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# Navigating contrast-enhanced digital mammography

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**C**ontrast-enhanced digital mammography (CEDM) takes sequential images at high and low energies that are used to construct a digitally subtracted image, highlighting areas of contrast medium enhancement. The low-energy image is of the same diagnostic quality as standard 2-dimensional mammography.<sup>1</sup> However, the digitally subtracted image is unlike those that mammographers are accustomed to interpreting and its use initially may be overwhelming.

With this paper, the authors aim to increase understanding of normal anatomic and non-anatomic structures encountered on subtracted images and increase awareness of commonly encountered artifacts. In addition, the authors outline a standardized reporting system to help further streamline interpretation and reporting of CEDM images.

## What is CEDM?

CEDM is a quick, well-tolerated, relatively low-cost breast imaging technique that combines standard full-field

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digital mammography (FFDM) with an intravenous, low-osmolar, iodinated contrast medium. After administration of contrast material in the antecubital vein, 2 sequential images are acquired at high and low energies. The low-energy image (26-32 kVp) yields soft tissue and calcification detail similar to standard FFDM;<sup>2</sup> the high-energy image (45-49 kVp) is specifically selected to be greater than the K-edge of iodine (33.2 keV).<sup>3</sup> These 2 images are then digitally subtracted from each other to produce a single contrast medium-enhanced image that highlights areas of neovascularity, similar to magnetic resonance imaging (MRI).

Numerous studies have demonstrated increased sensitivity and specificity of CEDM compared with either FFDM or FFDM combined with ultrasonography.<sup>4</sup> In addition, CEDM rivals the sensitivity of more costly and time-consuming examinations, such as MRI and molecular breast imaging.<sup>5-9</sup>

Dromain et al,<sup>4</sup> Jochelson et al,<sup>5</sup> Fallenberget al,<sup>3</sup> and Luczynska et al<sup>10</sup> compared the sensitivity and specificity of CEDM with FFDM. In all 4 cohorts, CEDM showed greater sensitivity (93%-100%) and specificity (41%-85%) in the

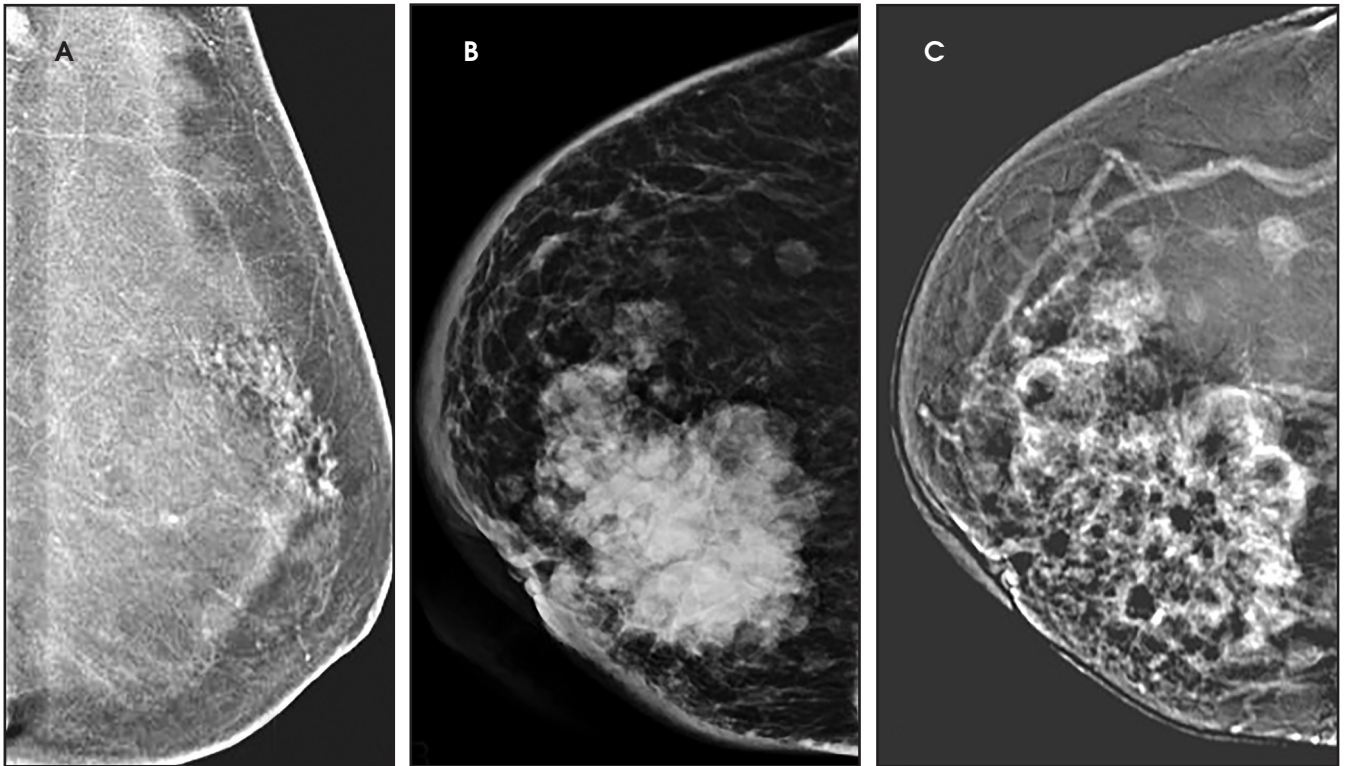
detection of breast cancer than FFDM (sensitivity, 78%-91%; specificity, 15%-58%). In 2011, Dromain et al<sup>4</sup> compared CEDM with FFDM and ultrasonography. They found that CEDM had a sensitivity of 93% vs a sensitivity of 90% for FFDM with ultrasonography, as well as improved specificity (63% for CEDM vs 47% for FFDM with ultrasonography). In a comparison of CEDM with MRI, 2 studies have shown that CEDM is similar to MRI. Jochelson et al<sup>5</sup> found that CEDM and MRI have equal sensitivity (96%), and Fallenberget al<sup>6</sup> found CEDM to have 100% sensitivity compared with 97% sensitivity for MRI.

