Clinical Radiology 71 (2016) 141–150

Contents lists available at ScienceDirect

Clinical Radiology

journal homepage: www.clinicalradiologyonline.net

Review

Digital breast tomosynthesis (DBT): a review of the evidence for use as a screening tool

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ARTICLE INFORMATION

Article history:
Received 24 September 2015
Received in revised form
29 October 2015
Accepted 3 November 2015

Breast screening with full-field digital mammography (FFDM) fails to detect 15–30% of cancers. This figure is higher for women with dense breasts. A new tomographic technique in mammography has been developed — digital breast tomosynthesis (DBT) — which allows images to be viewed in sections through the breast and has the potential to improve cancer detection rates. Results from retrospective reading studies comparing DBT with FFDM have been largely favourable with improvement in sensitivity and specificity. Increases in diagnostic accuracy have been reported as being independent of breast density; however there are mixed reports regarding the detection of microcalcification. Prospective screening studies using DBT with FFDM have demonstrated increased rates in cancer detection compared with FFDM alone. A reduction in false-positive recall rates has also been shown. Screening with the addition of DBT would approximately double radiation dose; however a simulated FFDM image can be generated from a DBT scan. The combination of simulated FFDM images and DBT is being evaluated within several studies and some positive results have been published. Interval cancer rates for the UK National Health Service Breast Screening Programme (NHSBSP) demonstrate the limited sensitivity of FFDM in cancer detection. DBT has the potential to increase sensitivity and decrease false-positive recall rates. It has approval for screening and diagnostics in several countries; however, there are issues with DBT as a screening tool including additional reading time, IT storage and connectivity, over-diagnosis, and cost effectiveness. Feasibility and cost-effectiveness trials are needed before the implementation of DBT in NHSBSP can be considered.

Introduction

Breast screening with mammography is widely acknowledged as the most effective method of detecting early stage breast cancer and reducing breast cancer mortality. A meta-analysis of 11 randomised trials concluded there was a 20% reduction in breast cancer mortality in women invited to screening[1]; however, the primary limitation of standard full-field digital mammography (FFDM) is that overlapping dense fibroglandular tissue within the breast can decrease visibility of malignant lesions or even obscure them completely resulting in a delay of diagnosis of cancer. It has been shown that 15–30% of cancers are not

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http://dx.doi.org/10.1016/j.crad.2015.11.008
0009-9260/

detected by standard screening,[2] and these are diagnosed when women present with breast symptoms in the interval between routine screens (interval cancers). This percentage is higher in women under 50 years[3] and in women with dense breasts.[4–7] Conversely, superimposition of normal fibroglandular tissue may mimic the appearance of malignancy leading to an increase in the number of false-positive recalls.[8]The advent of FFDM has allowed new techniques to be developed. The foremost of these is digital breast tomosynthesis (DBT).

Digital breast tomosynthesis is an X-ray mammography technique in which tomographic images of the breast are reconstructed from multiple low-dose projection images acquired by moving the X-ray tube in an arc over a limited angular range. The fundamentals of tomographic imaging were established in the 1930s, but clinical applications of tomosynthesis in mammography did not evolve until several decades later following the development of flat-panel digital display detectors, rapid computer processing, and advances in reconstruction and post-processing algorithms[9].

The range of angles employed varies by manufacturer from 15–50°. The exposure used for each projection is relatively small and the overall mean glandular dose for DBT is comparable with that of standard FFDM. The tomosynthesis projection images are processed by reconstruction algorithms to produce a set of parallel image planes through the whole breast, typically with 1 mm spacing. Conventional FFDM images can be acquired at the same breast compression. Readers view images on a workstation and are able to scroll vertically through the tomographic images (in 1 mm sections or in 10 mm slabs) and compare them with corresponding FFDM images. The image quality of DBT is highly dependent upon system geometry and the choice of optimal image acquisition, reconstruction, and display parameters.[10–12] Some manufacturers employ a larger angular range, which would theoretically improve the depth resolution between planes, but at the expense of in-plane resolution.[10,11] It is important to acknowledge the differences between the various manufacturers' systems and consider each on its own merits.

