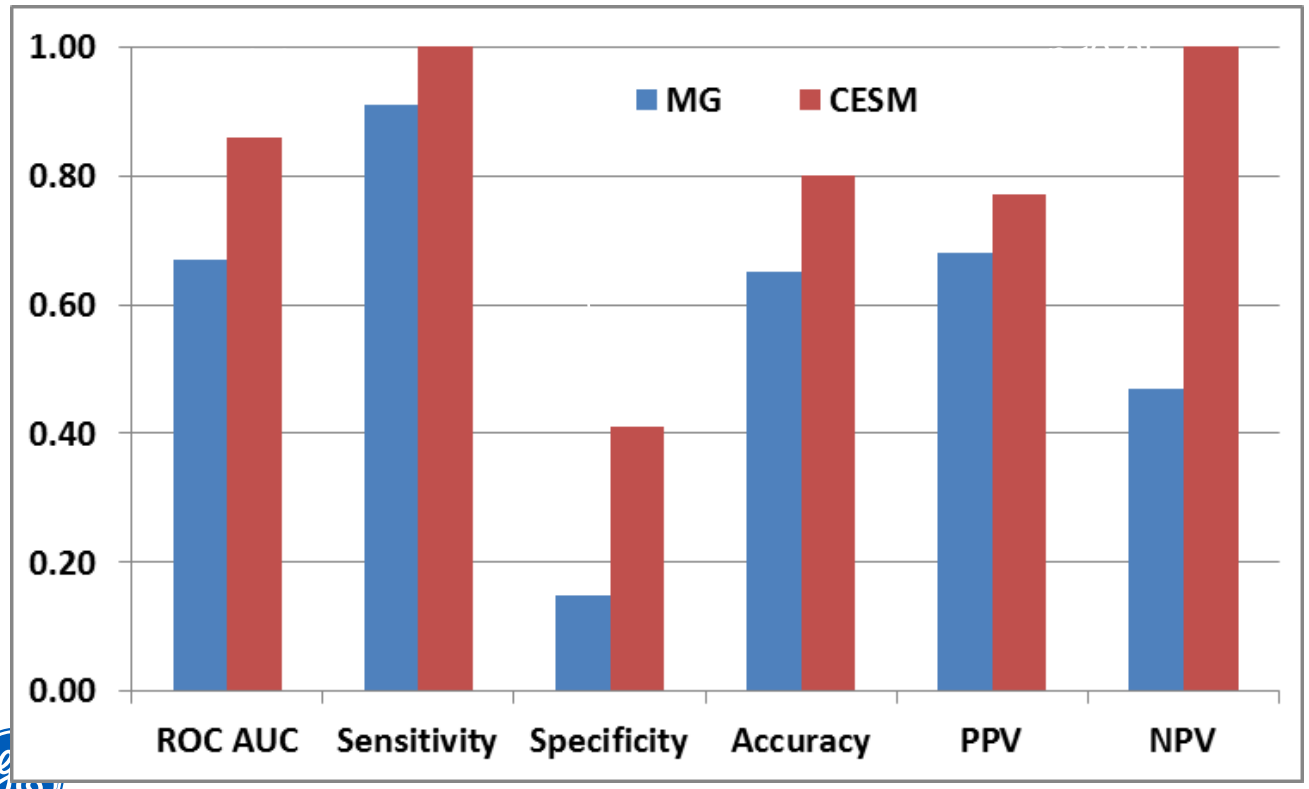
Many peer-reviewed publications, with 100+ on GE SenoBright™

CESM *vs Mammography*

Inclusion criterion was referral after mammography screening due to suspected breast cancer.

