Seminars in ULTRASOUND CT and MRI

Contrast Enhanced Spectral Mammography: A Review

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Contrast-enhanced spectral mammography (CESM) provides low-energy 2D mammographic images comparable to standard digital mammography and a post-contrast recombined image to assess tumor neovascularity similar to magnetic resonance imaging (MRI). The utilization of CESM in the United States is currently low but could increase rapidly given many potential indications for clinical use. This article discusses historical background and literature review of indications and diagnostic accuracy of CESM to date. CESM is a growing technique for breast cancer detection and diagnosis that has levels of sensitivity and specificity on par with contrast-enhanced breast MRI. Because of its similar performance and ease of implementation, CESM is being adopted for multiple indications previously reserved for MRI, such as problem-solving, disease extent in newly diagnosed patients, and evaluating the treatment response of neoadjuvant chemotherapy.

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Introduction

Screening mammography was proven in randomized clinical trials in the 1960s and 1970s to reduce breast cancer mortality and is a relatively low cost and rapid test for breast cancer screening.[1,2] The technology used in the original trials, screen-film mammography, has since been nearly completely replaced by full field digital mammography (FFDM), which was approved in 2000 for clinical use in the United States. Although more expensive in terms of equipment cost, FFDM improved efficiency, throughput, and digital information management. It was hoped that FFDM would also result in improved *diagnostic* performance, due to its superior contrast resolution (and despite its inferior spatial resolution). Unfortunately, FFDM did not prove to be significantly better than film mammography in sensitivity for cancer detection. Clinical studies in the US and Norway,[3-5] including the 50,000 subject U.S. ACRIN DMIST trial,[6] showed no overall sensitivity improvement, although the DMIST trial did demonstrate a modest benefit in younger women. Even as the results of these digital trials were being processed, research continued to progress on advanced applications of new digital technologies. Two applications that held the most promise included digital breast tomosynthesis and contrast-enhanced spectral mammography (CESM, or contrast-enhanced dual-energy mammography, CEDM).

The motivation for contrast-enhanced mammography (CEM) was the observation that cancers had been shown to preferentially take up intravenous contrast on breast magnetic resonance imaging (MRI) as its initial breast MRI results demonstrated nearly 100% sensitivity for invasive cancers.[7] The hope was that the increased contrast resolution of FFDM, as compared to film mammography, would enable contrast uptake to be demonstrated. However, because contrast resolution was still far inferior to that of CT or MRI, subtraction would have to be utilized. The commonly used method of *temporal subtraction*, where a pre-contrast image is subtracted from a post-contrast image, was first considered.[8] Although temporal subtraction was utilized in the cross-sectional modalities of both CT and MRI with great success, the technique had

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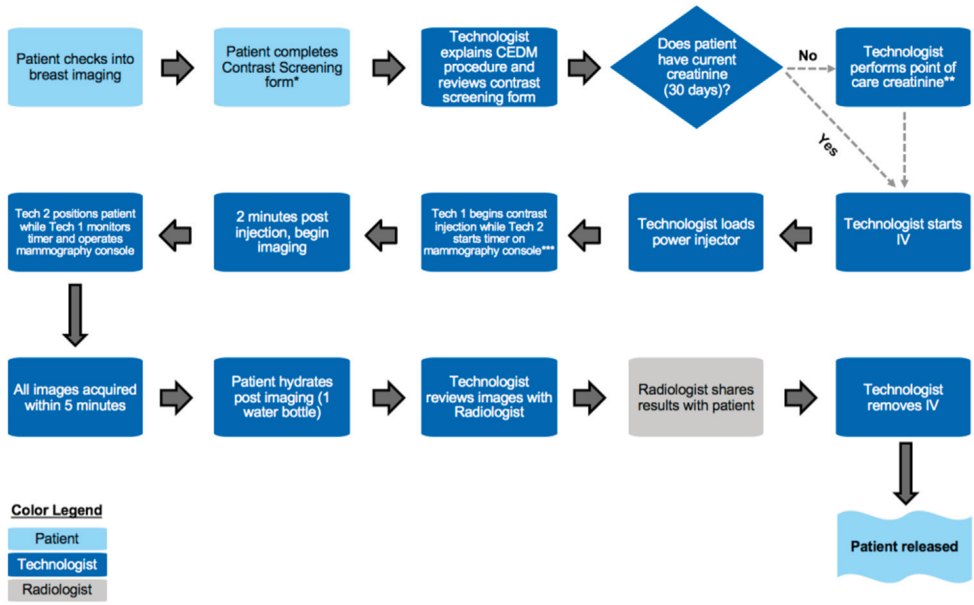
Table 1 Acquisition of the CESM Images