Hologic (Danbury, CT, USA) was the first manufacturer to have its DBT system approved by the US Food and Drug Administration (FDA) for use as a screening tool in February 2011. Since then both GE Medical Systems (Buc, France) and Siemens Healthcare (Erlangen, Germany) have had their DBT systems approved by the FDA. The Hologic and GE systems are also licenced for use in Canada and have received CE (Conformité Européene) clearance for use in the European Union (EU). The Giotto Breast Tomosynthesis System (IMS, Bologna, Italy) also has CE approval. As a result of the various approvals, DBT is currently used in routine clinical practice in a number of countries. The Hologic DBT system has also been approved in the UK by the National Health Service Breast Screening Programme (NHSBSP) for use in the diagnostic work-up of breast abnormalities detected as a result of screening with FFDM; however, more evidence is needed from high-quality clinical trials to support the implementation of DBT for routine screening in the UK.

Potential of DBT

DBT has the potential to overcome the primary limitation of standard FFDM that arises from overlapping fibroglandular breast tissue. By providing pseudo-three-dimensional (3D) images diagnostic accuracy can be improved as lesion conspicuity is increased and readers are more able to identify lesions and to differentiate between benign and malignant features. For screening programmes, this would result in a reduction in the number of false positives and a decrease in recall rates. The ability to identify more lesions would result in earlier detection of tumours and an increase in cancer detection rates. A more accurate delineation of a lesion, definition of the extent of disease, and identification of additional disease may be seen by DBT, and this would assist in surgical and treatment planning. Standard FFDM has suboptimal sensitivity in dense breasts and the improved visibility afforded with the addition of DBT has the potential to increase diagnostic accuracy in these cases.

Recent reviews of clinical studies measuring the accuracy of DBT compared with FFDM in breast cancer detection have been undertaken.[13–15] These have investigated studies measuring the performance of readers in the interpretation of test sets or a clinical series of cases (symptomatic and/or recalled from screening), often with a high proportion of cancer cases. This method introduces a selection bias as cancers detected with conventional FFDM screening predominate, whereas lesions only detectable by DBT are not included. Results mainly demonstrate that two-view DBT has equal or better accuracy than FFDM and also show the superiority of FFDM plus DBT over FFDM alone in terms of increased sensitivity and specificity and in reader performance.[16–20] One disadvantage cited is the additional time to read the DBT images.

Evidence from retrospective studies

Over the last 8 years, a number of retrospective reading studies of varying quality and size have been undertaken. These have either addressed the sensitivity of the technique or specificity or both, compared to standard FFDM. Most studies have used DBT in combination with FFDM and compared this with FFDM alone. The results have been largely favourable with both sensitivity and sensitivity improving; however, it is important to examine in more detail where the improvements have occurred.

Sensitivity

Using a Hologic system in 1083 women, Rafferty[21] demonstrated an improved sensitivity from 65.5% for FFDM alone to 76.2% with the addition of DBT.[21] In an enriched test set of 185 cases, consisting of normal, benign, and cancers obtained with a prototype DBT system based on the Siemens Mammomat Novation DR, increased sensitivity was demonstrated by single-view DBT (90%) compared with two-view FFDM (79%).[22] Michell *et al.*[17] conducted a study of 738 women recalled from routine screening. All

Table 1
Impact of digital breast tomosynthesis (DBT) on sensitivity: evidence from retrospective reading studies.

Author	Year	System	N	Single or two-view DBT	Summary
Gilbert *et al.*	2015	Hologic	7060	Two view	Borderline improvement in sensitivity (FFDM alone 87%; DBT+FFDM 89%)
Michell *et al.*	2012	Hologic	738	Two view	Increased sensitivity using DBT (58%) compared to FFDM (40%)
Wallis *et al.*	2012	Sectra	130	Single view Two view	Single view DBT comparable with FFDM; modest improvement with two-view DBT compared with FFDM
Svahn *et al.*	2012	Siemens	185	Single view	Increased sensitivity with DBT (90%) compared to FFDM (79%)
Gennaro *et al.*	2010	GE	200	Single view	Similar sensitivity for DBT compared with FFDM
Teerstra *et al.*	2010		513	Two view	Similar sensitivity for DBT and FFDM
Gur *et al.*	2009	Hologic	125	Two view	No increase in sensitivity shown
Rafferty *et al.*	2007	Hologic	1083	two view	Increased sensitivity using DBT+FFDM (76.2%) compared with FFDM alone (65.5%)

