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Can digital breast tomosynthesis accurately predict whether circumscribed masses are benign or malignant in a screening population?

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AIM: To evaluate whether digital breast tomosynthesis (DBT) can predict if circumscribed masses are benign or malignant by assessing margin sharpness.

MATERIALS AND METHODS: Circumscribed masses were evaluated on co-registered two-dimensional digital mammography (2DDM) and DBT. Lesions were categorised as follows: category 1=visible sharp border 0–25% of the total margin; category 2 = 26–50% category 3= 51–75%, and category 4=76–100%. Changes in category between 2DDM and DBT were analysed; if the category was lower on DBT the change was negative, if higher the change was positive.

RESULTS: Of 759 lesions, 121 masses classified as circumscribed on DBT were included; 25 were malignant and 96 benign. Of the benign lesions, 8/96 were within category 3 or 4 on 2DDM compared with 48/96 benign lesions within category 3 or 4 on DBT (Fisher's exact test $p<0.000527$). Forty-eight of 51 (94.1%) lesions categorised as 3 or 4 on DBT were benign and 65/67 (97.01%) of the positive category change group were benign. Lesions in category 1 on DBT had 45.4% chance of being malignant (20/44) compared with 22.72% (20/88) on 2DDM (chi-squared test $p<0.001$). Sixty-five of 67 (97.01%) lesions in the positive category change group were benign and 23/54 (42.6%) lesions with either no or negative category change were malignant.

CONCLUSION: The present study demonstrates 97% accuracy in predicting circumscribed lesions as benign when using positive category change and 94% accuracy when >50% of the margin is sharply defined on DBT.

Introduction

Circumscribed masses, i.e. non-spiculate masses, seen on two-dimensional digital mammography (2DDM) are a common cause of recall for assessment; however, the vast majority are benign.[1] Recall to assessment can result in unnecessary invasive procedures, general anxiety for

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patients, and has a significant impact on healthcare resources. The use of digital breast tomosynthesis (DBT) for screening patients for the detection of early breast cancer is gaining increasing credibility in light of recent published trials and may improve screening specificity.[2,3]

DBT has been shown to have greater diagnostic accuracy when compared to digital mammography (DM) for lesion characterisation.[4] The aim of this study is to assess whether DBT can accurately predict if circumscribed masses are benign or malignant by assessing percentage of margin sharpness and therefore potentially reduce false-positive recalls in routine screening. To the authors' knowledge no published studies to date have evaluated the predictive value of the percentage of lesion margin that is sharply defined on DBT.

Materials and methods

The database for the trial "A comparison of the accuracy of film-screen mammography, full-field digital mammography and digital breast tomosynthesis"[4] was interrogated for all lesions classified as circumscribed masses. For the purpose of this study all non-spiculate masses were considered to be circumscribed. In this study published in 2012, all women recalled for a mammographic abnormality following routine screening mammography as part of a National Health Service Breast Screening Programme between 2009 and 2010 were invited to participate. Ethics approval was granted by the institution's ethics committee and written informed consent was obtained from all of the participants. Clients underwent further assessment with bilateral two-view 2DDM and bilateral two-view DBT using a Full field digital mammography (FFDM) unit with tomosynthesis capability (Hologic Selenia Dimensions, Hologic, Bedford, MA, USA). The 2DDM and DBT images were obtained at the same time in the same compression, i.e. were co-registered. In this previous study, 759 lesions were analysed, to compare the accuracy of screen film, 2DDM and DBT using the Royal College of Radiologists mammographic suspicion score (M1–M5). From this dataset, all lesions classified as circumscribed masses on 2DDM and DBT were identified for the purposes of this study. Lesions that were classified as circumscribed on 2DDM, but showed spiculation on DBT were excluded from this study.

Two experienced consultant breast radiologists working within the National Health Service Breast Screening Programme with 8 years of experience of reading DBT, reviewed the co-registered 2DDM and DBT images blinded to the outcome of assessment. The images were double-read simultaneously. A consensus was reached on the percentage of the margin that was visualised as having a clear, sharp border on DM and DBT; on DBT this could be the summation of the sharp border seen on multiple image sections. Lesions were categorised as follows (see Fig 1): those lesions with a visible sharp border 0–25% of the total margin were assigned as category 1; 26–50% category 2; 51–75% category 3, and 76–100% category 4. The category was assessed visually. Where a score was on the threshold, the lower category was assigned; examples shown in Fig 2. Lesions that were not fully included on the mammograms were excluded from the study. On review of the DBT images, some lesions were deemed to be spiculate or asymmetric densities rather than true circumscribed mass and were also excluded. Correlation was made with final outcome of triple assessment consisting of clinical examination, further imaging, including ultrasound, and histopathology.

