



Contrast Enhanced  
Mammography  
**Implementation Guide**

## SECTION I: Introduction

**Purpose.** Contrast Enhanced Mammography (CEM) is a powerful tool combining functional information (derived from iodinated contrast administration) with structural imaging (derived from anatomic 2D and 3D mammographic views), previously only available from breast magnetic resonance imaging (MRI). CEM provides a comparably sensitive, more specific, and more cost-effective alternative to MRI. This manual will provide an in-depth guide for CEM implementation into clinical practice.

**Technical aspects of CEM image acquisition.** (Perry, et al., 2019; Ghaderi, Phillips, Perry, Lotfi, & Mehta, 2019) CEM utilizes a dual-energy technique predicated on the attenuation differences of breast tissue and iodinated contrast. A standard CEM acquisition requires two exposures per view: one at high-energy and the other at low energy.

The high-energy exposure utilizes a copper filter and is performed above the k-edge of iodine (33.2 keV). High energy x-ray photons are preferentially absorbed at the locations of increased iodine accumulation, relative to the absorption in these same locations with lower energy photons, whereas absorption in regions of normal breast tissue do not exhibit this large absorption change as a function of x-ray energy. The high-energy image is not interpretable but is used in the calculation of the iodine map.

The low-energy image is produced in the low-energy x-ray spectrum (28-32 kVp) and uses standard mammographic filters. The image produced is comparable to full-field digital mammography (FFDM) and may be utilized for morphologic characterization of lesions.

The recombined, or “subtracted”, image is created by post-processing subtraction of the low-energy image from the high-energy image. The recombined image appears as a subtracted image highlighting iodine accumulation while eliminating the surrounding breast tissue. Iodine accumulation is based upon principles of angiogenesis, similar to contrast enhancement in MRI. Following the CEM examination, only the low energy images and the recombined images are available for interpretation on PACS.

**Literature review.** Mammography is the only imaging modality known to reduce mortality from breast cancer. (Institute, 2020) The ability to detect a breast cancer at a smaller size, typically before palpation, is associated with reduced mortality. (Seely & Alhassan, 2018) The sensitivity of mammography for detecting a breast malignancy is reduced in women with dense breast tissue, reportedly 40-70%. (Pisano, ED; Gatsonis, C; Hendrick, E; Yaffe, M; Baum, JK; Acharyya, S; Conant, E; Fajardo, L; Bassett, L; D’Orsi, C; Jong, R; Rebner, M; Digital Mammographic Imaging Screening Trial (DMIST) Investigators Group, 2006) This decreases even further in those women with dense breast tissue and an inherited genetic predisposition/elevated lifetime risk for breast cancer. The masking effect of FFDM is partially overcome with DBT by obtaining multiple low dose images at various angles, producing a semi-3D image set. DBT has repeatedly shown to improve cancer detection rate (CDR) and positive predictive value (PPV) while lowering false positive rate. (Skaane, et al., 2013) However, the utility of DBT is constrained by a fundamental need for an attenuation difference between the malignant lesion and the surrounding normal glandular breast tissue. DBT has shown a modest performance improvement in women with dense breast tissue, yielding an additional 1.4 cancers per 1000 women screened and no statistically significant difference in CDR with the addition of DBT in women with extremely dense tissue. (Rafferty, et al., 2016)

CEM improves upon FFDM and DBT by adding functional information to established anatomic imaging. CEM demonstrates improved performance compared to FFDM in the diagnostic setting: sensitivity 100% vs 96%, specificity 97.7% vs 42.0%, PPV 76.2% vs 39.7%. (Lobbes, et al., 2014) In addition, CEM shows similar sensitivity compared to breast MRI (96% vs 96%). (Jochelson, et al., 2013) In a multi-reader study comparing CEM with breast MRI in women with known malignancy, 93-98% of known malignancies are seen at CEM compared to 89-93% at breast MRI. (Chou, et al., 2015) When CEM is utilized to assess extent of malignancy, there is no statistically significant difference between extent of disease on CEM compared with breast MRI when assessed at final pathology.

The use of CEM compared to breast MRI for neoadjuvant chemotherapy (NAC) response demonstrates that CEM outperformed MRI in sensitivity (100% vs 87%) and specificity (84% vs 60%). (Iotti, et al.)

