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Role of dual-energy contrast-enhanced digital mammography as a problem-solving tool in dense breasts: A case report

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Abstract

Breast density is strongly and independently related to the risk of breast cancer. Women with very dense breasts may have up to five times higher chances of developing malignancy as compared to those with less breast density. Detecting lesions in extremely dense or heterogeneous breasts on screening mammogram can be difficult. We report a case of incidental bilateral breast malignancy in an asymptomatic patient in whom mammogram and screening ultrasound were equivocal.

Key words: Contrast-enhanced digital mammogram; dense breast; dual-energy digital mammogram; mammogram

Introduction

Dense breasts are strongly associated with breast cancer risk and could be assessed qualitatively by assessment of the parenchymal pattern or quantitatively by calculating the percent breast density.[1] Studies have shown attributable risk from increased breast density to be 28%-30% for 50% or greater density and 40%-44% for any breast density.[2,3] In comparison, less than 5% of breast cancers were attributable to breast cancer gene (*BRCA1* and *BRCA2*) mutations, making breast density one of the strongest risk factors for malignancy. The sensitivity of mammogram decreases from 98% for fatty breasts to 48% for dense breasts.[2] Screening USG in such patients may at times be non-contributory or even confusing. We present a case where incidental bilateral breast malignancies were detected following a contrast-enhanced digital mammogram (CEDM) and in whom both mammogram and ultrasound were equivocal.

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Case Report

A 55 year-old lady who complained of occasional heaviness in the left chest was referred to us from cardiac OPD. As she required no active cardiologic intervention, a screening mammogram was undertaken as a part of routine health check-up. There was no family history of any breast or gynecological malignancy and no prior breast imaging had been undertaken. Digital mammograms in both craniocaudal [Figure 1] and mediolateral [Figure 2] views were taken on a GE Senographe Essential and viewed on an IDI work station. Both breasts were extremely dense (>90%) with no definite area of mass lesion being noted. Few prominent left axillary lymph nodes were noted. Benign scattered calcifications were noted bilaterally with no evidence of microcalcifications. Clinically, both breasts had an irregular lumpy feel on palpation. On USG, a suspicious hypoechoic area was noted within the dense glandular tissue of left breast with evidence of intralesional vascularity. Two enlarged left axillary nodes were noted measuring 2.5-2.7 cm each, with preserved hilar architecture. Screening of right breast appeared unremarkable. In view of dense

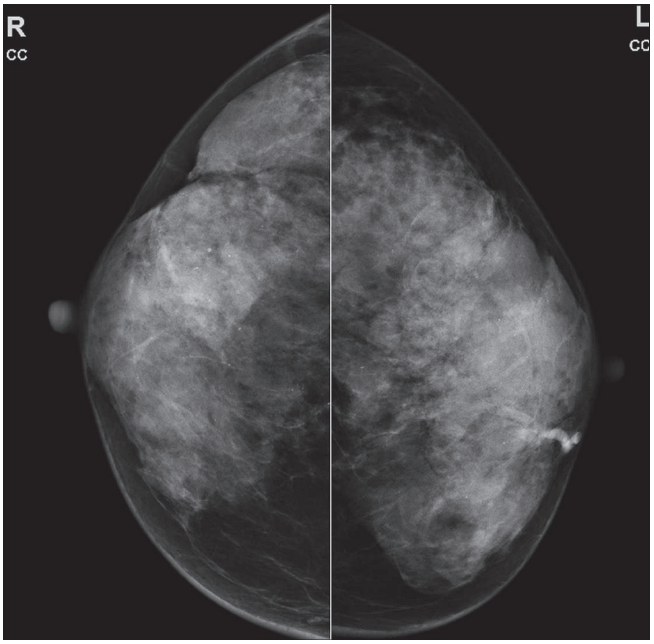

Figure 1: RCC and LCC views show dense fibroglandular breast tissue (>90%) in both breasts