FFDM, full-field digital mammography.

underwent bilateral two-view DBT and FFDM using a Hologic Selenia Dimensions system. The authors demonstrated an increase in sensitivity of 18% when DBT with FFDM (58%) was compared with FFDM alone (40%). However this study was unblinded and readers were aware of results from screening when reviewing DBT images.

There was no increase in sensitivity found in a smaller study of 125 women by Gur *et al.*[16] using a Hologic system. There were only 35 cancer cases and all but one of these were first detected by FFDM so this may provide a possible explanation for these findings. Gennaro *et al.*[23] using an investigational device based on the GE Senographe DS system, and comparing single view DBT with two view FFDM in 200 cases, also reported no significant difference in sensitivity. Small numbers may again account for this result although in another study Teertstra *et al.*[24] using a Hologic prototype system, with 513 cases of which 109 were cancers, similar sensitivity was also reported for DBT and FFDM (92.9%). It should also be noted that both the Gennaro *et al.* and Teertstra *et al.* did not investigate the use of DBT in combination with FFDM. In a UK study Wallis *et al.*,[25] using a prototype DBT system manufactured by Sectra (Stockholm, Sweden), examined 130 cases which were either symptomatic or recalled from screening. The authors compared the performance of single view DBT, two-view DBT and FFDM and found single view DBT was comparable with FFDM with a modest improvement in performance by two-view DBT.

In the most recent and largest study, a UK retrospective reading study of 7060 subjects conducted by Gilbert *et al.*,[20,26] women recalled following breast screening, and women below 50 years of age, with a family history of breast cancer, attending annual mammography screening were recruited from six centres. All participants underwent combined two-view FFDM and DBT. Results show a borderline significant improvement ($p = 0.07$) in sensitivity with the addition of DBT to FFDM (FFDM 87%; DBT + FFDM 89%). Cases for this study were read independently and readers were blinded to the outcome status of each.

The impact of DBT on sensitivity as demonstrated in retrospective reading studies is summarised in Table 1.

Specificity

Specificity was shown to be improved with the addition of DBT in a number of studies. The impact of DBT on specificity as demonstrated in retrospective reading studies is summarised in Table 2. Michell *et al.*[17] using a Hologic system, undertook receiver operating characteristic (ROC) analysis of 738 cases comparing FFDM with DBT and showed an improvement in specificity from 51% to 74%. In the Gur *et al.*[16] reading study, a 30% reduction in recall rate was reported when DBT was used in combination with FFDM compared with FFDM alone. When the same data were later analysed using free-response ROC (FROC) this translated into a 16% improvement in diagnostic accuracy

Table 2
Impact of digital breast tomosynthesis (DBT) on specificity: evidence from retrospective reading studies.

Author	Year	System	n	Single or two-view DBT	Summary
Gilbert *et al.*	2015	Hologic	7060	Two view	Specificity significantly higher for DBT+FFDM (69%) compared with FFDM alone (58%)
Bernardi *et al.*	2012	Hologic	158		Recall would have been avoided in 74% of cases using DBT compared with FFDM
Michell *et al.*	2012	Hologic	738	Two view	Increased specificity using DBT (74%) compared to FFDM (51%)
Wallis *et al.*	2012	Sectra	130	Single view Two view	Reduced recall rate of 11% for two-view DBT and 9.5% for single view DBT compare with FFDM
Svahn *et al.*	2012	Siemens	185	Single view	Diagnostic accuracy significantly better with DBT
Gennaro *et al.*	2010	GE	200	Single view	No significant difference in specificity for DBT compared with FFDM
Zuley *et al.*	2010	Hologic	125		No change in recall rates with DBT
Gur *et al.*	2009	Hologic	125	Two view	30% reduction in recall rate using DBT+FFDM compared with FFDM alone
Rafferty *et al.*	2007	Hologic	1083	Two view	30% reduction in recall rate using DBT in addition to FFDM