Women at elevated risk for breast cancer may additionally benefit from CEM. Not all women at elevated risk for breast cancer undergoes breast MRI, which may be secondary to inability to have a breast MRI for physical limitations (body habitus, anxiety), implanted devices, or financial burden. Hobbs et al demonstrated an increased overall patient preference of CEM compared to MRI citing a reduction in imaging time, anxiety, and noise. (Hobbs, Taylor, Buzynski, & Peake, 2015) In a study of evaluating CEM compared to breast MRI in 307 elevated risk patients for lesion detection, specificity and PPV are similar. Sensitivity is statistically higher in MRI secondary to a small number (n=3) of malignancies identified. (Jochelson, et al., 2017) Furthermore, CEM outperforms the sensitivity of FFDM (87.5% vs 50%). (Sung, et al., 2019) *References cited use equipment from various manufacturers.*

## SECTION II: Implementation

**Equipment requirements.** The addition of CEM requires I-View™ software and a hardware (addition of a Copper filter) upgrade to the 3Dimensions™ and a power injector for contrast injection. (Covington M. , 2021). Given resource constraints for many breast centers, the multifunctionality of Hologic Selenia Dimensions systems in screening mammography, upright stereotactic guided core biopsy (both 2D and 3D), CEM, image-guided localization and diagnostic mammography is particularly useful.

A power injector is the recommended method for CEM, allowing for a consistent, desired rate of 3 mL/second and the post injection saline bolus. (Zanardo, et al., 2019)

A crash cart or a contrast reaction kit should be easily assessable by staff in the breast center. Patients are monitored in the department for contrast reaction for 15 minutes following the CEM examination. Point of care methodology such as i-STAT (Abbott, NJ) allows for expeditious assessment of creatinine levels. To minimize the risk of contrast induced nephropathy (CIN), the ACR recommends serum creatinine level when patients meet 1 or more of the following factors: >60 years of age, a history of renal disease (dialysis, kidney transplantation, single kidney, renal cancer, renal surgery), hypertension (HTN) requiring treatment, diabetes mellitus (DM), or use of Metformin.

**Staffing requirements.** Preprocedural IV line may be placed by mammography technologists, breast center nurses/navigators or other radiology departmental technologists/nurses. Both nurses and technologists may perform pre-CEM contrast screening as well as postprocedural patient education. During the CEM exam, a radiologist or other licensed physician must be physically present in the facility to evaluate and treat any contrast associated reaction, as well as interpret this diagnostic examination. (Covington, et al., 2018)

**Radiologist requirements.** The time needed for radiologists to feel confident reading CEM is relatively short. (Lewin, Patel, & Tanna, 2020) CEM images are more efficiently and expeditiously interpreted than breast MR images, with a total mean interpretation time of 1-2 minutes. (Patel, Gray, & Pockaj, 2017) Serious contrast reactions necessitating physician involvement, as described below, are exceedingly rare.

The references related to CEM used in this document are a helpful collection of information new users will find beneficial as they implement CEM into their practices.

**Clinical workflow.** Separate areas designated for both IV insertion prior to the exam and for patient monitoring after the examination assist with efficiency of utilization of the 3Dimensions™ unit.

**Education.** Regarding initiating and expanding the CEM service line, referring provider education can be reliably performed through breast cancer multidisciplinary tumor board, grand rounds presentations, through the medical staff office, and via patient-specific direct communications to ordering providers. To maintain referring provider confidence in this modality, oftentimes the CEM reader pool is initially restricted to minimize downstream MR imaging following the CEM examination. Initial in-service for mammography technologists and breast center staff is critical for smooth clinical workflow.

**Gaining experience.** Even though reading CEM can be “easily learned”, it is helpful to gain experience with cases where you have some comparison to imaging findings on conventional and/or MRI. This can include patients with abnormal MRI, patients with imaging findings requiring biopsy or symptomatic patients like those with palpable findings. Spot compression images may be performed as part of the CEM encounter.

**Contrast.** The rate of severe contrast reactions is rare (0.04%), (Covington M. , 2021) with rare incidence of mortality reported at 0-10/1 million. (Radiology, 2020; Caro, Trindale, & McGregor, 1991; Katayama, et al., 1990) In general, protocols regarding administration of IV contrast for CEM parallel institutional protocols for computed tomography. Mild reactions may receive premedication per institutional protocols. Severe contrast reactions are a contraindication to the CEM examination. It is recommended to have a the ACR contrast reaction card in the mammography room for quick reference should a contrast reaction occur.

**Pre-imaging screening.** When scheduling, staff should ask questions related to history of allergies to contrast media, review of medications (specifically Metformin or HTN treatment), history of DM and HTN, and known renal disease.

Contraindications to intravenous contrast include a GFR of less than 30 mL/minute per 1.73 m<sup>2</sup> and a known moderate to severe allergy to iodinated contrast. CEM should also be avoided in pregnant patients and those under the age of 18.