E. Luczynska, et al, Korean J Radiol 2014;15(6):689-696

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



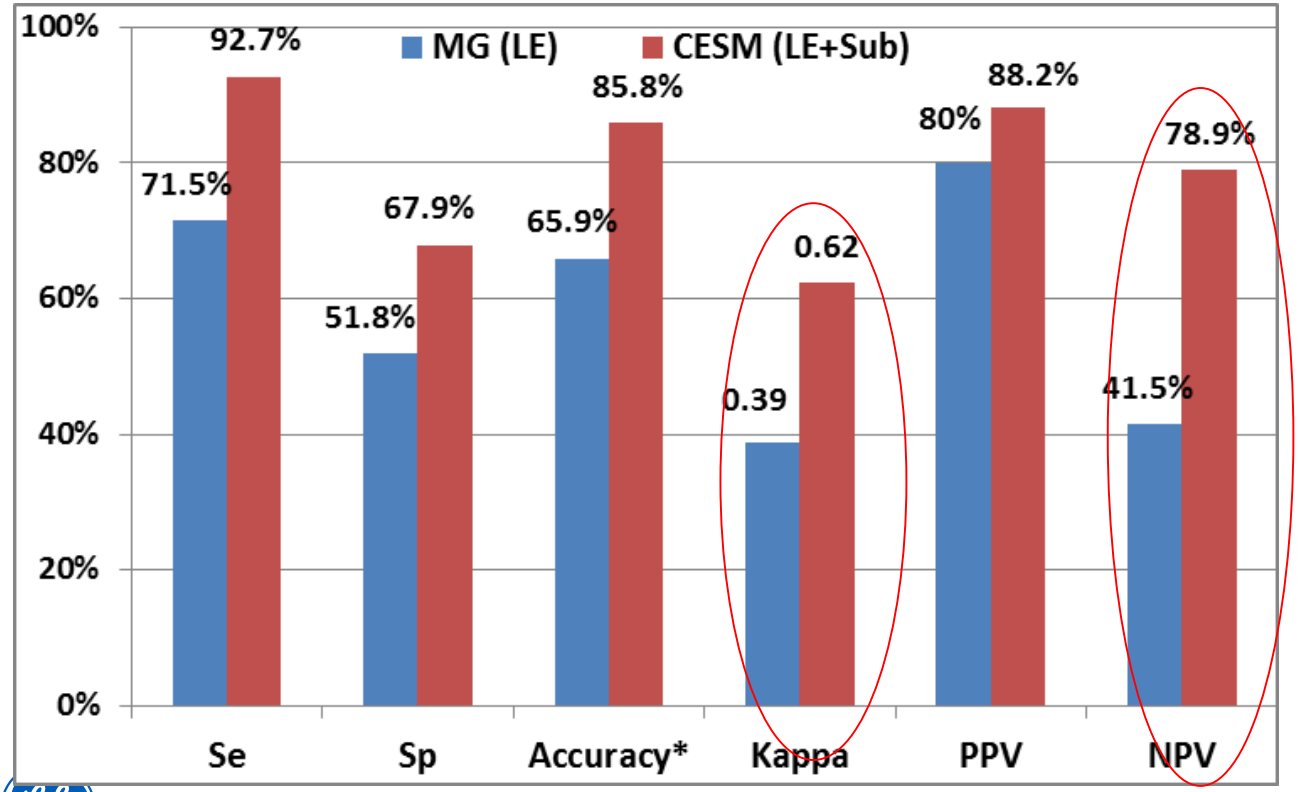
"CESM may provide higher sensitivity for breast cancer detection and greater diagnostic accuracy than conventional mammography"

CESM *vs Mammo for dense breasts*

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

Yun-Chung Cheung, et al - European Radiology (2014) 24:2394–2403

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.



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*

Inclusion criterion was recall from screening with unresolved findings after mammography and ultrasound.

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

	MG+US	MG+US+CESM	Difference	95% CI of Δ
ROC AUC (BI-RADS across readers)	0.827	0.871	0.043	(0.001, 0.085) p = 0.045
Per-Lesion Sensitivity	0.712	0.778	0.065	(0.019, 0.112) p = 0.006

CESM as an adjunct to MG+US improves diagnostic accuracy and per lesion sensitivity