FFDM, full-field digital mammography.

compared to FFDM alone.[27] Svahn *et al.*,[22] using a Siemens prototype DBT system, also found the diagnostic accuracy was significantly better with DBT than FFDM using ROC and jack-knife alternative FROC (JAFROC) methods; however, in the similar-sized study of 200 women comparing DBT alone with FFDM, Gennaro *et al.*[23] found no significant difference between areas under ROC curves (AUC) for Breast Imaging-Reporting and Data System (BIRADS) scores.

Wallis *et al.*,[25] reported a reduced recall rate of 11% for two-view DBT and 9.5% for single-view DBT compared with FFDM. In a study evaluating the impact of using DBT following FFDM screening of 158 women, Bernardi *et al.*[28] found that recall would have been avoided in 74% of cases using DBT compared to FFDM.

The multi-reader, multicentre trial of 293 conducted by Rafferty and Niklason,[29] reported increased diagnostic accuracy with the addition of DBT compared to FFDM alone, particularly in the detection of invasive cancers, and a reduction of 30% in the recall rate. Gilbert *et al.*,[20] in the much larger study of 7060 cases, found specificity was significantly higher ($p<0.001$) for DBT+FFDM (69%) compared with FFDM alone (58%); however, Zuley *et al.*,[30] looked at 125 cases using a Hologic system and reported no change in recall rates. This could possibly be attributed to the smaller number of cases studied.

Dense breasts

As stated previously, sensitivity is reduced in dense breasts with conventional FFDM, and it is anticipated that the addition of DBT to FFDM will improve diagnostic accuracy. Bernardi *et al.*[28] showed that the improved specificity they found using DBT in 158 cases seemed to be irrespective of breast density and Michell *et al.*[17] also found that the improved accuracy shown with DBT for the 738 cases in their study to be independent of breast density. Rafferty *et al.*[31] also found the addition of DBT significantly improved diagnostic accuracy across all breast densities, but that the overall gain for dense breasts (AUC, 0.091; $p<0.001$) was more than twice that for non-dense breasts (AUC, 0.035; $p=0.001$). In the TOMMY trial, Gilbert *et al.*[20,26] demonstrated significantly higher specificity ($p<0.001$) for all subgroups of breast density with the addition of DBT to FFDM; however, for breast density of <50%, sensitivity for FFDM alone and DBT+FFDM were similar (88% and 89%, respectively), whereas for breast density of ≥50%, sensitivity was 93% with FFDM +DBT compared to 86% with FFDM alone ($p=0.03$).

The impact of DBT on diagnostic accuracy in dense breasts as demonstrated in retrospective reading studies is summarised in Table 3.

Detection of microcalcification

The ability of DBT to improve the identification of microcalcification has been the source of much debate. Studies have produced varying results. The impact of DBT in detection of microcalcification as demonstrated in reading studies is summarised in Table 4.

Kopans *et al.*[32] reported that the detection of microcalcification was better with DBT, whereas both Michell *et al.*[17] and Poplack *et al.*[33] found DBT and FFDM to be equal. Spangler *et al.*[34] found DBT was worse than FFDM. The TOMMY Trial[20,26] demonstrated increased specificity (3%) with FFDM+DBT compared to FFDM alone, but specificity was lower for microcalcification than for soft-tissue masses (88% and 92%, respectively). In a recently published prospective reading study, Tagliafico *et al.*[35] compared the classification of microcalcification clusters on DBT with FFDM using BIRADS scoring. Cases from three centres were randomised and read by six radiologists. Of 107 cases, there were 11 discordant results of which three were cancers. The three malignancies were downgraded by DBT and the eight non-cancers were classified correctly by DBT, but not by FFDM. Sensitivity was reported as 100% for FFDM and 91.1% for DBT, whereas specificity was 94.6% for FFDM and 100% for DBT. The authors concluded that DBT may miss a small number of cancers.