The literature (James, Pavlicek, Hanson, Thomas, & Bhavika, 2017) demonstrates that CEM dose is approximately 1.5x that of FFDM and DBT is approximately 1.2x that of FFDM. In the latest Hologic software release, the CEM radiation dose is now lower at 1.25x of FFDM (Hologic Report VER-08953\_001).

Coordinating the CEM exam with the patient’s menstrual luteal phase, to minimize background parenchymal enhancement, may be considered although is not necessary, particularly for preoperative disease extent evaluation in recently diagnosed breast neoplasm. (Covington, et al., 2018)

**Imaging workflow.** Diagnostic radiologist reviews all images and clinical information to protocol the examination before patient arrives. Antecubital venous access using a  $\geq 20$ -g needle is preferred. (Covington M. , 2021) Care should be taken to place the IV into the arm contralateral to a prior axillary dissection. The patient should be informed about any side effects related to contrast injections such as a diffuse sensation of warmth, flushing, a metallic taste in mouth, and even urinary incontinence. Also, the patient can be educated about injection site issues including pain and swelling.

**Imaging protocol.** Contrast is typically administered to an upright, seated patient with a power injector. A multitude of iodinated contrast agents may be utilized. For CEM, it is helpful to parallel institutional CT iodinated contrast protocols. For Iohexol (Omnipaque 350, GE Healthcare) the suggested fixed dose is 1.5 mL/kg at a rate of 3 mL/s with a 10-mL saline flush.

Imaging should include the standard four views with imaging of both breasts. Spot compression and additional full views such as XCCL and ML can also be performed. Imaging should be started approximately 2 minutes after completion of the contrast injection and ideally completed by 12 minutes to minimize contrast washout, although imaging may be undertaken up to 20 minutes post contrast injection. (Polat, Evans, & Dogan, 2020) However, in those lesions with exceptionally low mitotic index, delayed images out to 20 minutes have occasionally been obtained.

Many institutions acquire images in the following sequence, affected breast MLO – unaffected breast MLO – affected breast CC – unaffected breast CC. (Zanardo, et al., 2019) In order to finish imaging within the ideal window, it is helpful for an institution to have a reproducible protocol.

For diagnostic CEM studies the radiologists may choose to be present in the imaging suite, especially in the initial stages of the CEM program. This can allow for real-time review of images and decision making regarding the need for additional views.

**Post imaging.** The injection site should be checked for any signs of contrast extravasation. Extravasation occurs from 0.1% to 1.2% in studies of patients having CT exams with power injectors. (Radiology, 2020) Signs of extravasation include patient complaints of swelling or tightness, stinging or burning pain at the site of extravasation, or no discomfort at all. (Wang, Cohan, Ellis, Adusumilli, & Dunnick, 2007) On physical examination, the extravasation site may be edematous, erythematous, and tender, although the vast majority recover without long term complications. (Wang, Cohan, Ellis, Adusumilli, & Dunnick, 2007) Patients who have had prior axillary dissection are at increased risk for extravasation in the affected extremity; therefore, contralateral extremity is typically utilized for the examination.

Mild immediate contrast reactions typically do not require medical treatment, although nursing should monitor vitals and the physician should be notified. The ability to check vital signs is important in a breast center that offers CEM. Any patient with a mild allergic-like reaction should be observed for a minimum of 30 minutes to ensure clinical stability or recovery. Treatment with an antihistamine may be instituted for mild symptomatic allergic-like urticarial reactions, but often is not necessary. (Caro, et al., 1991) Please refer to the ACR manual on contrast reaction for more information regarding managing contrast reactions.

### SECTION III: Clinical Utilization

Paradigmatically, CEM may be utilized in preprocedural or postprocedural diagnostic settings, and many other diagnostic indications. The CEM examination is pragmatic, efficient, and expeditiously interpreted in each setting, leading to high patient satisfaction, and often truncating the final time to diagnostic resolution in those patients recently diagnosed with breast neoplasm.

**Preprocedural setting.** CEM has been utilized for Diagnostic BI-RADS 4c/BI-RADS 5 lesions in which there is a high propensity of diagnosis of breast neoplasm, to present the breast surgeon with full breast staging prior to cancer consult.

**Postprocedural setting.** CEM is most utilized for preoperative disease extent evaluation in patients recently diagnosed with breast neoplasm, most commonly lobular origin neoplasm, diagnosis of breast neoplasm in the setting of heterogeneously dense or extremely dense breasts, unexpected histopathology upon breast biopsy (i.e., spindle cell neoplasm). CEM is used for post neoadjuvant follow-up, oftentimes in conjunction with targeted breast ultrasound and diagnosis of breast cancer metastases to the axilla without known breast primary location. CEM is also utilized for persisting clinical symptomatology with negative initial diagnostic breast imaging examination, such as persisting palpable abnormality, bloody nipple discharge, and unexplained unilateral breast dermal changes.