CESM *clinical performance vs MRI*

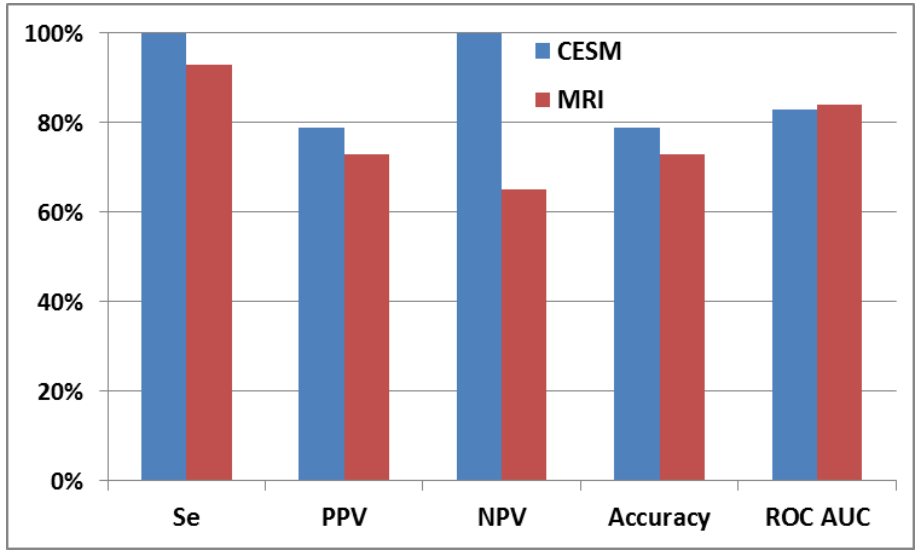
Luczynska et al, Med Sci Monit, 2015; 21: 1358-1367

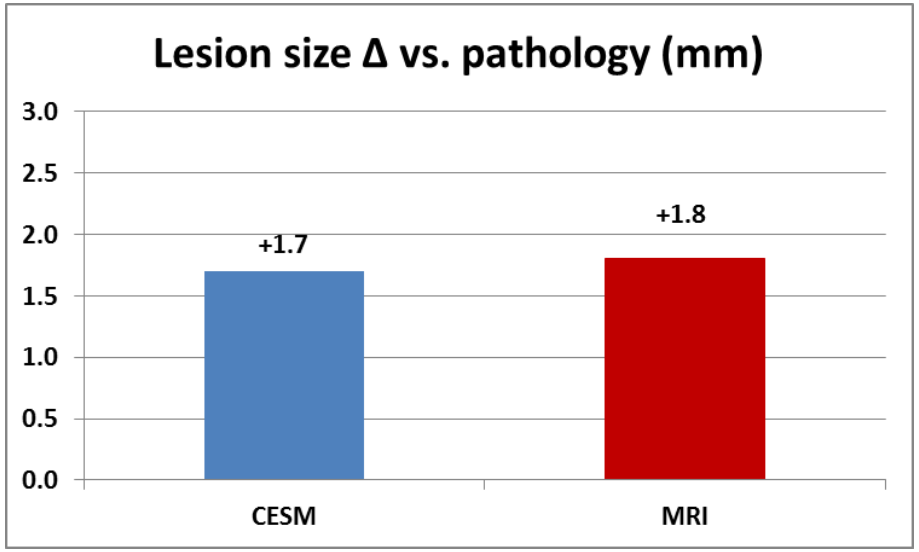
CESM and MRI examinations performed in 102 patients who had suspicious lesions in MG

