

# evidence | *note*

In response to an enquiry from Dr Gerald Lip on behalf of the SBSP  
(Scottish Breast Screening Programme) Clinical Directors Group.

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**In women who have been recalled from breast screening, what is the clinical and cost effectiveness of digital breast tomosynthesis (DBT) compared with coned views?**

## Questions addressed

- In women who have been recalled from breast screening for further assessment, what is the evidence that digital breast tomosynthesis (DBT) in place of coned views improves cancer detection?
- How does breast density and type/stage of cancer influence the results?

## Key points

- Evidence from ten studies suggests that, from a diagnostic perspective, digital breast tomosynthesis (DBT) can be used in place of supplementary mammographic views (SMVs) in women who have been recalled from initial breast screening for further assessment.
- Of eight studies that reported outcomes relating to diagnostic accuracy, six concluded that DBT demonstrated comparable diagnostic accuracy to SMVs. In the remaining two studies, the results suggested that DBT was superior to SMVs in terms of diagnostic accuracy.
- The existing evidence base suggests that the comparable/improved accuracy for DBT in the investigation of screen-detected abnormalities only applies to soft-tissue abnormalities, not to microcalcifications.
- The studies identified did not report any sub-analysis by lesion type, grade, or breast density.
- No economic studies were identified.

## What is an evidence note?

Evidence notes are rapid reviews of published secondary clinical and cost-effectiveness evidence on health technologies under consideration by decision makers within NHSScotland. They are intended to provide information quickly to support time-sensitive decisions. Information is available to the topic referrer within a 6-month period and the process of peer review and final publication of the associated advice is usually complete within 6–12 months. Evidence notes are not comprehensive systematic reviews. They are based on the best evidence that Healthcare Improvement Scotland could identify and retrieve within the time available. The evidence notes are subject to peer review. Evidence notes do not make recommendations for NHSScotland, however the Scottish Health Technologies Group (SHTG) produces an Advice Statement to accompany all evidence reviews.

## Definitions

**Coned mammographic view:** A type of mammogram that focuses on a specific area of the breast. Various terminology is used in the literature for the same thing, including ‘spot views’ or ‘spot compression views’

**DBT:** Digital breast tomosynthesis

**FFDM:** Full field digital mammography

**Magnification mammographic view:** A type of mammogram that allows the acquisition of ‘zoomed in’ images of a region of the breast

**SMVs:** Supplementary mammographic views. This term has been used in this evidence note to refer broadly to the additional diagnostic mammographic views (mostly coned or magnification views) that women recalled from breast screening may receive.

## Literature search

A systematic search of the secondary and primary literature was carried out on 13–15 December 2017 to identify systematic reviews, health technology assessments, other evidence based reports and primary studies. The Medline, Embase, and Web of Science databases were searched. Results were limited to the English language, and studies published from 2010.

Key websites were searched for guidelines, policy documents, clinical summaries, economic studies and ongoing trials.

Concepts used in all searches included: tomosynthesis; breast screening; recall; 3D mammography, digital breast tomosynthesis (DBT). A full list of resources searched and terms used are available on request.

Reference lists of relevant studies identified were checked.

## Introduction

Currently in Scotland women aged between 50 and 70 years are invited to participate in breast screening every 3 years, based on the fundamental principle of informed choice. Women over 70 years are encouraged to arrange an appointment. Over the last decade, most screening programmes have changed from 2D analogue mammography to full field digital mammography (FFDM). FFDM represents the current standard for mammography programmes in the UK<sup>1</sup>.

Screening with mammography can help identify breast cancer earlier, which is associated with reductions in mortality. At a population level, the estimated effect of the UK breast screening programmes is a 20% reduction in breast cancer mortality in women invited for screening<sup>2</sup>.

When a radiologist interprets a mammogram during an assessment, a score is assigned. For example, the American College of Radiology Breast Imaging Reporting and Data System (BI-RADS) is one scheme used for categorising the findings from breast imaging<sup>3</sup>:

- 0-incomplete
- 1-negative
- 2-benign findings
- 3-probably benign
- 4-suspicious abnormality
- 5-highly suspicious of malignancy
- 6-known biopsy with proven malignancy

The Royal College of Radiologists recommend a 5-point scoring system is used in the reporting of breast imaging examinations in the UK<sup>4</sup>:

- 1-normal
- 2-benign findings
- 3-indeterminate/probably benign findings
- 4-findings suspicious of malignancy
- 5-findings highly suspicious of malignancy

The assessment for women who have been recalled from screening mammograms normally involves supplementary mammographic views (SMVs; including coned and/or magnified views), clinical examination and an ultrasound scan. These are reviewed alongside the abnormal screening mammogram before a decision is made to proceed with a biopsy or discharge the woman (Dr G. Lip Clinical Director, North East Scotland Breast Screening Programme, Personal Communication, June 2017). These additional examinations are normally done at the same appointment, although women may be asked to make a separate appointment for a biopsy.