## CEDM Appearance of anatomic, non-anatomic structures

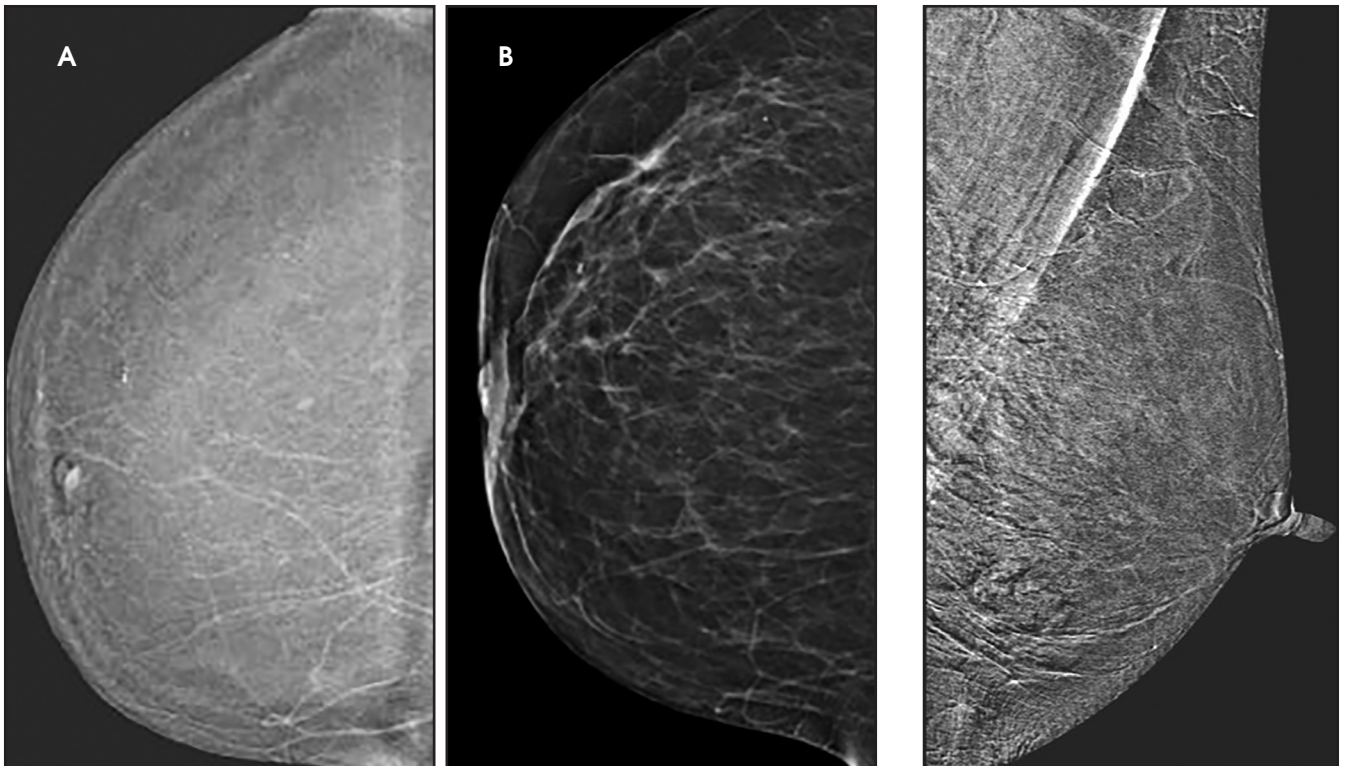
Two fellowship-trained breast imagers (B.K.P. and V.J.P.) performed a retrospective review of 110 CEDM cases conducted at our institution to evaluate the appearance of various anatomic and non-anatomic structures and artifacts in each subtracted image.