## SECTION IV: Reporting and Image Interpretation

CEM reporting and image interpretation parallels breast MRI reporting and image interpretation. Firstly, degree of background parenchymal enhancement is specified, as normal breast tissue can also enhance at CEM. This enhancement of breast tissue is described as background parenchymal enhancement (BPE). Normal background parenchymal enhancement is classified as minimal (<25% of glandular tissue demonstrating enhancement), mild (25%–50% enhancement), moderate (50%–75% enhancement), or marked (>75% enhancement). Degree of symmetry of BPE is also reported, as to whether BPE is symmetric or asymmetric. Standard BI-RADS nomenclature is followed. The technique section is inclusive of contrast dose and presence or absence of periprocedural complications. The report is often linked with any other diagnostic examinations performed during the CEM encounter, such as targeted breast ultrasound, to issue one comprehensive BI-RADS designation.

Notably, it is important to render image interpretation of both the morphologic 2D and/or 3D images as well as the recombined data set. Occasionally a patient with multifocal intraductal neoplasm has satellite regions of subtle microcalcifications discerned predominantly on morphologic imaging, which may not exhibit significant enhancement on recombined images and yet, may require further action in the pretreatment setting. Image interpretation and subsequent recommendations arising from the CEM encounter, as in other breast imaging modalities, is primarily governed by the most suspicious imaging feature, whether that is discerned from morphologic imaging (2D/3D) or the targeted ultrasound arising from the CEM encounter. Commonly, benign lesions such as fibroadenoma may exhibit brisk enhancement which parallels that of a malignant lesion. Lesions on CEM are characterized as solitary (unifocal) or multifocal, the degree of enhancement is characterized as non-mass enhancement (linear vs clumped, regional vs segmental) vs mass, and any concerning features in the axilla are described. In newly characterized neoplasms, comments may additionally be made regarding status of the nipple in the affected breast (ie. nipple inversion), degree (if any) of dermal thickening, parenchymal edema versus post biopsy hematoma about biopsied neoplasm, and distance from neoplasm to nipple anteriorly and chest wall posteriorly.

## SECTION V: Billing and Coding

CEM is uniformly billed as a Diagnostic Breast Imaging Contrast Examination with added charge for intravenous contrast. Adjunct targeted ultrasound or adjunct downstream ultrasound-guided or stereotactic-guided biopsy arising from CEM examination is billed separately. Even if CEM is performed for high-risk surveillance in patients with a known genetic predisposition to breast cancer or prior elevated risk benign biopsy, it is billed as Diagnostic Breast Imaging Contrast Examination. All these examinations are discussed with the patient as per your typical practice for diagnostic breast imaging. Currently, no screening code exists for CEM.

## SECTION VI: FAQs

**What were the barriers to implementation of Contrast Enhanced Mammography (CEM) in your practice?** The barriers to implementation of CEM at our institution are extrinsic to image quality and clinical workflow and primarily revolve around preprocedural operational measures such as IV placement, standardizing response to contrast reactions given presence in freestanding outpatient imaging center, and familiarizing mammography technologists with power injector for administration of intravenous contrast.

**What happens if the lesion of interest does not enhance?** If a lesion has a low mitotic index, represents intraductal neoplasm, or exhibits mucinous or papillary features, a delayed image in one view (MLO view, for example) may be necessitated at 4, 8 or even 12 minutes to optimize lesion conspicuity. In our institutional experience, delayed images of up to 20 minutes may be undertaken following contrast injection.

**What is the frequency of contrast reactions following CEM?** In our institutional experience of over 500 cases, there have been no severe contrast reactions following CEM examination. If patients historically demonstrated mild reaction to intravenous contrast administration, premedication protocol is administered (which parallels institutional premedication protocol for Computed Tomography (CT)). Patients should be forewarned prior to the examination that along with intravenous contrast examination, there is often a feeling of generalized full-body warmth/flushing and that they may have the sensation to urinate. No significant side effects have been observed because of intravenous contrast administration.

**Who places the IV for the CEM examination?** Who places the IV can depend upon whether the CEM examination is performed in the outpatient or inpatient setting. In the outpatient setting, the IV may be placed by the breast center nurse navigators, breast center nurses, or mammography technologists. At our institution, diagnostic imaging inclusive of MRI and CT is additionally performed in the breast center building and, as such, the IV is placed by the CT technologists. In the inpatient setting, Interventional Radiology nurses and CT/MR technologists may provide a useful adjunct to placing the IV to optimize the examination.

