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EDITORIAL COMMENT

# Contrast-enhanced mammography for screening recalls: a problem-solving assessment tool ready for use?

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Full-field digital mammography (DM) is the standard technique as of today for breast cancer screening, although digital breast tomosynthesis (DBT) is increasingly used in some countries, especially in the USA. Conventional DM has, however, two important limitations as a screening technique: a low sensitivity in women with dense breast parenchyma due to a masking effect, and a relatively low specificity due to superpositioning causing so-called pseudotumors. Non-conclusive findings at standard two-view mammographic screening need recall and further diagnostic work-up including supplementary mammographic views, ultrasound, digital breast tomosynthesis (DBT), MRI, and/or needle biopsy to confirm or exclude the presence of cancer. Adverse effects of mammography screening include false-negative interpretations causing interval cancer and false positive findings causing unnecessary recalls. Assessments of false-positive screening recalls represent a great problem not only to the women often causing psychologic distress and transient anxiety but also to the health care providers since unnecessary work-up including needle biopsies are expensive and represent a financial burden. Consequently, there is a need for a single diagnostic test with high diagnostic accuracy that could replace the several procedures included in today's standard work-up for screening recalls.

Contrast-enhanced mammography (CEM) has the potential to solve these challenges and make the assessment of screening recalls simpler and more straightforward. More than a decade ago it was shown that CEM has better diagnostic accuracy than mammography alone and mammography plus ultrasound [1]. The technique is based on the DM platform in which dual-energy mammograms of both breasts in standard projections (cc- and mlo-views) are acquired after intravenous injection of iodinated contrast material [1, 2]). The low-energy images are similar to conventional digital mammograms and consequently may replace the standard DM images. The high-energy images are used for post-processing purposes and may demonstrate changes in breast perfusion caused by tumor angiogenesis similar to MRI and may serve as an alternative to breast MRI [2]. The highest diagnostic performance is achieved when interpretation includes both low-energy and recombined images and jointly consider lesion morphologic characteristics and contrast enhancement [3]. Important is the high performance in women with dense breasts, and CEM was shown to have higher sensitivity and negative predictive value in females with dense breasts compared to DBT alone or DBT combined with ultrasound [4].

In this issue of *European Radiology*, Cozzi et al [5] present the effect of CEM on biopsy rate in women recalled for assessment after DM screening. The study included 207 women with 225 suspicious findings prospectively enrolled to undergo CEM alongside standard assessment. The two assessments were independently evaluated and the biopsy rates were compared. The reader interpreting CEM had access to the original screening mammograms, and therefore CEM interpretation was focused on recombined (rCEM) images in order to evaluate the added value of functional information provided by the contrast-enhanced images. Overall, 135 of the 225 findings were referred for biopsy: 90 by both assessments, 41 by standard assessment alone, and 4 by rCEM alone. The rCEM biopsy rate was significantly lower than for standard assessment ($p < 0.001$), and the rCEM sensitivity for 124 (80 malignant and 44 benign) lesions having final histopathology was 93.8% (all 5 false negatives being DCIS detectable as calcifications on low-energy images) and the specificity was 65.9%. The conclusion of this study was that rCEM-based assessment would have avoided biopsy for 16.4% suspicious mammographic findings compared with standard work-up.

Overall, the findings by Cozzi et al [5] confirm results from previous studies that CEM has the potential as a problem-solving tool for the assessment of screening recalls [6]. A

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practical advantage is the short learning curve as demonstrated by increased diagnostic accuracy even for less experienced radiologists [6]. Severe adverse reactions to iodinated contrast material are rare. Limitations of CEM, similar to all imaging tests, include both false positive and false negative results. Benign breast tumors including fibroadenomas may show contrast enhancement and requiring further assessment including ultrasound and/or core needle biopsy. Fibroadenomas and superposition densities have been reported as the most common causes of false positives [6]. DCIS presenting with calcifications may show no or extremely faint associated contrast enhancement on recombined (rCEM) images, but the low-energy images will demonstrate the calcifications and permit a correct diagnosis [5]. In general, CEM only slightly improves the diagnostic accuracy of calcifications and is not of added value compared to DM in guiding surgical decision-making [7]. Indication for CEM in the assessment of microcalcifications could be women with dense breasts to exclude invasive cancer components or masses not shown on DM. Breast cancers including invasive lobular carcinoma (ILC) presenting as small spiculated masses or architectural distortion represent a diagnostic challenge in screening and may easily be missed in women with dense breasts. ILCs may show weak or even no contrast enhancement at CEM, and enhancement is obviously more often weak in ILCs than in IDCs [2, 8]. Caution is mandatory when using CEM as assessment procedure for suspected distortions at DM screening. Overall, there is a significant correlation between the degree of contrast enhancement in CEM and malignancy [9], but there are no established enhancement thresholds between benign and malignant lesions. The highest diagnostic accuracy is achieved when CEM is interpreted using both low-energy and recombined images and jointly consider lesion morphology and enhancement [3]. There is a need for systematization of CEM interpretation, and future implementation of radiomics and artificial intelligence (AI)-based CAD technology has the potential to improve CEM diagnostics.

In conclusion, CEM is an emerging breast imaging tool that is easy to perform in daily clinical practice and is an alternative to MRI due to costs and availability. The main indication for this technique would be the assessment of screening recalls, but as of today, careful correlation of DM screening findings and CEM results is mandatory if CEM is used as a single assessment tool. Further studies, more evidence-based interpretation guidelines for benign-malignant criteria, and AI-based CAD technology might increase the usage of CEM as an important primary imaging tool in the assessment for subgroups of screening recalls.

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**Methodology**
• Editorial comment

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