### *Anatomic structures*

**Skin**—The appearance of the skin on a CEDM-subtracted image can be variable (Figure 1). Predominately, the skin



**FIGURE 1.** Skin appearance. (A) Mediolateral oblique subtraction image illustrates a thin line of skin enhancement, which is a common benign finding. The low-energy (B) and subtraction craniocaudal (C) views show pathologic skin thickening and enhancement of a biopsy-proven breast carcinoma.



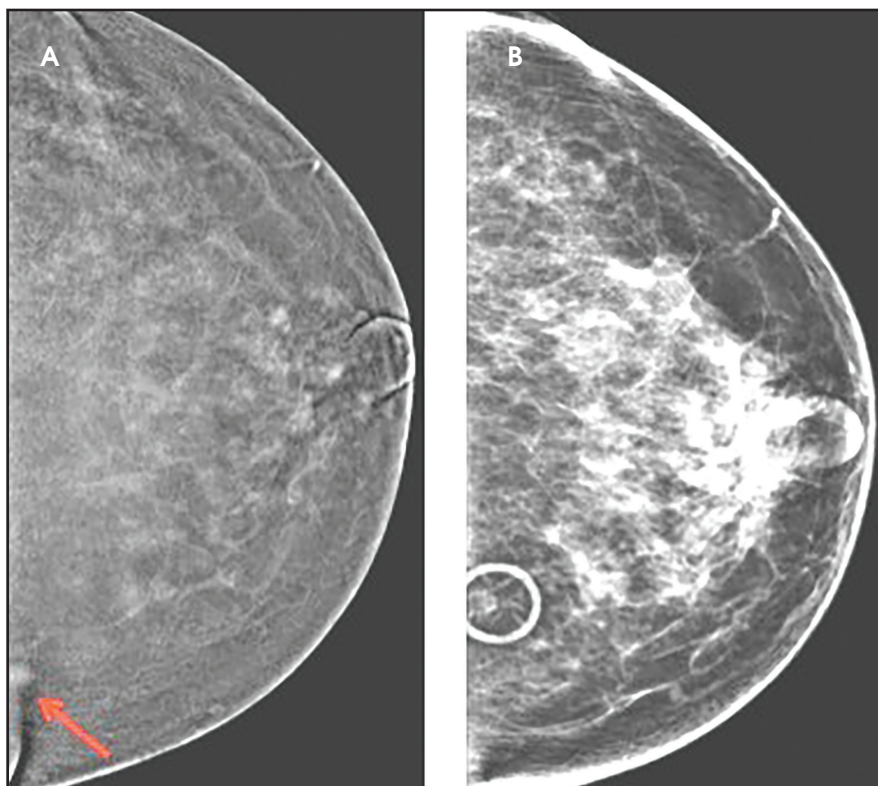
**FIGURE 2.** Nipple out of profile. (A) The subtraction view shows a mass with corresponding enhancement in the anterior right breast. This was thought to possibly represent an out-of-profile nipple, mimicking an enhancing mass. (B) Craniocaudal view with the nipple in profile, confirming no retroareolar mass.



**FIGURE 3.** Pectoral appearance. Mediolateral oblique subtraction image shows pectoral outlining.



**FIGURE 4.** Vessels. Similar to magnetic resonance imaging, subtracted images show enhanced vessels. Subtraction mediolateral oblique images show typical enhancing vessels on the right. The left image shows a breast with an enhancing biopsy-proven carcinoma with associated angiogenesis. Of note, a prominent enhancing axillary lymph node is also seen.