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



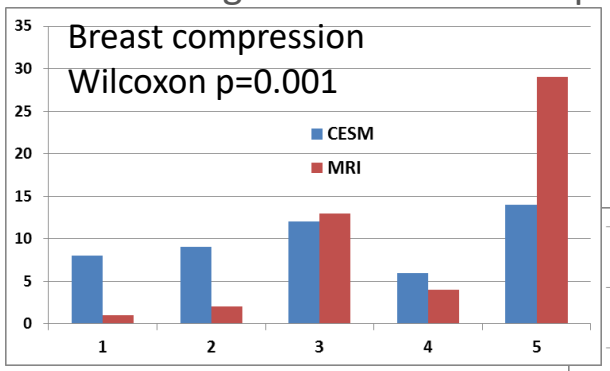


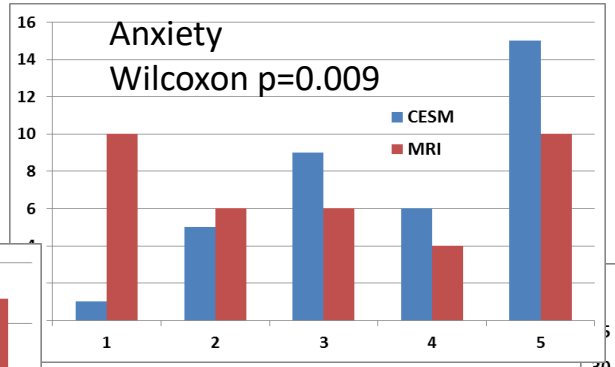
"CESM has the potential to be a valuable diagnostic method that enables accurate detection of malignant breast lesions, has high NPV, and a FPR similar to that of MRI"

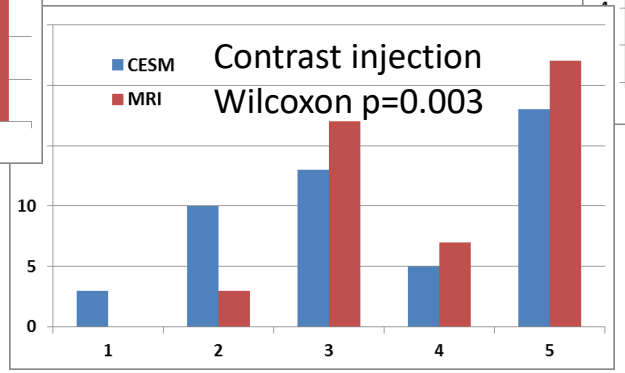
CESM *patient preference & tolerance vs MRI*

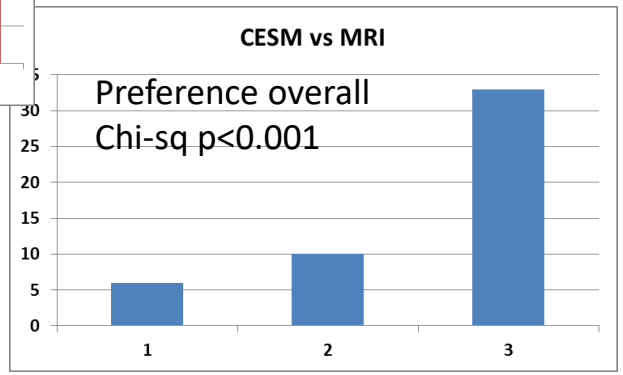
Hobbs et al (Royal Pereth Hospital), Jour of Med Im. and Rad. Onc. 59 (2015) 300–305

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









CESM:
faster procedure time
greater comfort
lower noise level
lower rates of anxiety