The purpose of the additional coned view mammograms (also known as spot compression) is to improve visualisation of the specific area of the breast where the abnormality is suspected. Unlike standard mammograms that compress the whole breast, coned views involve applying compression only to a specific area of the breast. The pressure is increased in that spot, resulting in better tissue separation and therefore improved visualisation. Although these views can accurately characterise the borders of masses and confirm the presence or absence of distortion, they are sometimes incorrectly interpreted. Some of these errors can arise because the lesion is displaced out of the field by the compression view<sup>5</sup>. This incorrect positioning may also result in repeat imaging, which among other things, can increase patient anxiety. Magnified views are normally used for calcifications, and errors are less common, although the radiation dose is greater than for non-magnified views<sup>6</sup>.

The focus of this evidence note is on using DBT instead of the additional coned mammographic views. Studies have also been included if they stated that they were comparing DBT with, for example, 'supplementary mammographic views', 'additional mammographic views' or 'diagnostic mammography'. Despite the different terminology used, these seemed to involve mostly coned or magnification mammographic views. The language used by the authors has been maintained. Studies that compared DBT to FFDM were not included.

## Health technology description

DBT is an advanced form of breast imaging, which provides three-dimensional information of the breast. In a conventional mammogram, two X-ray images are taken of the breast (top-to-bottom and from angled side-to-side) while the breast is compressed between a clear plastic paddle and an imaging detector. The purpose of compressing the breast is to reduce overlapping of the breast tissue. However, given that there is an inevitable degree of overlapping tissue, when a 2D mammogram is read, abnormal tissue can be hidden or normal tissue may appear abnormal. In DBT, the X-ray tube moves in an arc over the compressed breast, capturing multiple images, which can be synthesised into a set of 3D images by a computer<sup>7</sup>.

The use of DBT in place of SMVs in women who have been recalled from breast screening may improve accuracy, and possibly reduce the number of women receiving unnecessary biopsies resulting from increased clinician confidence. DBT takes an image of the whole breast and therefore negates the limitation of coned views whereby lesions are displaced out of the imaging field - which can result in repeat doses of radiation. Furthermore, DBT may also highlight additional lesions not seen on the original screening mammogram<sup>5</sup>.

Five DBT systems have received a CE mark, permitting distribution in the European Union (EU)<sup>8</sup>. These systems have numerous differences in their technical specifications, which would need to be considered if DBT was to be implemented in new settings. Public Health England has published practical evaluations for the GE SenoClaire DBT system and the Hologic [Selenia] Dimensions system, as equipment reports<sup>9</sup>. However, no studies compare the different DBT systems, and the effect of these differences on patient-oriented outcomes is unknown<sup>8</sup>.

All of the six screening centres in Scotland use the Hologic [Selenia] Dimensions mammography system. These systems have DBT capability, but this has been disabled on all but two systems. In the two units which have DBT enabled, one (in Dundee) is about to be used in a research project, and the other (in Glasgow) is occasionally used as an add-on for specific assessment cases (it cannot be used to replace existing imaging for assessment as it is not linked to the Picture Archiving and Communication System, PACS). Enabling DBT capability on the Hologic [Selenia] Dimensions systems requires a software upgrade and purchase of a license. Dundee also uses the Siemens Mammomat Inspiration System, which has DBT available, but it is only used for symptomatic patients (not for screening or assessment). In addition, Inverness have a Fuji Amulet unit, which cannot be upgraded to have DBT capability (Information provided by peer reviewers. Personal Communication, January 2018).

## Epidemiology

The incidence of breast cancer is highest in developed countries, with an age-adjusted incidence rate of 80 per 100,000 in the EU. It is the second most common cause of cancer death in women in developed countries<sup>1</sup>.

There are many different types of breast cancer. The first major division is between in situ and invasive carcinoma.