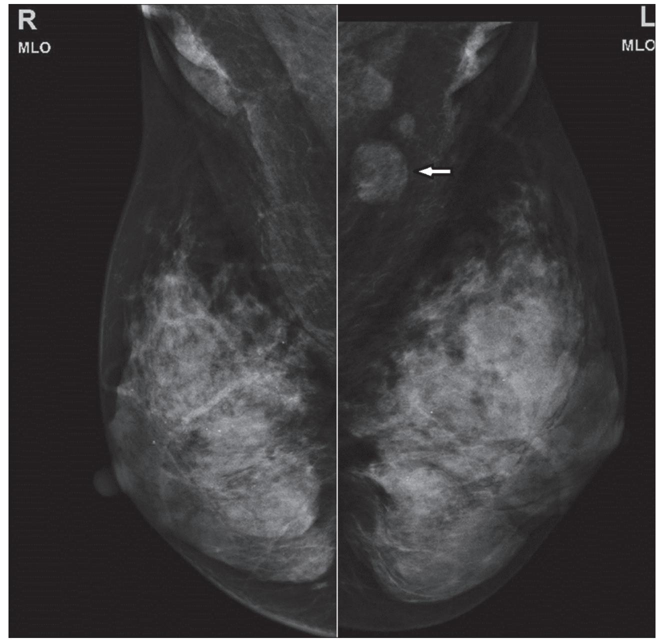

Figure 2: RMLO and LMLO views showing dense fibroglandular tissue with no definite mass lesion being noted. Enlarged left axillary node noted (white arrow)

mammogram and suspicious USG findings, the patient underwent a dual-energy CEDM. Baseline renal function of the patient was evaluated prior to contrast injection. Institutional review board approval and informed patient consent was obtained. Approximately 70 ml (at 1.5 ml/kg) of non-ionic contrast medium (Iomeron 350 mg/ml) was loaded into a Liebel-Flarsheim pressure injector. The rate was set at 3 ml/sec. The right (contralateral) antecubital vein was punctured and connected to the injector. A stopwatch on the console set at 0 sec was started simultaneously with initiation of contrast injection. The radiographer had a time gap of approximately 90 sec after cessation of contrast injection for positioning the patient for the right craniocaudal (RCC) view. This was taken at the 2nd minute. The left craniocaudal (LCC), right mediolateral (RMLO) and left mediolateral (LMLO) views were taken at 3rd, 4th, and 5th minute since start of the contrast, respectively. All images were acquired well within the 7-min cut-off as recommended by the manufacturer and as noted in various clinical studies.[4] Approximately 10 daN compression was applied for each exposure. All views were obtained using dual energy where the low-energy exposure was acquired using a Mo/Rh target/filter combination with tube voltages (kVp) ranging from 26 to 30 kVp. The high-energy images were acquired using Mo/Cu target/filter combination and with tube voltages in the range of 45-49 kVp. Within approximately 5 sec, a recombination algorithm, using the low-energy, high-energy X-ray spectra and the thickness of compressed breast produced dual-energy subtracted images which highlighted the iodine-enhanced areas. A small enhancing nodule was noted in the right breast centrally while a mass-like enhancement was noted in left breast lower inner quadrant in the respective CC views [Figure 3]. While the right breast lesion was no longer visualized, the left lesion was only subtly imaged in the respective MLO views, suggesting a probable rapid washout [Figure 4]. The enhancing left breast mass corresponded to the suspicious area noted on USG, while the focal nodular enhancement on the right corresponded to an isoechoic lesion which was completely missed on the initial scan. Both lesions were biopsied under ultrasound guidance in the same sitting. Histopathological evaluation revealed the right breast nodule to be a grade 1 and the left breast mass to be a grade 3 invasive ductal carcinoma. The patient preferred to pursue metastatic work-up and further treatment at her hometown.

Discussion

Women with extensive breast density are doubly disadvantaged as they are both at higher risk of developing breast cancer and at greater risk that cancer will not be detected because of "masking" of the radiological signs of cancer by increased density. Dense breasts are not only susceptible to primary malignancies but also to an increased incidence of second malignancy in the ipsilateral and the contralateral breasts.[5,6] While almost all cancers are visible in fatty breasts on mammogram, only half may be visualized in dense breasts.[7]

Contrast digital mammogram may also be performed by the temporal subtraction technique where a single breast in a single view is subjected to repeated exposures. This technique follows the same principle as in MR mammogram. The main disadvantages of this technique are that only a