Differing techniques used for image acquisition and reconstruction may partly account for the inconsistency in sensitivity for microcalcification reported from the various studies. In addition, it has been suggested there is a need to combine DBT planes into thicker slabs (e.g., 10 mm) for optimal visualisation of microcalcification clusters, and it is not clear whether readers in the studies have utilised this option or not.

Table 3
Impact of digital breast tomosynthesis (DBT) on diagnostic accuracy in dense breasts: evidence from retrospective reading studies.

Author	Year	System	N	Single or two-view DBT	Summary
Gilbert *et al.*	2015	Hologic	7060	Two view	Higher specificity for all breast densities with the addition of DBT to FFDM. For breast density 50% or more sensitivity increased from 86% with FFDM alone to 93% with the addition of DBT
Michell	2012	Hologic	738	Two view	Improved diagnostic accuracy found was independent of breast density – fatty breasts AUC, 0.934 with FFDM and 0.990 for DBT ($p<0.0002$); dense breasts AUC, 0.886 with FFDM and 0.962 for DBT ($p<0.0001$)
Bernardi *et al.*	2012	Hologic	158		Improved specificity shown irrespective of breast density. Reduction in recall rate was larger in denser breasts
Rafferty *et al.*	2014	Hologic	310	Two view Single view	Increase in diagnostic accuracy for non-dense (AUC, 0.035; $p=0.001$) and dense breasts (AUC, 0.091; $p<0.001$) with addition of two-view DBT

FFDM, full-field digital mammography; AUC, area under receiver operating characteristic curve.

Table 4
Impact of digital breast tomosynthesis (DBT) in detection of microcalcification: evidence from reading studies.

Author	Year	System	N	Single or two-view DBT	Summary
Gilbert *et al.*	2015	Hologic	7060	Two view	No difference in sensitivity but 3% increase in specificity with DBT+FFDM compared with FFDM
Tagliafico *et al.*	2015	Hologic	107	Two view	Sensitivity for DBT 91.1% compared with 100% for FFDM. Specificity for DBT 100%; FFDM 94.6%
Michell *et al.*	2012	Hologic	738	Two view	Detection of microcalcification equal for both DBT+FFDM and FFDM alone
Kopans *et al.*	2011	GE	119	Single view	Detection of microcalcification better with DBT
Spangler *et al.*	2011	Hologic	100	Two view	DBT worse in the detection of microcalcification than FFDM alone
Poplack *et al.*	2007	Hologic	98	Up to three views matched to mammograms	DBT and FFDM equal in the detection of microcalcification

FFDM, full-field digital mammography.

Synthetic two-dimensional images

The mean glandular doses (MGD) at DBT of average-sized breasts are typically about 2.3 mGy per view, which is about 1 to 1.5-times higher than the dose per view for FFDM.[36] The use of DBT in combination with FFDM, therefore, requires at least a doubling of radiation exposure.

Any additional radiation dose needs to be balanced with the benefit to women undergoing screening. It is unlikely that DBT would ever be used as a standalone imaging technique as it seems, at least for now, FFDM is still required for optimal microcalcification assessment[10,37,38]; however, it is possible to generate a synthetic two-dimensional (2D) image from a DBT scan[39] and the accuracy of combining DBT with a synthetic 2D image is currently being evaluated. Simulation of a 2D image from DBT data is being investigated by a number of manufacturers. Hologic have produced a commercial version called C-view that was evaluated by Gur *et al.*[39] Results from within the Oslo trial,[40] the TOMMY Trial,[20,26] and published by Zuley *et al.*[41], demonstrate that synthetic images are of acceptable diagnostic quality and that by employing them the conventional FFDM could be potentially eliminated. All used Hologic DBT systems; however, experiences of using synthetic images generated from a GE Healthcare DBT prototype reported at the European Congress of Radiology (ECR) meeting in Vienna 2014 were not so favourable. Low sensitivity and reduced conspicuity were reported by the authors who concluded the synthetic images could not replace FFDM even if used in combination with DBT.[42]

Prospective screening studies

Results from retrospective studies appear to support the use of DBT in addition to FFDM, particularly in the assessment of non-microcalcification lesions; however, the true potential of improvement in sensitivity when screening with the addition of DBT may not have been demonstrated due to case selection bias in these studies. Results from prospective screening studies should provide us with a more accurate picture of the impact of screening with DBT on cancer detection. There are three published screening studies and they are all paired studies, i.e., each woman is imaged at screening with both FFDM and DBT.