- In situ carcinoma is 'pre-invasive' carcinoma that has not yet invaded the breast tissue. These in situ cancer cells grow inside of the pre-existing breast lobules or ducts.
- Invasive cancers have cancer cells that infiltrate outside of the breast lobules and ducts to grow into the breast connective tissue.

Approximately 80% of breast carcinomas are invasive ductal carcinoma, followed by invasive lobular carcinomas which account for approximately 10-15% of cases. Invasive ductal carcinomas and invasive lobular carcinomas have distinct pathologic features<sup>10</sup>.

In NHSScotland 2015/2016, approximately four percent of women aged 53-70 who attended breast screening were recalled for further assessment (for women aged 50-52, this figure was higher, approximately 10%)<sup>11</sup>. The majority of women who are recalled for further assessment do not have breast cancer. In the current pathway of care, of the women who are recalled for further assessment, approximately 30% (roughly 2,500 women) will be referred for biopsy/cytology. Of these women, approximately 50% will receive a diagnosis of cancer (figures from the Scottish Breast Screening Programme, years 2013/2014 and 2014/2015; Information Services Division, NHS National Services Scotland. Personal Communication, January 2018).

## Clinical effectiveness

Two systematic reviews on the diagnostic accuracy of DBT were identified, but these did not compare the use of DBT in place of coned mammographic views (or SMVs more broadly) in women who had been recalled from screening<sup>12, 13</sup>. Therefore, a search of the primary literature was conducted, and this identified 10 studies. Finally, a search for clinical guidelines highlighted guidance from NHS Public Health England on breast cancer screening assessment (2016)<sup>14</sup>.

## Primary Studies

Table 1 provides a summary of the primary studies.

Table 1: Summary of primary studies

Reference	DBT system	Participant details	Comparison	Main Results	Authors' conclusion
Whelehan <i>et al</i> 2017 <sup>5</sup>  Retrospective multi-reader study (eight readers)	Siemens Mammomat Inspiration	n=238 participants  Germany  Women aged 50-69 years, recalled from initial screening for assessment of noncalcific screen-detected abnormalities	Standard screening images plus single-view DBT <i>versus</i> standard screening images plus supplementary mammographic views (SMV)	Area under the curve (AUC): DBT method: 0.870 SMV method: 0.857 p=0.489  Sensitivity / Specificity DBT method: 90% / 59% SMV method: 86% / 64% p=0.10 / 0.0002  4/35 malignant cases were multifocal (2 or more foci of cancer), with 10 detectable foci. Of 80 opportunities (10 foci x 8 readers) 49% were detected with SMV method, and 63% by DBT.  <i>A preliminary</i> description of measurement accuracy in unifocal malignant lesions was also given. Accuracy within 5mm was obtained for 60% (95% CI 53 to 66) of lesions with the SMV method and 62% (95% CI 56 to 68) using DBT.	'Siemens DBT demonstrates equivalent diagnostic accuracy according to ROC curve analysis when used in place of SMVs in screen-detected soft-tissue mammographic abnormalities.'
Heywang-Köbrunner <i>et al</i> (2017) <sup>15</sup>  Prospective and retrospective reader study (two readers)	Siemens Mammomat Inspiration	n=311 lesions in 285 participants  Germany  Women aged 50-69 years with a screen-detected abnormality.	Single view DBT <i>versus</i> DBT with additional views (AV) <i>versus</i> AV  Images viewed with screening mammograms	Sensitivity / Specificity DBT+AV: 96.4% / 54.3% DBT: 96.4% / 56.6% AV: 90.9% / 42.2%  Negative Predictive Value (NPV) / Positive Predictive Value (PPV) DBT+AV: 95.6% / 25.3% DBT: 97.4% / 32.3% AV: 98.6% / 31.2%	'DBT appeared to be at least equivalent to AV for assessing indeterminate screen-detected lesions and could replace AV for most lesions. To obtain the extra information appears possible without increasing the overall radiation dose.'
Ni Mhuircheartaí	Hologic [Selenia] Dimensions	n=341 lesions	DBT <i>versus</i> spot compression mammography	No asymmetry, distortion or mass where spot compression provided more diagnostic information than DBT alone.	'From our initial experience with tomosynthesis we conclude that spot