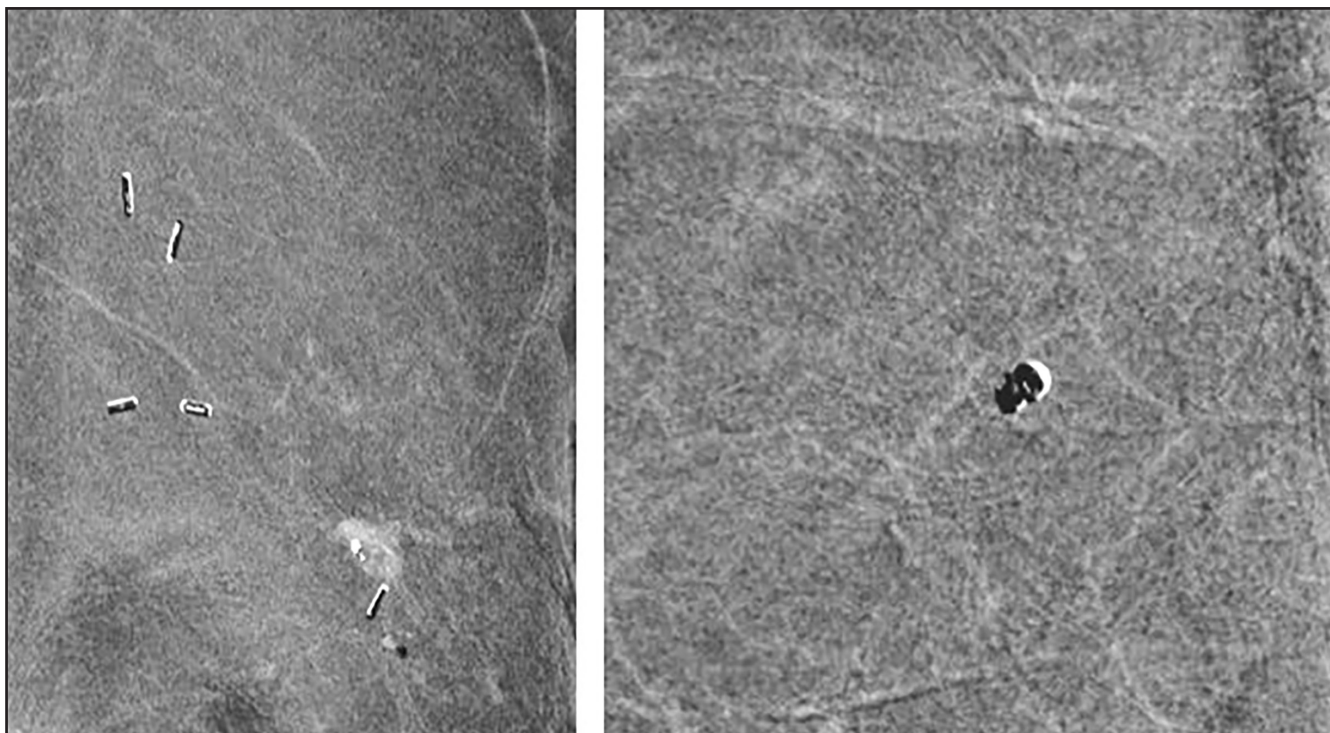
**FIGURE 5.** Mole enhancement. (A) Left craniocaudal subtraction image shows a small oval area of enhancement (arrow) in the medial, posterior breast. On further examination of the low-energy image, a rim of air appears to surround an oval density in this area, suggestive of a skin lesion. (B) Repeat craniocaudal 2-dimensional image of the left breast taken after a mole marker was placed, confirming that the oval enhancing lesion corresponded to a cherry angioma.

is nonenhancing or shows a thin line of enhancement. Rarely, it shows artifactual thickening not seen on the standard 2-dimensional image. This artifact is thought to be related to current detector limitations in regard to high-energy X-ray doses. Given the variable appearance of the skin on subtraction images, any findings should be correlated with the low-energy image. Patient presentation of skin enhancement and thickening on the subtraction images can differ and should be evaluated on the standard low-energy mammography image.

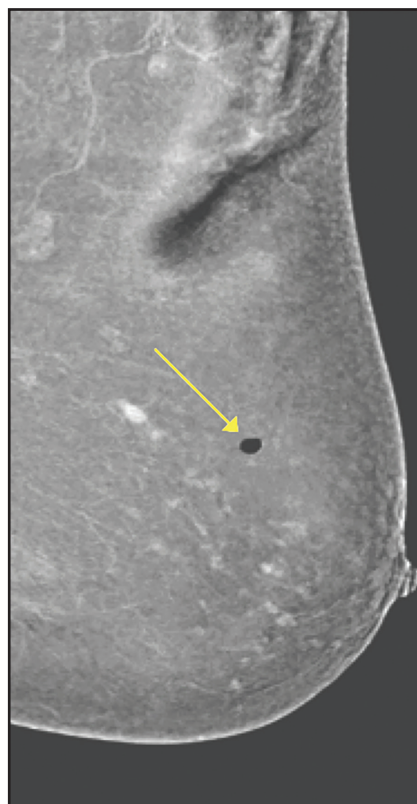
**Nipple**—Peripheral superficial enhancement of the nipple is commonly seen on MRI, attributable to the rich blood supply of the nipple areolar complex.<sup>11, 12</sup> Conversely, the subtraction image on CEDM can yield various appearances of the nipple. The most common is that of no enhancement. Occasionally, a thin dark line is seen at the base of the nonenhancing nipple, which may give the illusion of a thin rim of peripheral enhancement. A less common appearance is minimal enhancement at the base of the nipple. In patients with flat nipples, a prominent thin rim of enhancement may be seen contiguous with the adjacent skin. The differences in nipple enhancement between MRI and CEDM are likely secondary to a combination of the differing contrast agents used and the compression applied with CEDM.