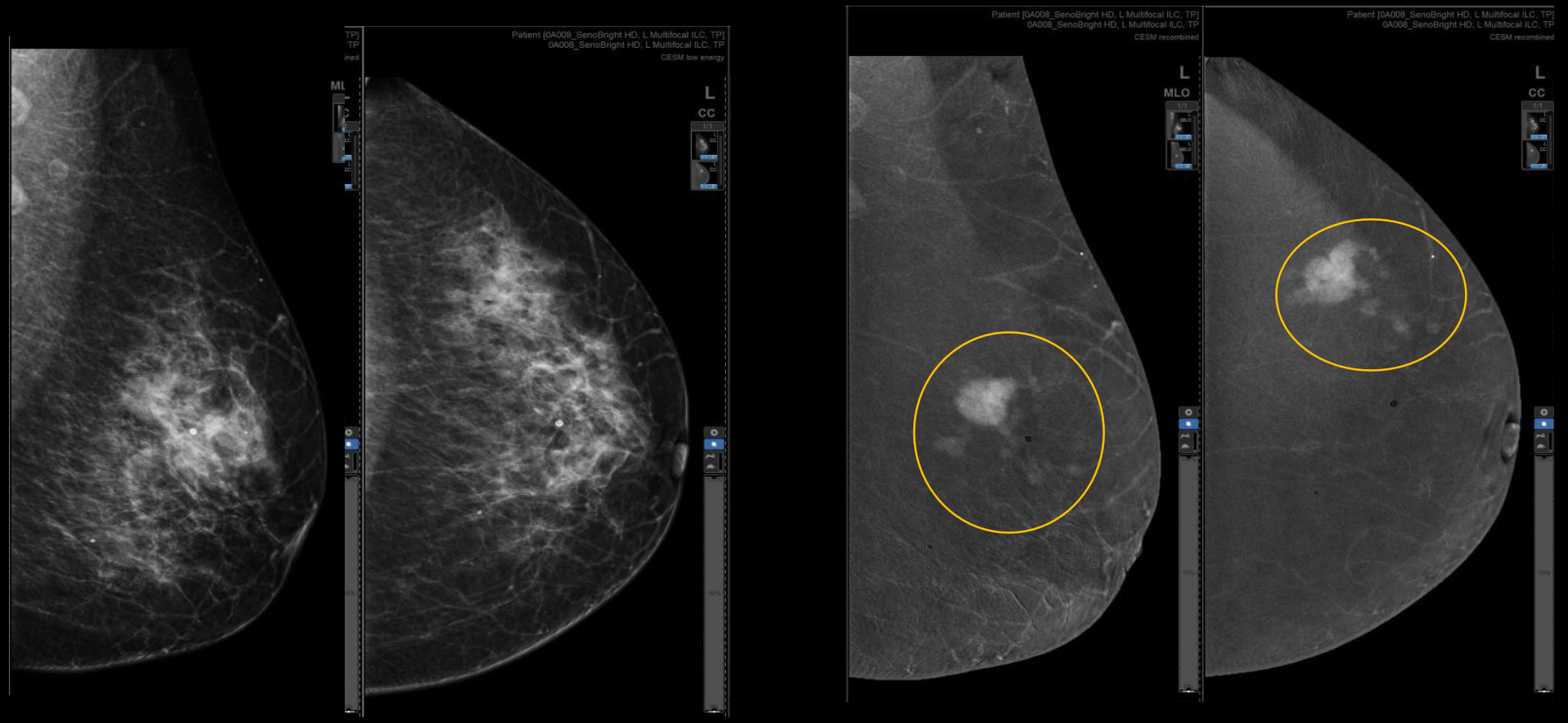
MRI:
breast compression comfort
contrast injection comfort

"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