Reference	DBT system	Participant details	Comparison	Main Results	Authors' conclusion
gh <i>et al</i> (2017) <sup>16</sup>  Retrospective reader study (three readers)		Ireland Women aged 50-64 years with a screen-detected abnormality (four were recalled based on clinical abnormality)		Three additional cancers detected that had not been seen on screening mammogram.	compression mammography is now obsolete in the assessment of screen detected masses, asymmetries and distortions where tomosynthesis is available.'
Cornford <i>et al</i> (2016) <sup>17</sup>  Prospective (two readers) and retrospective (one of eight readers) reader study	GE Health Care (SenoClaire®)	n=342 lesions in 322 women  England  Women recalled for soft-tissue mammographic abnormalities	Two-view DBT plus two-view mammogram <i>versus</i> 'standard' supplementary views (typically spot compression views) plus two-view mammogram	AUC <i>Prospective analysis</i> DBT method: 0.946 (95% CI 0.917 to 0.968) Supplementary views method: 0.922 (95% CI 0.899 to 0.948) Difference not statistically significant  <i>Retrospective analysis</i> DBT method: 0.900 (95% CI 0.864 to 0.929) Supplementary views method: 0.873 (95% CI 0.834 to 0.906) Difference not statistically significant  Authors also reported absolute sensitivity, complete sensitivity, specificity, PPV and NPV for both the prospective and retrospective analyses.	'The accuracy of GE DBT in the assessment of screen detected soft-tissue abnormalities is equivalent to the use of standard supplementary mammographic views.'
Morel <i>et al</i> (2014) <sup>18</sup>  Retrospective reader study (one of seven readers)	Hologic [Selenia] Dimensions	n=354 lesions  England  Women (aged 47-73 years) recalled from routine screening; recalled from family history	Two-view mammogram plus one-view DBT <i>versus</i> two-view mammogram plus coned compression magnification mammography (CCMM)	AUC: <i>Full data set</i> CCMM method: 0.87 (95% CI 0.83 to 0.91) DBT method: 0.93 (95% CI 0.91 to 0.95) Difference: 0.06 (p=0.0014)  <i>Soft-tissue lesions subset</i> CCMM method: 0.90 (no confidence interval given) DBT method: 0.97 (no confidence interval given) Difference: 0.07 (p=0.005)	'Two-view mammography with one-view DBT showed significantly improved accuracy compared to two-view mammography and CCMM in the assessment of mammographic abnormalities. These results show that DBT can be used effectively in the further evaluation of mammographic

Reference	DBT system	Participant details	Comparison	Main Results	Authors' conclusion
		screening (40-49 years); recalled from symptomatic mammography (35 years and above).		<i>Microcalcifications subset</i> No statistically significant difference (no other details given)  Authors also reported sensitivity, specificity, PPV and NPV	abnormalities found at screening and in symptomatic diagnostic practice.'
Brandt <i>et al</i> (2013) <sup>19</sup>  Retrospective reader study (three readers)	Hologic [Selenia] Dimensions	n=146 women with 158 abnormalities  USA  Women with noncalcified findings recalled from screening mammography	Screening mammogram plus two-view DBT <i>versus</i> screening mammogram plus conventional diagnostic mammography	The median number of additional mammographic views per abnormality was three (range 1-6).  Ultrasound was used clinically to further evaluate and/or determine biopsy route in 49% of the abnormalities.  Agreement between DBT and diagnostic mammography BI-RADS categories (weighted kappa statistics): Reader 1: excellent (0.91) Reader 2: excellent (0.84) Reader 3: good (0.68)  DBT sensitivity and specificity for breast abnormalities: Sensitivity: reader 1 (100%), reader 2 (100%), reader 3 (88%) Specificity: reader 1 (94%), reader 2 (93%), reader 3 (89%)  DBT was considered an adequate mammographic evaluation by 99% for readers 1 and 2, and 93% for reader 3.  Readers 1, 2 and 3 stated that they would have ordered ultrasound in addition to the DBT images for further evaluation in 44%, 28% and 48% of cases.	'The results of this study suggest that DBT can replace conventional diagnostic mammography views for the evaluation of noncalcified findings recalled from screening mammography and could achieve similar sensitivity and specificity. Two-view DBT was considered adequate mammographic evaluation for more than 90% of the findings. There was minimal change in the use of ultrasound with DBT compared with diagnostic mammography.'
Zuley <i>et al</i> (2013) <sup>20</sup>	Hologic [Selenia] Dimensions	n=182 women with 217 lesions  USA	Standard mammogram plus Two-view DBT <i>versus</i> standard	AUC: DBT: 0.87 Supplemental views: 0.83 p<0.001	'Tomosynthesis significantly improved diagnostic accuracy for noncalcified lesions compared with supplemental mammographic views.'