As with typical FFDM, every effort should be made to place the nipple in profile. When the nipple is not in profile (Figure 2A) the nipple may be mistaken for an enhancing mass within the anterior breast. By comparison, an image showing the nipple in profile allows for better detection of subareolar masses and helps prevent the nipple from being mistaken for a mass (Figure 2B). When limitations prevent the nipple from being placed into profile, a BB marker should be used to denote its location.

**Pectoralis muscle**—The majority of pectoralis muscles do not show enhancement on subtracted images. However,



**FIGURE 6.** Misregistration artifact. Subtraction images from two patients show misregistration artifact. Surgical clips seen on the subtraction image of the left panel show side-by-side bright and dark lines, causing so-called zebra artifact from the misregistration. Zebra artifact is present in the right panel as well, on the subtraction image of a dystrophic calcification.



**FIGURE 7.** Calcifications. A round calcification (arrow) shows the expected dark appearance on subtraction image.

a small percentage (11%) of subtracted images demonstrate pectoral outlining, which mimics faint enhancement (Figure 3). Pectoral outlining is an artifact attributed to patient motion and does not indicate inflammation or pathologic change within the muscle itself. Therefore, misregistration artifact, similar to that seen in MRI with patient motion, may be present when pectoral outlining is seen.

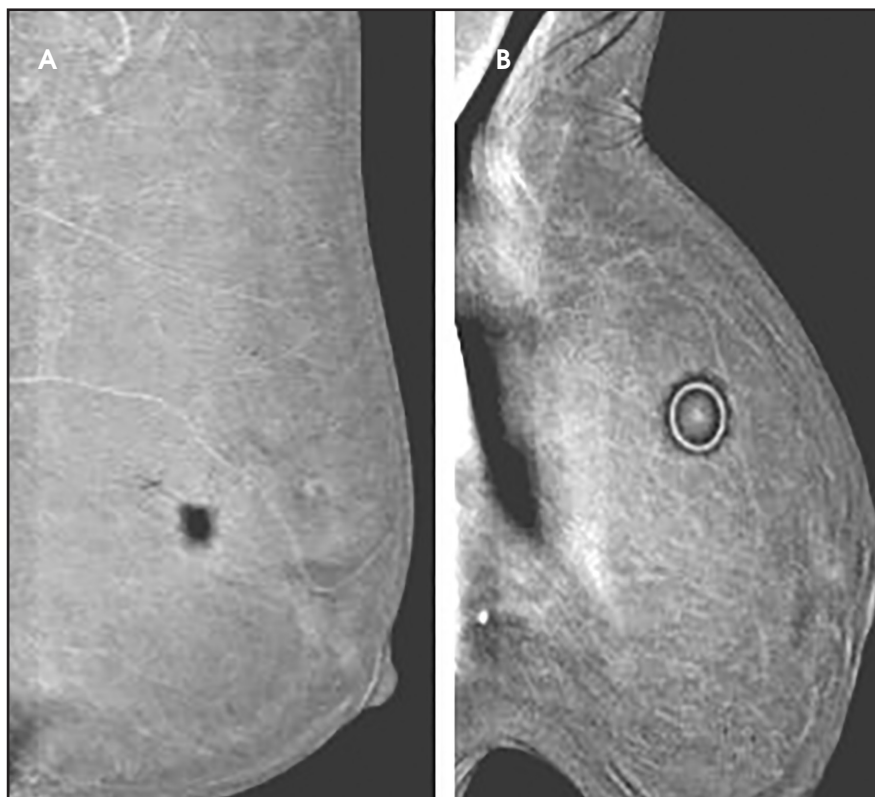
**Vessels**—Vessels enhance more prominently and wash out on the first view than on subsequent views, similar to results of MRI (Figure 4). Also similar to MRI, when breast cancer is present, neoangiogenesis results in an increased number of enhancing vessels supplying the affected breast.<sup>13</sup>

**Lymph nodes**—Although lymph nodes are most commonly found in the axilla, intramammary lymph nodes can be seen in up to 47% of breasts.<sup>14</sup> These findings are typically seen in the upper outer quadrants. Normal axillary and intramammary lymph nodes have