Oslo trial

The Oslo breast tomosynthesis trial[43,44] is being undertaken within the Norwegian screening programme and plans to screen 18,000 women with two-view FFDM and two-view DBT and compare various screen reading protocols. Images are assessed by four different radiologists reading different arms in parallel. The use of each radiologist is not totally balanced over the arms, but the authors feel that given the size of the study, this is unlikely to significantly impact on their findings. All images were taken using the Hologic DBT system. Interim results have shown an increase in cancer detection rate of 27%, a significant (40%) increase in the detection of invasive cancers, and an estimated 13% decrease in false-positive recall rate using DBT in combination with FFDM compared with FFDM alone. Employing independent double reading with arbitration, as practiced in many European screening programmes, resulted in an increase in the cancer detection rate to 30% and a decrease in recall rate to 18% when using DBT in combination with FFDM compared with FFDM alone.[43]

The FFDM+DBT arm found an additional 25 invasive cancers of which 40% were grade 2 or higher; a 26% increase in higher-grade cancers. This compares to routine FFDM screening where 49% of cancers detected are of grade 2 or higher.

Results from the trial comparing the use of FFDM+DBT and the Hologic synthetic 2D images (C-view) + DBT have also been published.[40] Recall rates and cancer detection were similar for each arm.

STORM trial

Results from the Italian, population-based screening study by Ciatto *et al.*,[45] STORM, also using the Hologic Dimensions DBT system, comparing sequential FFDM reading with combined DBT and FFDM reading, are consistent with the data from the Oslo trial. Images from 7292 women attending for routine bi-annual screening were read independently by two radiologists, first with FFDM alone and then FFDM+DBT. As is clinical practice for most European breast screening programmes, images in this study were double-read, unlike in the main Oslo trial. The authors reported a 34% increase in cancer detection across all age

groups and breast densities, and the potential to reduce the false-positive recall rate by 17%; however, they found that reading time was doubled. Cancers detected by FFDM alone and the additional cancers detected by combined FFDM and DBT were of similar size and node status.

Malmö 2 trial

The Malmö breast tomosynthesis screening trial conducted a paired analysis of sensitivity and specificity of single-view DBT compared with two-view FFDM in a population-based screening programme in Sweden using the Siemens Inspiration DBT system. Results for 7500 women were presented at the ECR meeting in 2014[46] and subsequently published online.[47] The trial demonstrated a 40% increase in cancer detection rate using DBT alone compared with FFDM, comparable with results from both the Oslo and STORM trials. An increase of 15% in sensitivity with DBT compared to FFDM was also reported but with a significant increase in recall rate of 46%; however, as the recall rate only actually increased from 2.6% to 3.8% the rate is still very low. Of the cancers detected in the DBT arm, 61% were of grade 2 and 3 compared to 68% of those detected using FFDM. The proportion of grade 2 and 3 cancers amongst those that were only detected by DBT was 48%.

Time series studies

As some screening centres in the USA have been switching from screening with FFDM to screening with DBT, a number of them have undertaken time series studies to report on the effect of adding DBT to routine practice and the impact on cancer detection.[19,48–51] Screening performance measures before and after the introduction of DBT were assessed; however, it should be noted that in the prospective studies each woman is screened with and without DBT for comparison, whereas in these time series studies, different cohorts of women are being compared, which could produce misleading findings.

Overall the four smaller studies demonstrated a reduction in recall rate of between 16% and 37%. Results for cancer detection rates varied with one study[50] showing similar rates before and after the introduction of DBT and another[49] showing the cancer detection rate varying by reader. In another[19] there was no statistically significant improvement and this was attributed to study design limitations. The final study[48] was also underpowered to demonstrate a significant increase in cancer detection rate.