**How often is MRI performed for problem solving following CEM examination?** MRI is not utilized for problem solving following CEM examination at our institution. If there are additional foci of enhancement within the ipsilateral affected breast or contralateral unaffected breast on CEM, a targeted ultrasound is performed to discern these lesions. An ultrasound slot and biopsy slot are held for all CEM patients. If the enhancing lesion(s) of interest are not discerned upon targeted breast ultrasound, upright 3D-directed biopsy is performed based upon landmarks for the CEM-detected lesions of concern.

**How is a meaningful referral base for CEM built?** CEM was initially presented in our breast oncologic multidisciplinary tumor board; every time a CEM is performed which subsequently alters surgical management or in which impactful new data is discerned from the CEM examination, these cases are presented in tumor board. In this manner, a virtuous feedback loop was built with all our CEM ordering providers across disciplines inclusive of medical oncology and breast surgery. Additionally, these cases are presented in Grand Rounds to the primary care specialties of internal medicine, obstetrics and gynecology, and family medicine. Patient stories, with patient consent, are also profiled in the online "Health eNews" platform of our health care system.

**Has CEM negatively impacted diagnostic MRI volumes at your institution?** No. CEM has heightened awareness of the importance of preoperative disease extent evaluation in newly diagnosed neoplasms, particularly in those patients with heterogeneously dense/extremely dense breasts or in those with unexpected pathologic findings. As such, many newly diagnosed neoplasms are counseled by breast surgery regarding the importance of preoperative disease extent evaluation and given the option of pretreatment breast MRI vs CEM. Many of those patients subsequently elected for CEM. The volume of breast MRI has remained stable to slightly increased in our institution.

**What is the imaging protocol for CEM?** There are many ways to perform the imaging sequence for CEM. At our institution, following a delay of 2 minutes after contrast injection for intraductal neoplasms, 4 minutes following contrast injection for lobular neoplasms, and 2-minute contrast delay for all other indications, the affected MLO performed first, followed by MLO view of unaffected breast, affected CC, followed by unaffected CC view. Finally, in those CEM cases performed for preoperative disease extent evaluation in newly diagnosed neoplasms, an axillary spot view is performed of the affected axilla for enhanced axillary visualization. At our institution, we have nearly 100% utilization of DBT for screening and diagnostic purposes. By the time of the CEM encounter, many of our patients have already had two separate DBT encounters. Therefore, the CEM is performed as a 2D examination coupled with the subtracted sequences.

**Power injector for CEM?** It is advised to parallel institutional guidelines for contrast. However, a power injector will significantly help to improve workflow. If you are interested in a power injector, please contact manufacturers of CT injectors. Guerbet, Sinomdt, and MEDRAD are examples of power injector manufacturers. It is the sole responsibility of the medical professional to determine which technique or protocol is appropriate. The websites below are for your reference.

**Do radiologists monitor CEM examinations?** All these examinations are performed as diagnostic mammographic examinations and, as such, are only performed when a breast imaging radiologist is on site. For the first 50 examinations, a diagnostic breast imaging radiologist monitored these examinations in the actual Imaging suite to monitor for contrast extravasation, monitor efficiency of protocol, and monitor the actual images and the imaging protocol. Once the clinical protocol had been optimized, in-suite monitoring was no longer necessary. All patients are counseled following CEM examination by the diagnostic radiologist, paralleling the diagnostic breast imaging workflow.

- <https://www.radiologysolutions.bayer.com/products/injection-systems/medrad-stellant-flex-ct>
- <https://www.guerbet.com/products-solutions/>
- <https://sinomdt-global.com/product/contrast-media-injector/>