*Includes pregnancy test if indicated
**Patients screened for contrast induced nephroptahy if >70 years of age, history of diabetes or eGFR<30 in the past 2 years, history of renal disease, history of previous pelvic surgery in past 2 years, history of heart failure, or history of pre-cardiac transplant
***Imaging can be performed with one technologist if timer is available

specific limitations for a projection technique such as mammography. Because of the requirement for the pre-contrast (mask) image to be registered with the post-contrast image, only a single view of one breast could be obtained. Additional views or images of the other breast would require re-injection after the contrast had washed out, necessitating a second study on a different day. An added problem unique to mammography was that evidence from MRI biopsy suggested that breast compression, which is required to minimize movement between the mask image and the post-contrast images, limited contrast uptake to the breast 9. Overcoming this last obstacle by using only limited compression and reducing motion artifacts with image processing, Jong et al[10] published a series of single projection temporal subtraction CEM cases in 2003.

To overcome the limitations inherent in temporal subtraction, the technique of *dual-energy subtraction* was applied to CEM.[11] In dual-energy subtraction, a pair of low-energy and high-energy images are acquired *after* contrast administration and used to construct the final recombined image. Because the contrast has already been delivered to the breast, full compression can be used and, because a mask image is not needed, multiple images can be taken in a single examination, allowing both breasts to be studied and lesions to be localized using orthogonal projections. The two source images are combined to make an image that, by equalizing the density of fibroglandular tissue and fat, minimizes the appearance of breast tissue and increases the conspicuity of iodinated contrast agent. The low- and high-energy beams are created by adjusting the peak kilovoltage (kVp) of the x-ray tube and changing the filtration. kVp values between 28 and 32 are typically used for the low-energy beam and those between 45 and 49 are typically used for the high-energy beam. In addition, copper filtration is added to the high-energy beam to further harden it and images are combined using a weighted logarithmic subtraction. Before its use in contrast mammography, dual-energy imaging was utilized in chest radiography systems to increase the visibility of soft tissue by eliminating overlapping bones. More recently, body imagers have become familiar with dual-energy through its application to CT to improve the quantification of contrast uptake for perfusion studies.[12]

In comparison to temporal subtraction, dual-energy subtraction offers many advantages and has therefore become the standard for CEM. Dual-energy CEM-capable devices are commercially available from multiple vendors and are approved for clinical use in most countries, including the U.S. Over 100,000 CEM examinations have been performed to date in both research and clinical settings (Table 1).

To perform a CESM examination, a low osmolar iodinated contrast agent, similar to what is used in CT, is administered using a power injector at a rate of 2-3 mL/s. Contrast agents with concentration between 300 and 370 mgI/ml are typically used and the volume of contrast is like that used for an abdominal CT scan, approximately 1.5 mL/kg of body weight. Approximately 2 minutes after the injection, the patient is positioned as they would for a standard mammogram and a dual-energy image pair is acquired. Acquisition of an image pair typically takes less than 6 seconds and additional projections may then be obtained. A typical 4-view exam takes about 10 minutes to perform, similar to the time needed for a standard 4-view mammography exam, although the total "room-time" is slightly more than standard FFDM given the time required to prepare and administer the intravenous contrast administration (Table 2). The order of image