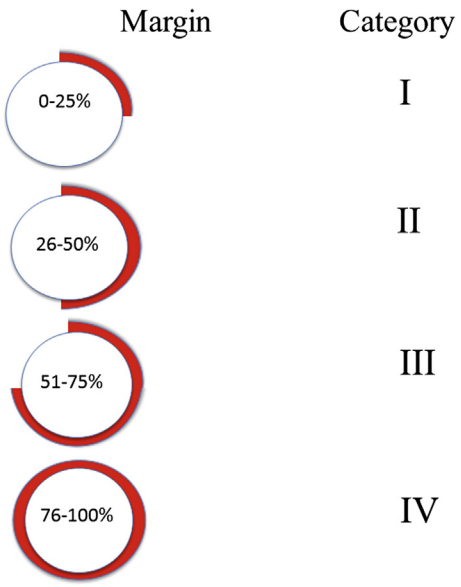

Figure 1 Margin categorisation.

The second part of the study looked at the difference between the categories assigned for 2DDM and DBT to determine if changes in category had any correlation on final outcome of assessment. If the category was lower on DBT, i.e., the margin less sharp than 2DDM the change would be negative, but if the lesion sharpness was better on DBT, e.g., category 1 on 2DDM, but 2 on DBT, then the category change was positive. Fig. 3 demonstrates assignment of category change.

Results

The trial database consisted of a total of 759 lesions, of which 122 met the criteria for this study. Of these 122 lesions, 25 were malignant with 24 invasive cancers and one in-situ carcinoma. Ninety-seven lesions were benign with the majority being cysts 59/97 (60.8%). Cysts accounted for 59/122 (48.4%) of all of the lesions classified as circumscribed masses on DBT. The remaining benign lesions included fibroadenomata (n=15), lymph nodes (n=6), benign change with varying proportions of fibrosis (n=7), fibrosis alone (n=2), normal glandular tissue (n=5), hamartoma (n=1), papilloma (n=1), and a sebaceous cyst (n=1). The majority of all circumscribed masses 88/122 (72.1%) assessed on 2DDM were in category 1 (<25%) as shown in Fig 4.

Fig 5 demonstrates the category distribution for benign lesions only. The majority of these lesions, even though they

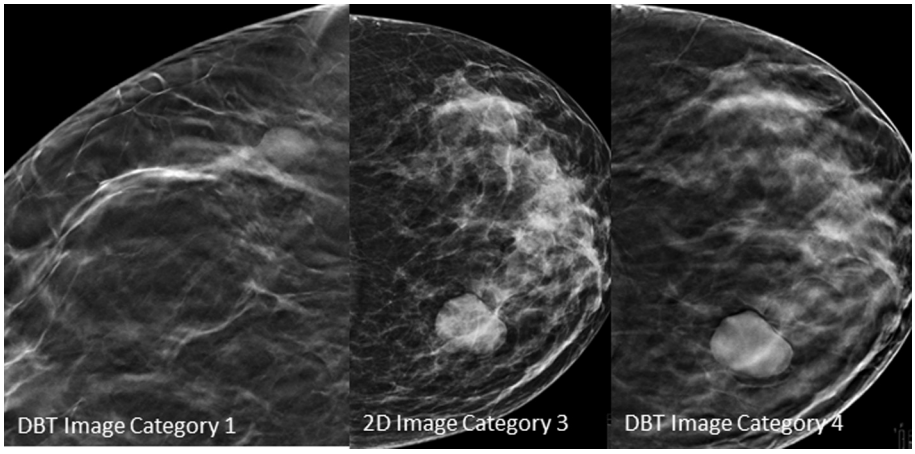

Figure 2 Example images of margin sharpness from study cases.

are benign, are in category 1 on 2DDM. Fig 6 shows the effect of combining category 1 and 2 together and comparing it with category 3 and 4 combined. The advantage of combining categories is that margin sharpness is assessed as either <50% or as >50%, which is an easy visual assessment to make. Fig 6 demonstrates that for the majority of benign lesions on 2DDM <50% of the margin was sharply defined, 88 of the 97 (90.7%) benign lesions were in category 1 or 2. For the same benign lesions assessed on DBT over five times as many lesions were classified as having a sharply defined margin of >50%, i.e., category 3 or 4 on DBT (49/97 = 50.5%) compared with 2DDM (9/97 = 9.3%). The difference between the two proportions was statistically significant via Fisher's exact test ($p<0.0002$).

Of all lesions categorised as 3 or 4 on DBT 49/50 (98%) were benign. There was one case with a category 4 margin, which was malignant. In this case, there were other suspicious radiological features that will be reviewed within the discussion section.