Left Multifocal ILC



Prior Right Mastectomy - Indication: Palpable area

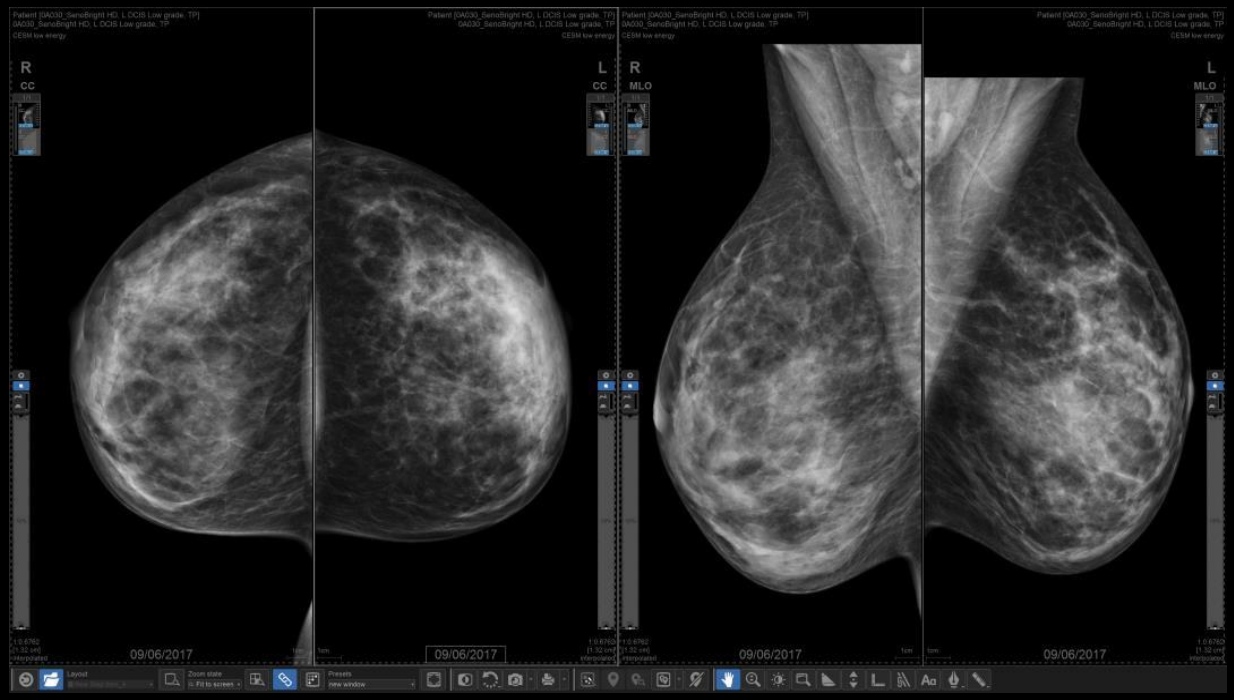
CESM LE finding: Spiculated mass, Left UOQ