## REFERENCES

- (2021, January 3). Retrieved from National Cancer Institute: [https://www.cancer.gov/types/breast/hp/breast-screening-pdq#\\_524\\_toc](https://www.cancer.gov/types/breast/hp/breast-screening-pdq#_524_toc)
- Beatty, A., Lieberman, P., & Slavin, R. (2008, Feb). Seafood allergy and radiocontrast media: are physicians propagating a myth? *Am J Med*, 121(2), 158.e1-4.
- Caro, J., Trindale, E., & McGregor, M. (1991). The risks of death and of severe nonfatal reactions with high- vs low-osmolality contrast media: a meta-analysis. *AJR*, 825-832.
- Chou, C., Lewin, J., Chiang, C., Hung, B., Yang, T., Huang, J., . . . Pan, H. (2015, Dec). Clinical evaluation of contrast-enhanced digital mammography and contrast enhanced tomosynthesis--Comparison to contrast-enhanced breast MRI. *Eur J Radiol*, 84(12), 2501-8.
- Covington, M. (2021). Contrast-Enhanced Mammography Implementation, Performance, and Use for Supplemental Breast Cancer Screening. *Radiology Clinics of North America*, 113-128.
- Covington, M., Pizzitola, V., Lorans, R., Pockaj, B., Northfelt, D., Appleton, C., & Patel, B. (2018). The Future of Contrast Enhanced Mammography. *AJR*, 292-300.
- Fallenberg, E., Dromain, C., Diekmann, F., Engelken, F., Krohn, M., Singh, J., . . . Renz, D. (2014, Jan). Contrast-enhanced spectral mammography versus MRI: Initial results in the detection of breast cancer and assessment of tumour size. *Eur Radiol*, 24(1), 256-64.
- Ghaderi, K., Phillips, J., Perry, H., Lotfi, P., & Mehta, T. (2019). Contrast-enhanced Mammography: Current Applications and Future Directions. *Radiographics*, 39(7), 1907-1920.
- Hobbs, M., Taylor, D., Buzynski, S., & Peake, R. (2015, June). Contrast-enhanced spectral mammography (CESM) and contrast enhanced MRI (CEMRI): Patient preferences and tolerance. *J Med Imaging Radiat Oncol*, 59(3), 300-5.
- Institute, N. C. (2020, August 27). *Breast Cancer Screening (PDQ®)–Health Professional Version*. Retrieved February 28, 2021, from [https://www.cancer.gov/types/breast/hp/breast-screening-pdq#\\_524\\_toc](https://www.cancer.gov/types/breast/hp/breast-screening-pdq#_524_toc)
- Iotti, I., Ravaioli, S., Vacondio, R., Coriani, C., Caffarri, S., Sghedoni, R., . . . Pattacini, P. (n.d.). Contrast-enhanced spectral mammography in neoadjuvant chemotherapy monitoring: a comparison with breast magnetic resonance imaging.
- James, J. R., Pavlicek, W., Hanson, J. A., Thomas, F. B., & Bhavika, K. P. (2017). Breast radiation dose with CESM compared with 2D FFDM and 3D tomosynthesis mammography. *AJR*, 362–372.
- Jochelson, M., Dershaw, D., Sung, J., Heerd, A., Thornton, C., Moskowitz, C., . . . Morris, E. (2013, Mar). Bilateral contrast-enhanced dual-energy digital mammography: feasibility and comparison with conventional digital mammography and MR imaging in women with known breast carcinoma. *Radiology*, 266(3), 743-751.
- Jochelson, M., Pinker, K., Dershaw, D., Hughes, M., Gibbons, G., Rahbar, K., . . . Sung, J. (2017, Dec). Comparison of screening CEDM and MRI for women at increased risk for breast cancer: A pilot study. *Eur J Radiol*, 97, 37-43.
- Katayama, H., Yamaguchi, K., Kozuka, T., Takashima, T., Seez, P., & Matsuura, K. (1990). Adverse reactions to ionic and nonionic contrast media. A report from the Japanese Committee on the Safety of Contrast Media. *Radiology*, 621-628.
- Lewin, J., Patel, B., & Tanna, A. (2020). Contrast-Enhanced Mammography: A Scientific Review. *Journal of Breast Imaging*, 7-15.
- Lobbes, M., Lalji, U., Houwers, J., Nijssen, E., Nelemans, P., van Roozendaal, L., . . . Wildberger, J. (2014, July). Contrast-enhanced spectral mammography in patients referred from the breast cancer screening programme. *Eur Radiol*, 24(7), 1668-7.
- Patel, B., Gray, R., & Pockaj, B. (2017, June). Potential Cost Savings of Contrast-Enhanced Digital Mammography. *AJR*, 208(6), W231-W237.
- Perry, H., Phillips, J., Dialani, V., Slanetz, P., Fein-Zachary, V., Karimova, E., & Mehta, T. (2019). Contrast-Enhanced Mammography: A Systematic Guide to Interpretation and Reporting. *AJR*, 212(1), 222-231.
- Pisano, ED; Gatsonis, C; Hendrick, E; Yaffe, M; Baum, JK; Acharyya, S; Conant, E; Fajardo, L; Bassett, L; D’Orsi, C; Jong, R; Rebner, M; Digital Mammographic Imaging Screening Trial (DMIST) Investigators Group. (2006, Oct). Diagnostic performance of digital versus film mammography for breast-cancer screening. *N Engl J Med*, 355(17), 1840.
- Polat, D. S., Evans, W. P., & Dogan, B. E. (2020). Contrast-Enhanced Digital Mammography: Technique, Clinical Applications, and Pitfalls. *AJR*, 1267-1278.
- Radiology, A. C. (2020). *ACR manual on contrast media 2020*. Retrieved Feb 28, 2021, from [https://www.acr.org/-/media/ACR/Files/Clinical-Resources/Contrast\\_Media.pdf](https://www.acr.org/-/media/ACR/Files/Clinical-Resources/Contrast_Media.pdf)