The most recent time series report by Friedewald *et al.*,[51] which combined data from 13 academic and non-academic breast screening sites, including studies mentioned above, is by far the largest and potentially the most likely to provide reliable and statistically significant results. Performance metrics including recall rate and cancer detection rate were compared for the 12-month period before DBT was introduced and an average period of 17 months afterwards. All sites used the Hologic Selenia Dimensions DBT system. The addition of DBT to the screening process resulted in a reduction in the recall rate of 15% and the invasive cancer detection rate was increased by 41%. These findings are consistent with those reported in the prospective screening trials. The evidence from prospective screening trials is summarised in Table 5.

Why should DBT be approved for routine screening?

The most recent published interval cancer rate for the UK NHSBSP of 2.67 per 1000 women screened over a 3-year period[52] demonstrates the potential to increase cancer detection and diagnose cancers earlier by adding DBT to FFDM. Women with dense breasts have a reduced screening programme sensitivity[53–56] and tend to have larger screen-detected and interval cancers.[55,57,58] These issues are of concern for the UK NHSBSP as it extends the screening age to include pre- or peri-menopausal women and are relevant for younger women being screened due to moderate or high risk of developing familial breast cancer.[59,60]

Superimposition of normal tissues may produce features on mammography, which are suspicious for cancer and lead to unnecessary recall for further assessment and diagnostic tests to exclude malignancy. By facilitating the analysis of superimposed breast structures, DBT may enable the reader to identify features that, for example, appear to be asymmetric density on FFDM image as normal composite shadows, thereby decreasing the number of false-positive recalls,[16,18,44,61] associated health costs,[28] and reducing patient anxiety.[62,63]

Table 5
Comparison of evidence from prospective screening trials.

Author	Year	System	N	Single or two-view DBT	Summary
Skaane *et al.*	2013	Hologic	12,631	Two view	Increase in cancer detection rate of 27% (with double reading this increased to 30%) Predicted 13% reduction in recall rate (with double reading a reduction of 18% in recall rate was predicted)
Ciatto *et al.*	2013	Hologic	7,292	Two view	Increase in cancer detection rate of 40% Predicted reduction in recall rate of 17%
Lång *et al.*	2015	Siemens	7,500	Single view	40% increase in cancer detection rate 46% increase in recall rate (although actual recall rate is still low at 3.8%)
Friedewald *et al.*	2014	Hologic	173,663		Increase in cancer detection rate of 41% 15% reduction in recall rate

DBT, digital breast tomosynthesis.

Issues with DBT as a screening tool

Despite mounting evidence that the addition of DBT to FFDM has clear benefits for diagnosis, there are several issues to be addressed regarding the implementation of DBT as a screening tool. These include increased radiation dose, the increased costs associated with using DBT technology, including IT and data storage, increased screen reading times and changes to diagnostic practice.[64] Another is how many additional clinically insignificant cancers might be detected by employing DBT in routine screening leading to potential over-diagnosis. These concerns have led to speculation that the place for DBT within the screening programme would be for group(s) of women who might benefit most from its addition to standard FFDM. Further research needs to be undertaken to assess whether such group(s) of women can be identified and to assess the cost implications of the addition of DBT into routine screening.

Additional reading time

Skaane *et al.*[44] reported reading times of 45 seconds for FFDM and 91 seconds for DBT ($n = 12{,}631$). Wallis *et al.*[25] confirmed an approximate doubling of reading time with average times of 67 seconds for FFDM and 124 seconds for DBT ($n = 130$). An increase in reading time of 33% was reported by Zuley *et al.*[65]. This increase in time will clearly impact on clinics and have cost implications.

IT storage and connectivity

DBT images require a large amount of storage space and with the numbers of women participating in the breast screening programme many departmental PACS will be unable to cope. Initially, DBT images could only be read on dedicated workstations; however, the increasing use of the DICOM (digital imaging and communications in medicine) standard format for storing DBT images (BTO) makes it possible to read DBT images on PACS workstations. The availability of PACS workstations that can adequately display DBT images for multidisciplinary team meetings (MDTs) and other NHS sites needs to be verified. It is important that all manufacturers make the standard format of DBT images available for export from their systems.