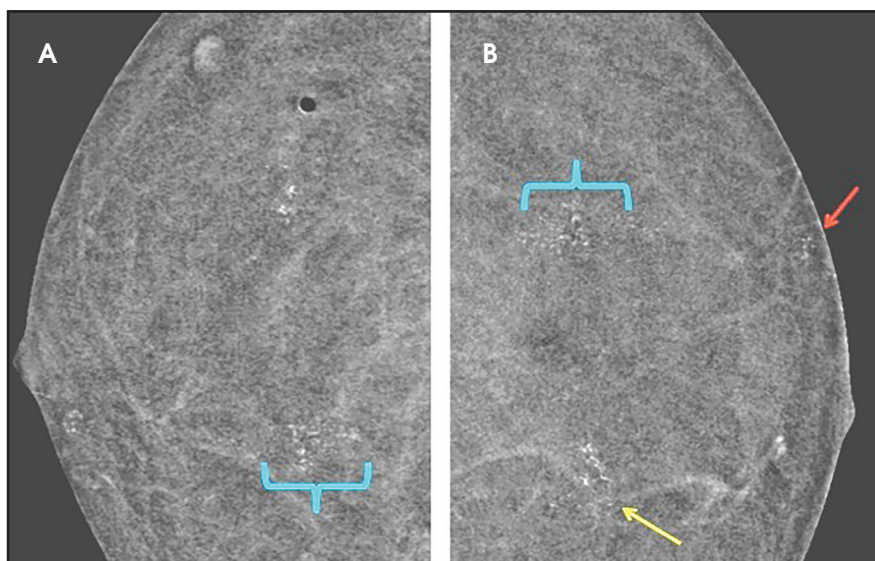
characteristically benign appearances, including circumscribed margins; oval, round, or reniform shape; a fatty hilum; and proximity to a vessel.

Lymph nodes show various degrees of enhancement on CEDM images whereby the enhancement is not necessarily indicative of pathologic characteristics. Similar to MRI, normal lymph nodes may enhance avidly, whereas abnormal lymph nodes may not enhance at all.<sup>15</sup> Evaluation of lymph node size and morphologic characteristics, as well as assessment of stability over time, is essential. Abnormal lymph nodes may show a more rounded appearance because the typical nonenhancing hilum becomes replaced by tumor. The enhancement pattern usually becomes more heterogeneous with increased lymph node size and may be secondary to metastatic implants or areas of necrosis.

**Enhancing skin lesions**—Skin lesions with increased vascularity, especially cherry angiomas, can demonstrate contrast enhancement on CEDM images



**FIGURE 8.** Additional artifacts. Incomplete contact of the skin with the paddle creates air gaps, causing a dark artifact. (A) shows an air gap in the mid left breast. (B) shows a dark curvilinear artifact with the skin fold of the left upper breast and axillary tissue. In addition, a dark halo, resulting from image processing artifact, is depicted surrounding the mole marker.



**FIGURE 9.** Contrast contamination. Subtracted right and left craniocaudal images show multiple areas of non-mass enhancement in both breasts (arrows and brackets). On further examination, the imaged areas of presumed enhancement in the right breast are exact mirror images of those in the left breast. For example, the small area of presumed enhancement in the right medial breast, anterior depth (A, bracket), corresponds to a similar area of enhancement in the left lateral breast, anterior depth (B, bracket and arrows). The mirror-image nature of the presumed enhancement suggests external contrast medium contamination of paddle and detector.

and mimic cancers. However, in our experience, typical moles and seborrheic keratoses do not enhance. An example of the importance of placing mole markers on potentially enhancing skin lesions is shown in Figure 5.

### *Non-anatomic structures*

**Clips**—Placing clips after breast biopsy is common. Highly attenuated objects, such as clips and calcifications, can show a variable appearance. This variation depends on a demetal function that is intrinsic to CEDM software (Hologic, Inc). When the demetal function is off, clips and calcifications appear dark; in the enabled position, these structures appear bright. Currently, because artifacts can be caused by the demetal function, the default within the Hologic system is the off position. Future Hologic software upgrades are expected to fix these artifacts and allow the demetal function to remain on, giving clips and calcifications the bright appearance of which most mammographers are accustomed. A third type, that of alternating bright and dark appearance, gives a zebra artifact and is secondary to motion-causing misregistration (Figure 6). Misregistration is commonly seen.