- Rafferty, E., Durand, M., Conant, E., Copit, D., Friedewald, S., Plecha, D., & Miller, D. (2016, Apr). Breast Cancer Screening Using Tomosynthesis and Digital Mammography in Dense and Nondense Breasts. *JAMA*, 315(16), 1784-6.
- Seely, J., & Alhassan, T. (2018). Screening for breast cancer in 2018-what should we be doing today? *Curr Oncol*, 25(Suppl 1), S115-S124.
- Skaane, P., Bandos, A., Gullien, R., Eben, E., Ekseth, U., Haakenaasen, U., . . . Gur, D. (2013, April). Comparison of digital mammography alone and digital mammography plus tomosynthesis in a population-based screening program. *Radiology*, 267(1), 47-56.
- Sung, J., Lebron, L., Keating, D., D'Alessio, D., Comstock, C., Lee, C., . . . Jochelson, M. (2019). Performance of dual-energy contrast-enhanced digital mammography for screening women at increased risk of breast cancer. *Radiology*, 293, 81-88.
- Wang, C. L., Cohan, R. H., Ellis, J. H., Adusumilli, S., & Dunnick, N. R. (2007). Frequency, management, and outcome of extravasation of nonionic iodinated contrast medium in 69,657 intravenous injections. *Radiology*, 80-87.
- Zanardo, M., Cozzi, A., Trimboli, R., Labaj, O., Monti, C., Schiaffino, S., . . . Sardanelli, F. (2019). Technique, protocols and adverse reactions for contrast-enhanced spectral mammography (CESM): a systematic review. *Insights Imaging*.

## ADDITIONAL REFERENCES

- Ali-Mucheru, M., Pockaj, B, Patel, B. et al. Contrast-Enhanced Digital Mammography in the Surgical Management of Breast Cancer. *Ann Surg Oncol* (2016); 23 (Suppl5): 649-655. American Cancer Society, Cancer Facts and Figures. Atlanta, *American Cancer Society*, 2019.
- Badr S., Laurent N., Regis C et al. Dual-energy contrast-enhanced digital mammography in routine clinical practice in 2013. *Diagn Interv Imaging* (2014), 95(1):245-258.
- Bhimani, C., Matta, D., Roth, RG et al. Contrast-enhanced Spectral Mammography: Technique, Indications, and Clinical Applications. *Acad Radiol* (2017) 23(1): 84-88.
- Boehm, I. (2008). Seafood allergy and radiocontrast media: are physicians propagating a myth? *Am J Med*, e19.
- Cheung, Y-Z., Lin Y-C., Wan Y-L et al. Diagnostic performance of dual energy contrast-enhanced subtracted mammography in dense breasts compared to mammography alone: interobserver blind-reading analysis. *Eur Radiol* (2014) 24(10):2394-2403.
- Diekmann, F., Freyerm N., Diekmann, S., et al. Evaluation of contrast-enhanced digital mammography. *Eur J of Radiol* (2011): 78 (1): 112-121.
- Dromain C., Thibault, F., Diekmann, F et al. Dual-energy contrast-enhanced digital mammography: initial clinical results of a multireader, multicase study. *Breast Cancer Res* (2012) 14(3): R94.
- Dromain C., Thibault, F., Muller, S. et al. Dual-energy contrast-enhanced digital mammography: initial clinical results. *Eur Radiol* (2011): 21(3): 565-574.
- Fallenberg, EM, Schmitzberjger FF., Amer H. et al. Contrast-enhanced spectral mammography vs mammography and MRI- clinical performance in a multi-reader evaluation. *Eur Radiol* (2017): 27: 2752-2764
- Fallenberg, EM., Dromain, C., Diekmann, F. et al. Contrast-enhanced spectral mammography: Does mammography provide additional clinical benefits or can some radiation exposure be avoided? *Breast Cancer Res Treat* (2014): 146 (2): 371-381.
- Francescone MA., Jochelson MS, Dershaw DD et al. Low energy mammogram obtained in contrast enhanced digital mammography (CEDM) is comparable to routine full-field digital mammography (FFDM). *Eur J Radiol* 2014 83(8): 1350-1355.
- [https://www.cancer.gov/types/breast/hp/breast-screening-pdq#\\_524\\_toc](https://www.cancer.gov/types/breast/hp/breast-screening-pdq#_524_toc) (National Cancer Institute, 2021)
- Jo, JM, Jafferjee, N., Covarrubias GE et al. Dense breasts: a review of reporting legislation and available supplemental screening options. *AJR* (2014) 203(2): 449-456.
- Kachelmeyer, S., & Blonski, D. (2013). FDA 510K Summary Hologic CESM. Retrieved from [https://www.accessdata.fda.gov/cdrh\\_docs/pdf12/K123873.pdf](https://www.accessdata.fda.gov/cdrh_docs/pdf12/K123873.pdf)
- Kerlikowki, J., Zhu W., Hubbard RA, et al. Outcomes of screening mammography by frequency, breast density, and postmenopausal hormone therapy. *JAMA intern Med* (2013) 173(9): 807-816.
- Lee-Felker SA, Tekchandani L., Thomas, M. et al. Newly Developed Breast Cancer: Comparison of Contrast-Enhanced Spectral Mammography and Breast MR Imaging in the Evaluation of Extent of Disease. *Radiology* (2017): 285(2): 389-400.
- Patel BK., Garza SA, Eversman S et al. Assessing tumor extent on contrast-enhanced spectral mammography versus full-field digital mammography and ultrasound. *Clin Imaging* (2017), 46: 78-84.
- Saslow, D., Boetes, C., Burke, W., et al. American Cancer Society guidelines for breast screening with MRI as an adjunct to mammography. *CA Cancer J Clin* (2007), 57(2): 75-89.
- Tuczynska, E., Heinze-Paluchowska, S., Hendrick, E. et al. Comparison between Breast MRI and Contrast Enhanced Spectral Mammography. *Med Sci Monit* (2015): 21: 1358-1367.