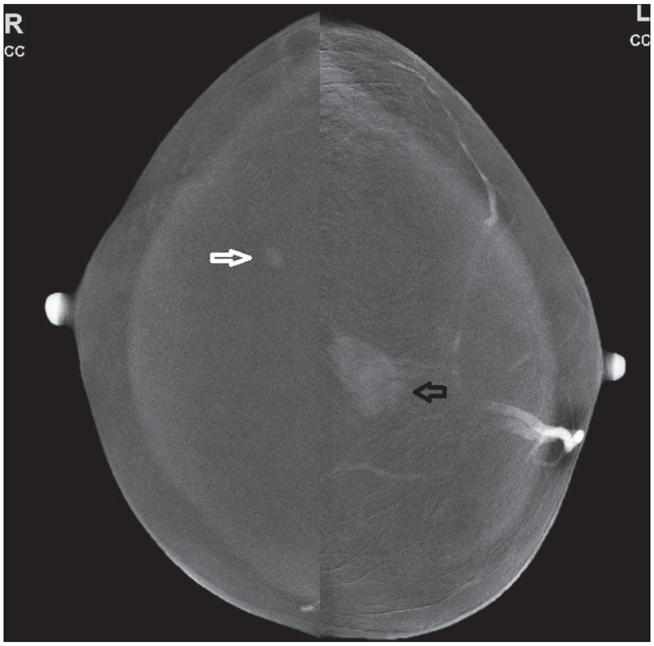

Figure 3: Dual energy subtracted CEDM images in RCC and LCC views. A small enhancing nodule is noted in the right breast centrally (white arrow) while a mass-like enhancing lesion is noted in the left breast (black arrow)

single breast can be imaged, patients have to maintain a particular position (usually MLO) for a prolonged period, and motion artifacts are more as breast is under compression when contrast arrives in the blood stream. Moreover, the kinetics of time enhancement curves obtained from these studies were not reliable and both benign and malignant lesions had shown progressive enhancement.[4,8]

To overcome these limitations, dual-energy CEDM was developed. This is a technique based on dual-energy acquisitions, where two images are acquired using distinct low-energy (standard mammography kV and filtration) and high-energy (higher kV with strong filtration) X-ray spectra. The differences between X-ray attenuation of iodine and breast tissues at these two energy levels are exploited to suppress the background breast tissue. Dual-energy CEDM depicts areas in the breast associated with increased vascularity. Contrast is injected with the patient in the sitting position in dual-energy CEDM, which takes approximately 20-30 sec. It is only 2 min after the start of contrast injection that images are acquired. This gives the patients time to recover from any discomfort related to contrast injection and gives radiographers enough time to position the patient**.** Absence of compression during contrast injection also ensures non-occlusion of small tumor feeders and, hence, adequate uptake by even small lesions.[9]

Dual-energy CEDM is non–operator-dependent and has doses comparable to that of standard DM. The dose estimated from low- and high-energy views combined is about 1.2 times the dose delivered in standard single-view

Figure 4: Dual energy subtracted CEDM images in the RMLO and LMLO views. The right breast nodule is no longer visualized while the left lesion is only subtly imaged (black arrow) suggesting probable rapid wash out. Enhancing left axillary nodes were also noted (asterisk)

DM.[10] The procedure takes approximately 10 min and could be followed by either a stereotactic or an USG-guided biopsy in the same sitting, reducing the critical time patients often have to wait from detection to diagnosis.

Preliminary studies with temporal subtracted CEDM have shown sensitivity in the range of 80%-91%.[11] This method showed enhancement in 8 out of 10 biopsy proven malignant lesions (80%) in a 22 patient study . Using the dual-energy CEDM technique, Lewin *et al.* had shown strong enhancement in 11/13 (85%) malignancies and moderate or weak enhancement in the remaining two cases.[12] The role of dual-energy CEDM as a problem-solving tool versus the standard techniques of mammography or the paired use of mammography and USG was evaluated by Dromain *et al*. in their study published in *European Radiology* in 2012.[9] They concluded that dual-energy CEDM used as an adjunct to these modalities improved the diagnostic accuracy of lesions.

Conclusion

USG is a complementary technique to mammography, but is time consuming, operator dependent, and may not aid in a definitive diagnosis especially in dense breasts. Contrast MRI, though extremely sensitive for detecting breast malignancies, has the disadvantage of higher false-positive rates, lower availability, and higher costs.[13] Dual-energy CEDM is marginally more expensive than a digital mammogram and works out at least five times cheaper than an MR mammogram. As seen with this case, we believe a major clinical indication for dual-energy CEDM could be its use as a "problem-solving" modality in case of equivocal mammographic and ultrasound assessments. A recent study in 2013 comparing dual-energy CEDM and breast MRI has shown similar sensitivities and superior specificity for contrast mammogram in the detection of primary breast malignancy.[14] In our experience with dual – energy CEDM till date, all pathology-proven malignancies had shown enhancement including subcentimetric lesions and a case of ductal carcinoma *in situ*. We, however had a few false positives with fibroadenomas, complicated cysts and apocrine metaplasia. Hence, studies need to be undertaken in a larger series of patients to assess contrast uptake in benign and indeterminate lesions, which would help assess the specificity of this emerging technique better.

We feel short acquisition times, high-quality subtracted images, and excellent patient cooperation make dual-energy CEDM a cost-effective alternative to breast MRI in some clinical settings. Dual-energy CEDM is a fast emerging technique gaining interest in the non-screening setting with its potential for detecting cancer, staging malignancy, detecting contralateral disease, and improving the selection of patients for biopsy.

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