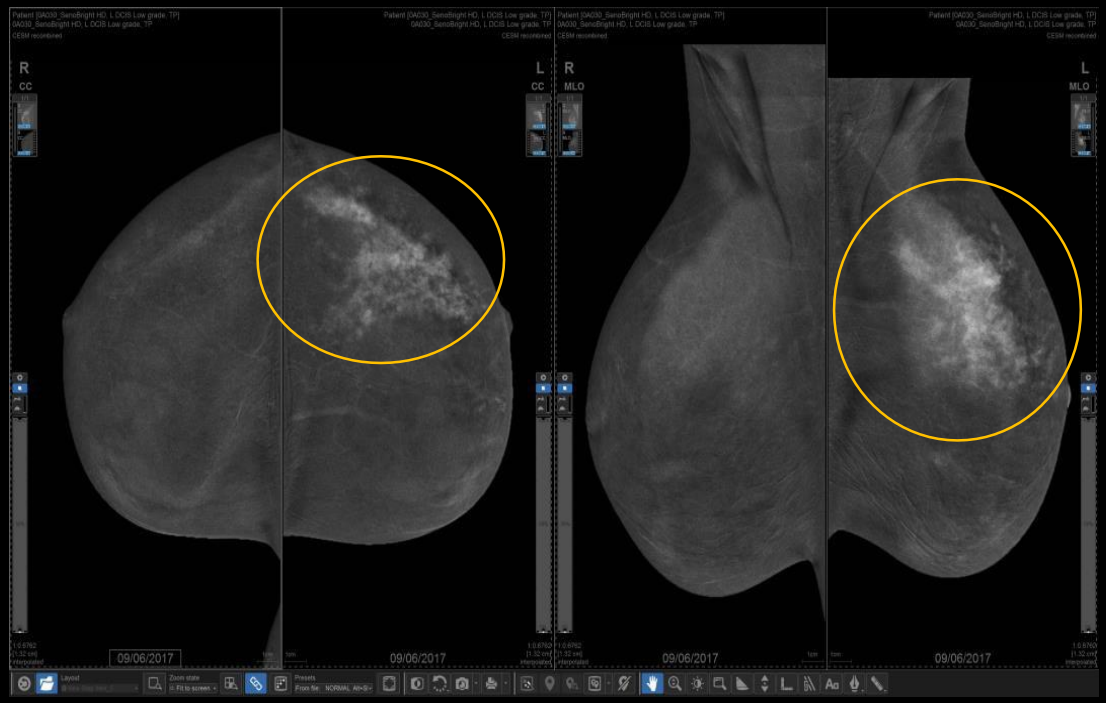
CESM finding: UOQ uptake, satellites

Biopsy Result: Invasive Lobular Carcinoma

Case 2

Left DCIS Low Grade





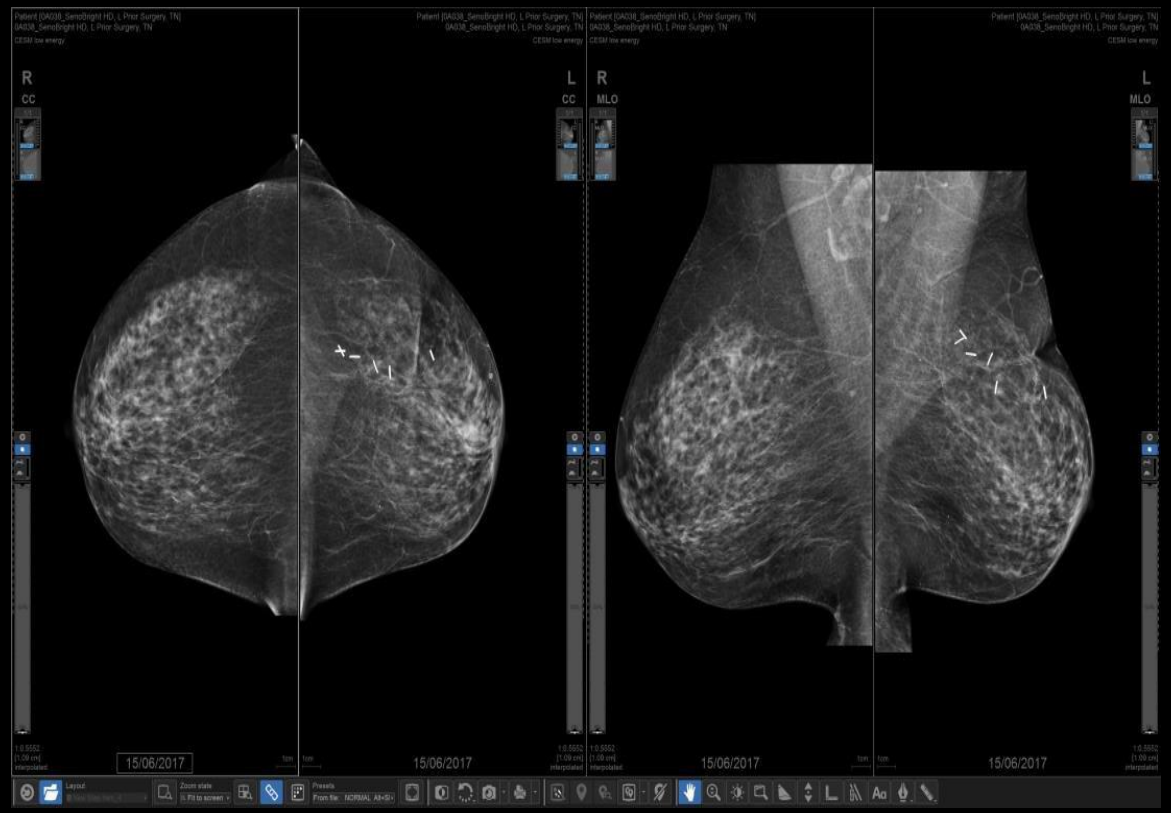
Indication: Induration palpation Left UOQ