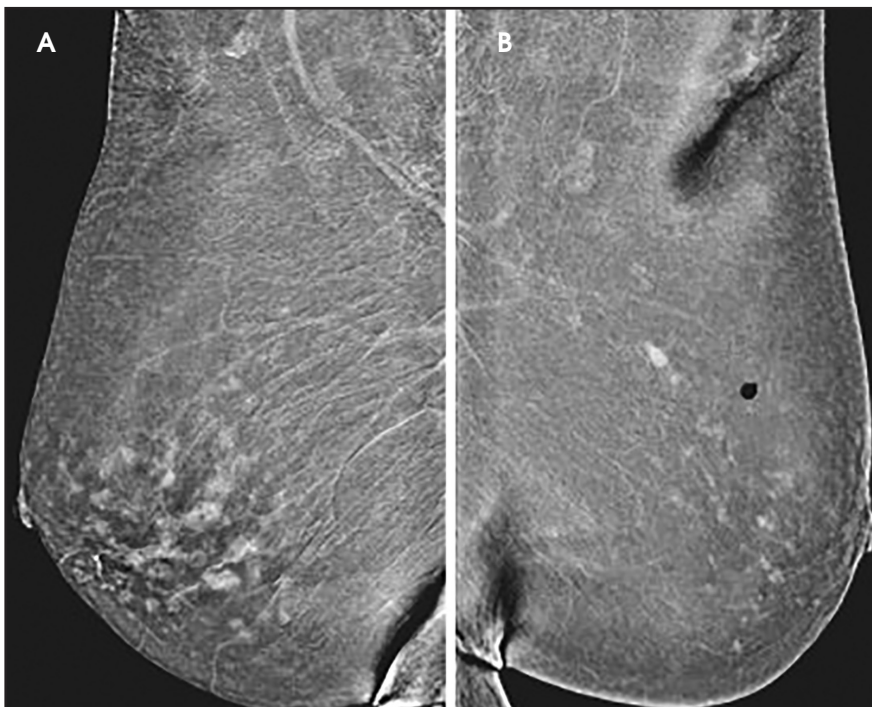
**Calcifications**—Because the demetal function is defaulted to the off position, most calcifications are dark on subtracted images. However, microcalcifications (<0.5 mm) seen on the low-energy image appear to be occult, without a dark (Figure 7) or bright appearance. In some instances where the demetaling function was inadvertently turned on between views, calcifications appeared dark on one view but bright on the other view. Larger calcifications may not appear uniformly dark when misregistration is present (Figure 6, right panel). For these reasons, it is important to use the low-energy images to evaluate breasts for microcalcifications.

### *Artifacts*

**Misregistration**—Given that the high-energy and low-energy images



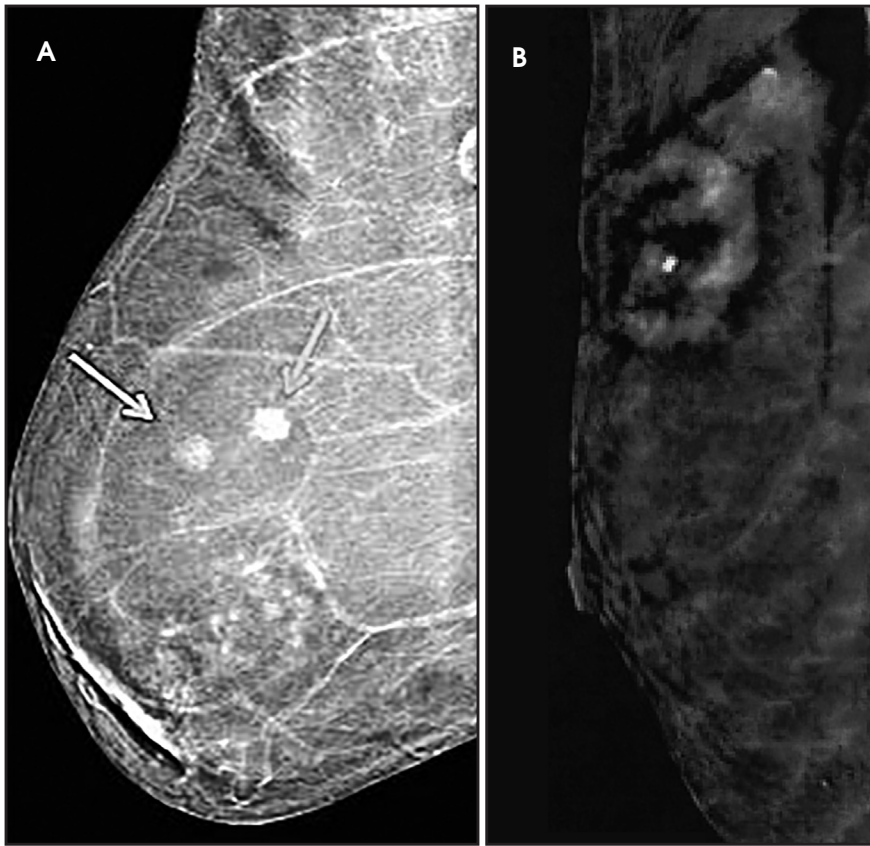
**FIGURE 10.** Background enhancement. Contrast-medium enhanced digital mammography reports should include the degree and symmetry of background enhancement. Subtraction images from three patients show minimal (A), mild (B), moderate (C), and marked (D) background parenchymal enhancement.