Reference	DBT system	Participant details	Comparison	Main Results	Authors' conclusion
Retrospective reader study (8 readers)		Women aged 31-60 years who underwent diagnostic mammography with supplemental views and DBT for a tissue-density finding, including a mass, architectural distortion, or asymmetry.	mammogram plus supplementary mammographic views	<p>For cases that were BI-RADS category 3 or higher, the average false-positive rate decreased to 74% for DBT from 85% for supplementary views (<math>p &lt; 0.01</math>), without a meaningful change in sensitivity (remaining roughly 96% for both).</p> <p>For cases that were BI-RADS category 4 or 5, the average false-positive rate decreased to 48% for DBT from 57% for supplementary views (<math>p &lt; 0.01</math>), without a meaningful change in sensitivity (remaining roughly 90% for both).</p> <p>With DBT, more cancers were classified as BI-RADS category 5 (39% versus 33%), without a decrease in specificity.</p>	
Noroozian <i>et al</i> (2012) <sup>21</sup>  Retrospective reader study (four readers)	GE Health Care (not clear if it is SenoClaire®)	n=67 women with 67 lesions  USA  Women (mean age 55 years; range 34-88) enrolled after clinical recommendation for a breast interventional procedure. A 'cancer-enriched' study population was selected	Two view DBT <i>versus</i> mammographic spot view (MSV)	<p>Mean mass visibility ratings (10-point scale) DBT: range 3.2-4.4 MSV: range 3.8-4.8</p> <p>'All readers reported that, on average, masses appeared more obvious on DBT images, although only one reader achieved a statistically significant difference (<math>p = 0.001</math>).</p> <p>Area under the curve DBT: range 0.89-0.93 MSV: range 0.88-0.93 <math>p = 0.23</math></p> <p>Readers characterised seven additional malignant masses as BI-RADS 4 or 5 with DBT than with MSVs, at a cost of five false-positive biopsy recommendations.</p>	'In this small study, mass characterization in terms of visibility ratings, reader performance, and BI-RADS assessment with DBT was similar to that with MSVs. Preliminary findings suggest that MSV might not be necessary for mass characterisation when performing DBT.'
Tagliafico <i>et al</i> (2012) <sup>22</sup>	Hologic [Selenia] Dimensions	n=52  Italy	DBT <i>versus</i> digital spot	Sensitivity: DBT: 100% (95% CI 91 to 100%) DSCV: 100% (95% CI 91 to 100%)	'In this dataset, diagnostic accuracy is at least equal to

Reference	DBT system	Participant details	Comparison	Main Results	Authors' conclusion
Retrospective reader study (two readers)		Women with a screening abnormality (women with calcifications were excluded). Mean age 51 ± 12years.	compression view (DSCV)  It is not stated whether single-view or two-view DBT was used.	Specificity: DBT: 100% (95% CI 91 to 100%) DSCV: 94% (95% CI 91 to 100%)  Area under the curve: DBT: 1 DSCV: 0.963 p=0.43	that of digital spot compression.'
Hakim <i>et al</i> (2010) <sup>23</sup>  Retrospective reader study (four readers)	Hologic [Selenia] Dimensions	n=25 (4x25 reader ratings)  USA  Identified from screening as having an abnormality, or women during a diagnostic evaluation were found to have an abnormality. One architectural distortion; four multiple cysts; 17 masses. No cases depicting only microcalcifications	FFDM and two-view DBT <i>versus</i> FFDM and additional diagnostic views	Perception of readers: FFDM and DBT were perceived to be better for diagnosis in 50% (50/100) of cases, compared with FDDM and additional diagnostic views. The methods were considered equivalent in 31% of cases, and DBT was perceived as worse for diagnosis in 19% of cases.  Over all readers, 92% of ratings for verified cancer cases and 50% of the ratings for high-risk cases were rated as BI-RADS 4 or 5.  In 12% of the ratings, radiologists indicated that the availability of DBT would have eliminated the need for ultrasound as part of the diagnostic process.	'DBT may be an alternative to obtaining additional mammographic views in most but not all cases of patients with a lesion that is not solely calcifications. In a fraction of cases, the use of DBT may eliminate the need for ultrasound.'