Over-diagnosis

DBT has been shown to be better than standard FFDM in detecting small/subtle cancers leading to earlier detection of disease; however, whether the detection of these additional cancers will be of benefit or harm to the patient is a strongly debated issue. There are limited data presented on the pathological characteristics of the additional cancers detected with the addition of DBT, but preliminary data from the Oslo study[43,44] reported that 60% of additional cancers were Grade 1, whereas the remaining 40% were grade 2 or 3. This is reflected in results from the Malmo study[46] where 48% cancers detected only by DBT were grade 2 or 3. These findings seem to suggest that the addition of DBT into routine screening will not increase the ratio of over-diagnosis to lives saved. In addition to this, rather than regarding this facet of screening with DBT as a negative, the view could be taken that current screening with FFDM risks under-diagnosis resulting in later diagnosis and more interval cancers and a limited reduction in mortality from breast cancer.

Radiation dose

The cost-to-benefit equation must be considered in any population screening programme where there is a radiation dose. Adding DBT to FFDM more than doubles the radiation dose a woman would receive in routine breast screening. As mentioned previously, there is an opportunity to use synthetic 2D images in combination with DBT instead of conventional FFDM with only a slight increase in dose compared with FFDM and DBT. Once synthetic 2D images have been shown as an acceptable alternative, the marginal increase in radiation dose becomes much less of an issue.

Cost effectiveness

In the USA, Lee *et al.*[66] used modelling to estimate the cost effectiveness of screening with FFDM+DBT versus FFDM alone for women between the ages of 50–74 with dense breasts. The authors reported incremental cost per quality-adjusted life year gained by adding DBT to FFDM screening was $53,893. They concluded that biennial screening with DBT+FFDM in this group of women is likely to be cost effective if priced at $226 as compared to $139 for FFDM alone.

To date, the additional cost of screening with DBT has not been reported for the UK. Capital cost for upgrade to the tomosynthesis version of mammography systems, increased capacity for data storage, and additional time for radiologists to read DBT images are amongst the factors to be considered. Extra costs for the latter could potentially be offset if a reduced recall rate is achieved, meaning that radiologists would have to spend less time in assessment clinics.

Summary

In general, studies have demonstrated the potential for DBT to decrease recall rates and increase cancer detection rates; however, the use of DBT systems with different technical configurations coupled with variations in study methodologies and case configurations have produced conflicting results regarding the efficacy of DBT. Studies comparing analogue mammography or FFDM to DBT have reported improved lesion visibility in terms of size and classification for DBT[67–72] and the possibility that DBT could reduce the need for additional mammographic views for non-calcified lesions has been suggested.[65,73,74] The gain in diagnostic accuracy has been established for soft-tissue masses and architectural distortions, but there are mixed reports for the sensitivity of DBT for the detection of microcalcifications[17,25,32–34,75,76].

Published data from studies of DBT combined with FFDM in routine screening have demonstrated increased rates of invasive cancer detection compared with FFDM alone. In the three prospective studies[44–46] and the time series study by Friedewald *et al.*,[51] the increase ranges from 27–51%, but with no significant change in detection rate for ductal carcinoma *in situ* (DCIS). Results also show cancers being detected at a smaller size and a decrease in false-positive recall rates of 15–20%.

The reported level of increase in cancer detection rate may only be found during the first round of changing to screening with DBT and may decline in subsequent rounds; however, this does not diminish the benefit of screening with DBT. Instead, the advantages should be viewed in terms of earlier detection, reduced numbers of interval cancers, and improved clinical outcomes. The impact on interval cancers and mortality from breast cancer from screening with the addition of DBT has not been reported, nor can these data be provided from the current screening trials as participants were screened with and without DBT. Further studies are needed to assess the effect of screening with DBT on mortality.

Although data from screening centres in the USA have demonstrated reduced recall rates and increased cancer detection, in the UK, cost effectiveness and feasibility studies are needed before implementation into the UK NHSBSP can be considered; however, this technology is undoubtedly an improvement on conventional 2D imaging.

Acknowledgements

The authors acknowledge the NIHR Cambridge Biomedical Research Centre, Cambridge, UK.

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