**FIGURE 11.** Asymmetrical background enhancement. Subtraction images show asymmetrical enhancement: mild on the left breast (A) and moderate on the right breast (B).

are acquired one immediately after another, the potential for motion exists and can cause misregistration artifact. Misregistration between the two images results in adjacent dark and bright areas, causing so-called zebra artifact. This artifact has been seen related to clips, vessels, and calcifications (Figure 6).

**Air gap and other high-attenuation artifacts**—In our experience with CEDM, the most common artifact results from an air gap. Partial contact between the skin and the detector or compression paddle creates a dark artifact that takes the configuration of an area of incomplete contact. Imperfect contact may result from improper compression, skin dimpling, or skin folds (Figure 8). Similar to clips and calcifications, a dark halo appearance can be seen around other high-attenuation items, such as mole markers, scar markers, BB markers, pacemakers,



**FIGURE 12.** Lesion enhancement. Contrast-enhanced digital mammography reports should include the degree of lesion enhancement. Subtraction images from two different patients show various degrees of enhancement. (A) The anterior lesion (yellow arrow) shows mild enhancement and corresponds to a biopsy-proven hamartoma. The posterior lesion (red arrow) shows moderate enhancement and was a biopsy-proven invasive ductal carcinoma. (B) Marked enhancement can be seen in the large biopsy-proven invasive ductal carcinoma of the right upper breast.

and chest ports secondary to an image-processing artifact.

**Contrast contamination**—Contrast material external to the patient, such as on the skin, the paddle, or the detector, can cause superimposed bright artifacts. In a CEDM examination, caution is critical to prevent contamination. Figure 9 shows a case that was initially presumed to have multiple, bilateral areas of abnormal enhancement. On further review of the images, the areas of supposed enhancement showed a mirror image configuration suggestive of contrast contamination of the paddle or detector, or both.

### CEDM Evaluation and reporting

No reporting method for high-energy subtracted CEDM images has been established. Our institution has

adopted a standardized reporting system through the Breast Imaging–Reporting and Data System (BI-RADS) lexicon, similar to those already published for mammography, ultrasonography and MRI.<sup>16</sup>

The low-energy image is interpreted as a standard mammography scan. Breast density (ie, almost entirely fat, scattered areas of fibroglandular densities, heterogeneously dense or extremely dense)<sup>16</sup> is included in the report, in addition to pertinent imaging findings.

The next section in the CEDM report describes the findings on the subtracted image. The background parenchymal enhancement (BPE) is described (similar to BI-RADS MRI BPE) in 1 of 4 categories: minimal, mild, moderate, and marked (Table

and Figure 10). Minimal BPE is defined as enhancement of 0% to 24%; mild as enhancement of 25% to 49%; moderate as enhancement of 50% to 74%; and marked as diffuse generalized enhancement of 75% to 100%.

Similar to MRI, increased BPE may result in increased call-back rates. BPE is graded as symmetrical or asymmetrical between the breasts and, similar to MRI, asymmetrical enhancement can be seen because of benign and malignant causes, including those in patients with a history of radiation treatment or extensive pathologic manifestation in one breast (Figure 11).<sup>17</sup>

Findings described on low-energy mammography, such as calcifications, asymmetries, and masses, are further evaluated for any corresponding areas of abnormal enhancement on the subtracted images. Areas of abnormal enhancement are described further as *mass* or *non-mass* enhancement.

The term *mass enhancement* is used to describe a space-occupying lesion with mass-like borders; the term *non-mass enhancement* describes an asymmetry without clear borders.<sup>16</sup> Determination of mass or non-mass enhancement is best made through interrogation of the low-energy image in conjunction with the subtracted image, because the shape and margins are often better delineated on the low-energy image. Both mass and non-mass enhancements are described by their quadrant location and given a 3-dimensional measurement.

In addition, areas of mass enhancement are described by their enhancement pattern, including homogeneous, heterogeneous, or rim enhancing. The degree of mass or non-mass enhancement is documented using 1 of 4 categories: none, mild, moderate, or marked. Finally, pertinent findings regarding structures outside the breast parenchyma (eg, axilla, skin, nipple) are reported (Figure 12).

### Conclusion

CEDM is a novel modality that continues to show improved sensitivity

in breast cancer detection compared with standard mammography. Studies reported in the literature continue to measure the performance of CEDM compared with standard mammography, MRI, and other breast-imaging modalities. We provide the first guide, to our knowledge, for radiologists and clinicians in interpreting the contrast-enhanced subtracted images. In providing case examples of the encountered anatomic and non-anatomic artifacts in our practice, we hope to ease the transition and help troubleshoot questions that may arise during the initial interpretation. A BI-RADS-based reporting structure is offered to enable consistent, quality-driven reports for clinicians.

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