An interesting and potentially clinically relevant finding was obtained from the sub-analysis of the DBT lesions in category 1. A lesion in category 1 on DBT had a nearly 50% chance of being malignant (22/45 = 48.9%) compared with 23.9% (21/88= 23.9%) for a lesion in category 1 on 2DDM.

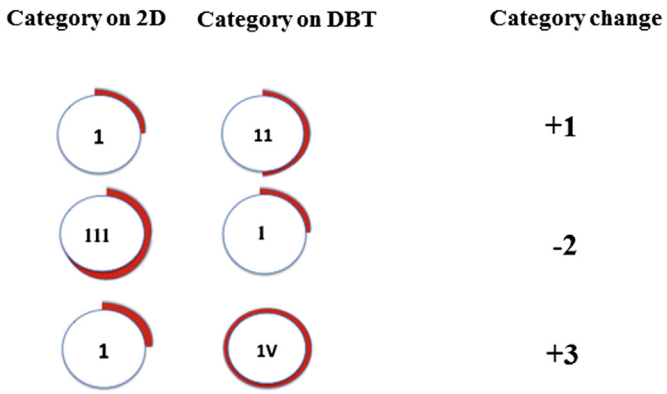

Figure 3 Assignment of category change.

This difference was statistically significant via Fisher's exact test ($p<0.005$).

Change in category between DBT and 2DDM was also analysed for all lesions as shown in Fig 7. All 82 lesions in the positive category change group were benign. No malignant lesions demonstrated a positive category change. There were a total of 39 lesions showing no category change, with 24 (61.5%) of these being malignant. One lesion had a negative category change which was malignant. Images for this case are shown in Fig 8.

Discussion

The present study shows that margin visibility was seen more confidently on DBT compared to current standard of care, 2DDM. More benign lesions were classified as having a sharply defined margin of >50%, i.e., category 3 or 4 on DBT 49/97 (50.5%) compared with 2DDM where only 9/97 (9.3%) had a margin visibility of >50%

In the cases where the proportion of the margin that was clearly visualised was >50% (i.e., category 3 and 4 combined) 49 out of 50 lesions were benign on DBT and 9/10 on 2D. There was one malignancy that had a category 4 margin on both 2DDM and DBT. This lesion was a solitary high-density mass in an adipose breast in a 76-year-old women, and therefore, had additional mammographic features suspicious of malignancy. The sonographic

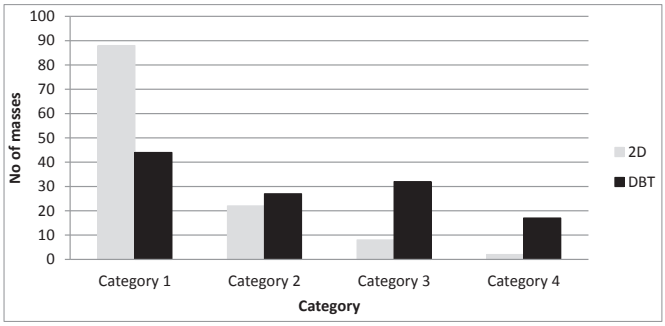

Figure 4 Category distribution for the complete data set for all circumscribed masses.

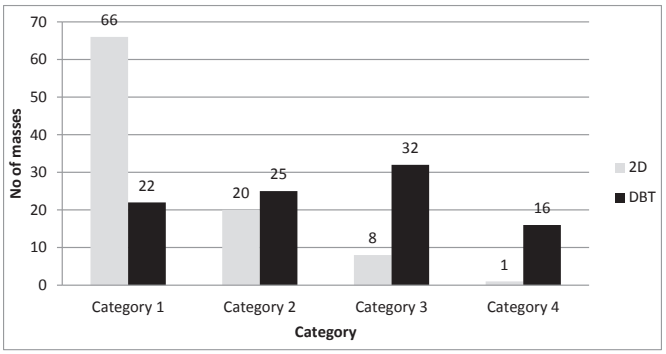

Figure 5 Category distribution for all benign lesions.

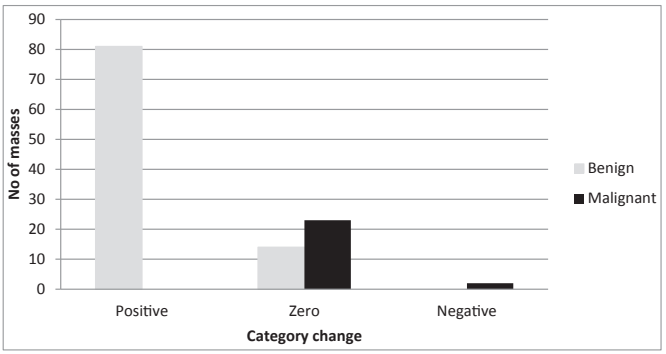

Figure 7 Change in category between 2DDM and DBT.

appearance of this malignancy was of an intracystic mass, thus explaining the mammographic features of a dense cyst (Fig 8). At final histopathology, the diagnosis was grade 3 ductal carcinoma. This emphasises the importance of taking all clinical and radiological features in to account in the decision to recall a patient.