Fast diagnostic: No FFDM

CESM finding: Left UOQ extensive uptake

Biopsy Result: DCIS Low grade

Case 3 Left Surgical Follow up

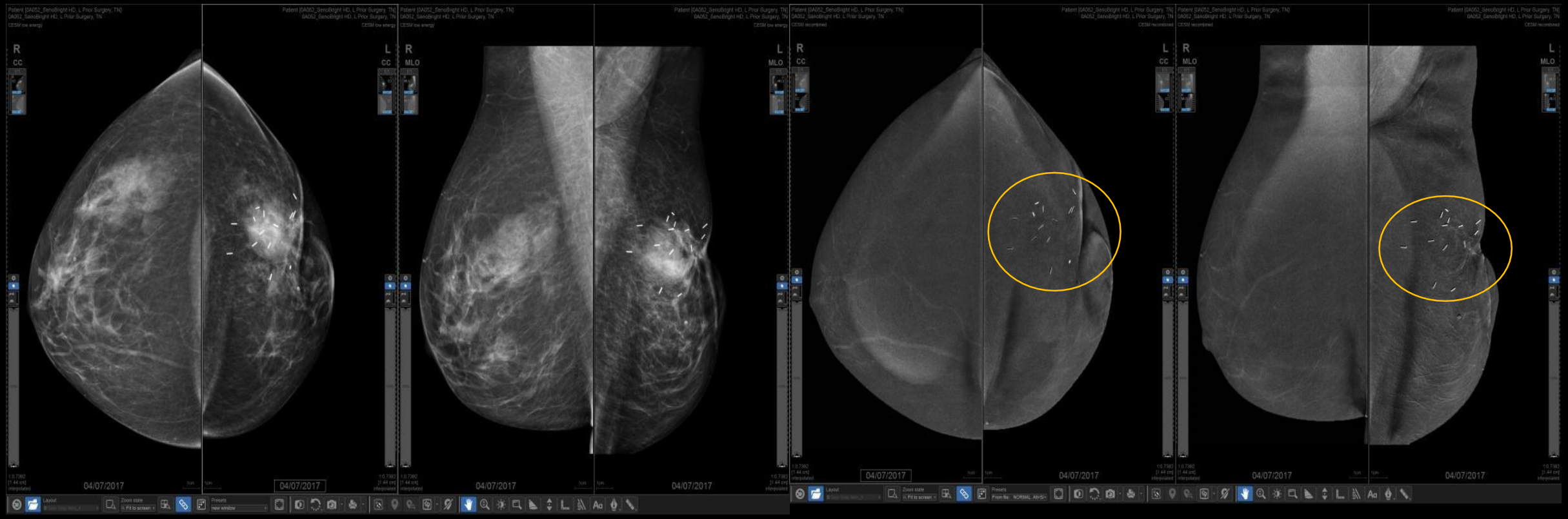


59 Yr, Prior surgery left breast. Indication: Nodule palpated in the surgery bed

Fast diagnostic, surgery follow up: No FFDM

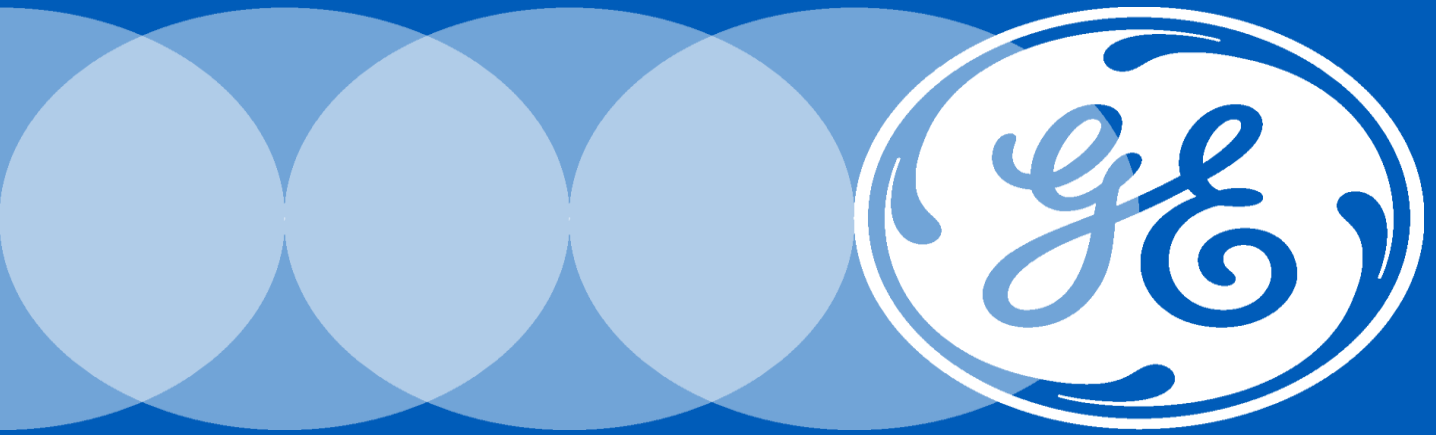
CESM finding: No uptake – True Negative

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