# Contrast-Enhanced Digital Mammography

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**KEYWORDS**

• Digital mammography • Contrast • Neovascularity • MR imaging

**KEY POINTS**

- Contrast-enhanced mammography can improve the sensitivity of digital mammography.
- Contrast-enhanced mammography is less sensitive but more specific than breast MR imaging.
- Contrast mammography is significantly less expensive than MR imaging and could potentially be used for screening patients who are unable to undergo breast MR imaging.

## CONTRAST-ENHANCED MAMMOGRAPHY

Mammography remains the only breast screening examination proved to reduce breast cancer mortality in the general screening population. Multiple randomized studies have demonstrated a 30% to 40% reduction in mortality for women actually screened.[1–3] Mammography is inexpensive and widely available, but its sensitivity is limited: 70% to 85% overall but dropping to 30% to 50% in high-risk women with dense breast tissue.[4–6]

Certain breast cancers are more likely to be associated with false-negative mammograms. Among them are lobular carcinomas, which grow in a linear pattern and, therefore, may not form a discrete mass, and noncalcified ductal carcinoma in situ. Small nonspiculated masses are common sources of false-negative mammograms. Oval-shaped circumscribed masses may be misinterpreted as benign.

Once a cancer is diagnosed, mammography may underestimate the size and/or extent of a primary tumor. As a result, re-excision is necessary in approximately 30% of patients[7,8] undergoing breast conservation. Also, mammography may not identify additional foci of malignancy in other quadrants of the breast.

There is continuing improvement in mammography, most recently due to the conversion from analog to digital mammography. Although digital mammography does not improve the overall sensitivity of mammography, it has been shown to improve sensitivity in women with dense breast tissue.[9] More importantly, digital mammography has provided a template on which to develop more-advanced breast imaging technology. Tomosynthesis was developed as a method to image the breast by removing overlying layers of breast tissue so that lesion characteristics and margins are better seen. This topic has been discussed in an article elsewhere in this issue. As stated by Johns and Yaffe,[10] however, removal of overlying structures may not be sufficient to guarantee lesion detection because the difference in attenuation coefficients between fibroglandular and cancerous tissue ranges from only 4% at 15 keV to 1% at 25 keV.

Contrast-enhanced mammography is the second type of advanced technology stemming from the digital platform. The theory behind contrast mammography is based on the success of breast MR imaging, which is currently the most sensitive of all breast imaging techniques, with sensitivities reported up to 98%.[11,12] MR imaging detects

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occult breast cancers in approximately 4/100 to 5/100 high-risk women. It also detects occult multifocal or multicentric cancers in approximately 16% of all patients with known breast cancer.[13] The exquisite sensitivity of MR imaging is the result of a combination of anatomic and physiologic imaging. The physiologic component of MR imaging is primarily its ability to detect enhancing tumor vascularity after contrast administration. Tumor vascularity may be detected before a discrete mass is present. As a result, MR imaging has been shown to demonstrate cancers at an earlier stage in high-risk women who are screened yearly with MR imaging compared with those screened with mammography alone.[14] In this population, MR imaging has also been shown to improve overall survival (93% vs 74.5% in historical cohorts).[15,16]

MR imaging is expensive and time consuming, however, and cannot be performed on all patients. Additionally, good-quality MR imaging is not universally available. Women who are claustrophobic and women with pacemakers or other implanted metallic materials cannot undergo breast MR imaging. Therefore, there is a need for an alternate method to use both contrast enhancement and anatomy for detection of breast cancer. The performance of mammography using contrast material to diagnose breast cancer has been studied for several decades.

## DIGITAL SUBTRACTION ANGIOGRAPHY

In 1985, Ackerman and colleagues[17] reported their experience using digital subtraction angiography (DSA) of the breast in 22 patients in an attempt to differentiate benign from malignant disease without performing a surgical biopsy. They injected 30 mL of contrast at 25 mL/s into the right atrium; 32 to 40 images were obtained. In this initial group there were 7 true positive results, 11 true negative results, 2 false-positive results, 1 false-negative result, and 1 equivocal case. These results must be interpreted, however, with caution. One of the malignant lesions was considered a true negative because the mammogram was negative. Additionally, lesions less than 2 cm were not well seen. This somewhat invasive procedure, therefore, did not perform well enough to continue with its use.

It was observed that the degree of tumor angiogenesis correlates with tumor growth and metastatic potential.[18] Haga and colleagues[19] investigated whether tumor enhancement on DSA correlated with disease-free survival. They performed DSA in 103 women and found all tumors enhanced. They compared maximum densities of enhancement and demonstrated that higher densities of enhancement were associated with decreased disease-free survival.

## TEMPORAL TECHNIQUE

More recently, contrast-enhanced mammography has been performed using a temporal technique. A baseline image is obtained in a single view performed just above the K-edge of iodine (33 KeV) with the breast mildly compressed. The same iodinated contrast used for CT scans is injected intravenously after which multiple images of the breast are obtained over a period of 5 to 7 minutes. The noncontrast image is subtracted from the contrast images. This technique is successful in detecting cancers. Jong and colleagues[20] studied 22 women who were to undergo breast biopsies for suspected breast cancers. They demonstrated enhancement in 8/10 (80%) of the cancers in their study. Seven of 12 benign lesions did not enhance, but there were 5/22 (23%) false-positive examinations. These included 3 fibroadenomas and 2 patients with fibrocystic changes.

Diekmann and colleagues[21] performed a multireader study involving 70 patients with 80 lesions and demonstrated that the addition of contrast to digital mammography improved sensitivity from 43% to 62%. Not surprisingly, improvement in sensitivity was more likely to occur in women with dense breasts than women with fatty breasts. Dromain studied 20 women with suspicious mammographic findings. There was enhancement in 16/20 (80%) cancers. The size of 97% of the tumors correlated well with size at histology. In her study, the enhancement curves in the cancers differed from those seen with MR imaging. With contrast-enhanced mammography, most cancers demonstrated gradually increasing enhancement as opposed to the rapid enhancement with washout pattern classically seen with cancers on MR imaging. Rapid enhancement with wash out was only seen in 4 of the patients having contrast mammography. It is uncertain as to whether this difference in enhancement pattern is related to the breast compression performed with the temporal technique or is a characteristic of the difference between gadolinium and the iodinated contrast used for contrast mammography. Additionally, the enhancement patterns in Dromain and colleagues'[22] series did not correlate with the microvessel counts demonstrated on pathology.

Although the technique of temporal contrast-enhanced mammography is able to demonstrate cancers with good sensitivity, there are several disadvantages associated with this technique.