Noting a sharply defined margin of >50% is a quick and easy decision to make. The visualisation of a sharply defined margin of >50% correlated with benignity on both 2DDM (90%) and DBT (98%). The important benefit of DBT being that it allows the radiologist to correctly interpret many more lesions as benign than 2DDM allows; 49 cases with DBT compared with only nine with 2DDM.

Identifying a sharply defined margin of <25% (category 1) on 2DDM is not helpful in differentiating malignancy from benignity. In the present study, 88 lesions had a margin visibility where <25% of the margin was sharply defined with the majority, 67 (76.1%), being benign; however, seeing a sharply defined margin of <25% using DBT was a useful finding, out of 45 lesions in this category 22 were malignant (48.9%)

Looking for a change in category from the classification on 2DDM to DBT was also helpful in this study; 82 benign lesions had a positive category change, i.e., greater percentage of margin sharpness on DBT, and in this group, there were no malignant lesions. Of those lesions with no category change 24/39 (61.5%) were malignant.

The single lesion that had a negative category change, i.e., less margin visibility on DBT compared with 2D, was malignant.

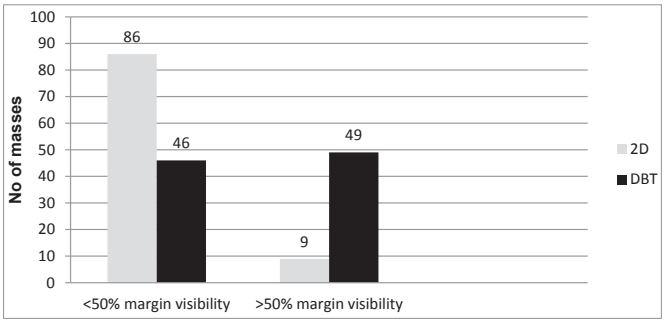

Figure 6 Benign lesion data set according to less than or greater than 50% visibility.

The use of DBT is becoming standard in the screening assessment setting[5] and symptomatic clinic setting. Margin analysis on DBT may help with diagnostic confidence.

In the context of breast screening, recall to assessment can result in unnecessary invasive procedures, general anxiety for patients, and has an impact on healthcare resources. There is growing evidence from studies in Europe[2,3,6–9] and North America[10] to support the use of DBT in screening. These studies show a consistent improvement in sensitivity across the studies with a more variable improvement in specificity. In their 2016 paper, Lee *et al.* demonstrated DBT to have a higher diagnostic accuracy compared with ultrasound for the assessment of breast lesions in women with dense breasts.[11] The present study indicates that careful analysis of margin sharpness on DBT more accurately predicts whether a circumscribed mass is benign or malignant compared with 2DDM and may therefore further improve specificity in the context of screening with DBT. This study demonstrates 100% accuracy in determining if a circumscribed lesion is benign with the use of positive category change. In addition, 98% accuracy in determining if a circumscribed lesion is benign was determined by using a cut-off of 50% of the margin visualised as sharply defined on DBT. Assessing margin visibility by eye is

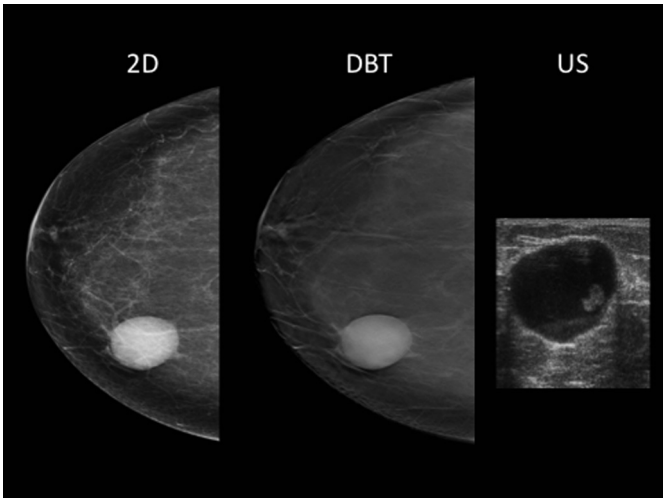

Figure 8 Category 4 malignancy.

quick and the classification is simple to incorporate in to everyday practice.

This study is from a single institution with a relatively small study size and limited number of readers. Further larger multi-reader studies are required to validate these results.

Conflict of interest

The authors declare no conflict of interest.

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