## AUTHORS:

### **Nila Alsheik, MD**

Chief of Breast Imaging  
Advocate Lutheran General Hospital  
Chair of the Breast Imaging Medical Directors Committee  
Advocate Health Care  
Park Ridge, IL

### **Ryan Gabriel, MD**

Diagnostic Radiologist  
Radiology Associates of Richmond  
Director of Breast Imaging  
Henrico Doctors' Hospital  
Richmond, VA

### **Brandi T. Nicholson, MD**

Breast Imaging Fellowship Director  
University of Iowa College of Medicine  
Iowa City, IA

Views and opinions expressed herein by third parties are theirs alone and do not necessarily reflect those of Hologic. This is a general information tool for medical professionals and is not a complete representation of the product(s)' Instruction for Use (IFU) or Package Insert, and it is the medical professionals' responsibility to read and follow the IFU or Package Insert.

The information provided may suggest a particular technique or protocol however it is the sole responsibility of the medical professional to determine which technique or protocol is appropriate. At all times, clinicians remain responsible for utilizing sound patient evaluation and selection practices, and for complying with all applicable rules and regulations regarding accreditation, anesthesia, reimbursement, and all other aspects of in-office procedures. In no event shall Hologic be liable for damages of any kind resulting from your use of the information presented.

This information is intended for medical professionals in the U.S. and other markets and is not intended as a product solicitation or promotion where such activities are prohibited. Because Hologic materials are distributed through websites, e-Broadcasts and tradeshow, it is not always possible to control where such materials appear. Not all products featured are available in all markets. For specific information on what products are available for sale in a particular country, please contact your local Hologic representative or write to [womenshealth@hologic.com](mailto:womenshealth@hologic.com).

Hologic, its products and The Science of Sure, including all associated logos are trademarks and/or registered trademarks of Hologic, Inc. and/or its subsidiaries, in the United States and/ or other countries.

**For additional resources and educational opportunities, please visit [www.HologicED.com](http://www.HologicED.com)**

MED-00525 Rev.001 (3/21) © 2021 Hologic, Inc. All rights reserved. Printed in USA. Specifications are subject to change without prior notice. Hologic is a trademarks and/or registered trademarks of Hologic and/or Hologic subsidiaries in the United States and/or other countries. All other trademarks and registered trademarks are the property of their respective owners. This information is intended for medical professionals in the U.S. and other markets and is not intended as a product solicitation or promotion where such activities are prohibited. Because Hologic materials are distributed through websites, eBroadcasts and tradeshow, it is not always possible to control where such materials appear. For specific information on what products are available for sale in a particular country, please contact your local Hologic representative or write to [womenshealth@hologic.com](mailto:womenshealth@hologic.com).