## Description of studies

Ten studies were identified. Six evaluated DBT using the Hologic [Selenia] Dimensions system<sup>16, 18-20, 22, 23</sup>; two used the Siemens Mammomat Inspiration system<sup>5, 15</sup>; and two used systems from GE Healthcare<sup>17, 21</sup> (one was the SenoClaire system<sup>17</sup>, it is not clear whether the other study used SenoClaire or an earlier model<sup>21</sup>). Four studies were conducted in the USA<sup>19-21, 23</sup>, two were from England<sup>17, 18</sup>, two were from Germany<sup>5, 15</sup>, one was from Ireland<sup>16</sup> and one was from Italy<sup>22</sup>. For one of the studies using cases from Germany, a retrospective reading study (which involved evaluating existing images) was done in the UK, using radiologist 'readers' from breast screening programmes in England, Scotland or Northern Ireland<sup>5</sup>. Some of the same cases were used in two studies<sup>5, 15</sup>.

In five studies, the included cases were women who had been recalled because of abnormalities seen on screening mammograms<sup>5, 15, 17, 19, 22</sup>. The other five studies had slightly broader inclusion criteria, also including women who had been referred for assessment following symptomatic mammography, findings on ultrasound or Magnetic Resonance Imaging (MRI), or because they had presented with symptoms (for example, a palpable lump)<sup>16, 18, 20, 21, 23</sup>. The study participants all attended further assessment, and part of the work-up involved SMVs (mostly coned or magnification views) in addition to DBT. In most of the studies, participants were prospectively enrolled, or consecutively acquired<sup>5, 15-20, 22</sup>. A more selective approach was used in one study to produce a 'cancer-enriched study population'<sup>21</sup>, and another used a 'small nonrandomized set of cases'<sup>23</sup>.

Eight of the studies were retrospective reader studies<sup>5, 16, 18-23</sup>. Two studies had a prospective and retrospective reading element<sup>15, 17</sup>. The retrospective studies mostly involved readers evaluating two sets of images for each study participant: (1) the screening mammograms with the DBT images, and (2) the screening mammograms with the SMVs<sup>5, 15, 17, 18, 20, 23</sup>. To reduce bias from readers' memories, most (but not all) studies stated that the DBT and SMVs for each participant were reviewed at different times (varying between 2 and 9 weeks apart). Most studies also stated that the readers were blinded to the assessment outcome. The number of readers in the studies ranged from two to eight, and encompassed varying levels of clinical experience. In most studies, all the readers reviewed every case, however in two studies a single reader was assigned to each case<sup>17, 18</sup>.

Eight studies reported outcomes relating to diagnostic accuracy (for example, area under the curve, sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV)<sup>5, 15, 17-22</sup>. Two reported results relating to the subjective opinion of readers<sup>19, 23</sup>, and one provided a description of the additional diagnostic information provided from DBT<sup>16</sup>. Other outcomes of interest included statistical measures of agreement between DBT and diagnostic mammography views<sup>19</sup> and mass visibility ratings<sup>21</sup>.

Most studies stated that the comparative evaluation of diagnostic accuracy was based on histopathology and/or 1-3 years follow-up for benign findings<sup>5, 15, 17, 18, 20-23</sup>.

## Study quality

The three oldest studies (conducted between 2010 and 2012) were small and preliminary in their design, whereas the studies from 2013 tended to be larger. All studies were generally consistent in their main conclusions.

Despite the retrospective nature of most studies, the authors appear to have taken efforts to minimise bias with regards to selection of cases, blinding of readers to true diagnoses, and reader recall/memory.

The comparators in the studies were not entirely consistent. Studies were included that talked about ‘supplementary mammographic views’, ‘diagnostic mammograms’, and ‘additional views’. These generally seemed to be coned or magnification views (both analogue and digital), depending on what had been deemed suitable/was available for each participant. The impact of this on the results is not clear, but may reflect real life clinical practice.

## Main results

All ten studies concluded that DBT could be used in place of SMVs in women who have been recalled for assessment because of abnormal screening mammograms.

## Diagnostic accuracy

Of the eight studies reporting outcomes relating to diagnostic accuracy, six concluded that DBT demonstrated comparable diagnostic accuracy when used in place of SMVs<sup>5, 15, 17, 19, 21, 22</sup>. In the remaining two studies, the results suggested that DMT was superior to SMVs in terms of diagnostic accuracy<sup>18, 20</sup>. Both these studies had slightly broader inclusion criteria than the other six studies, including not just women who had been recalled because of abnormal screening mammograms, but also women who had, for example, been referred for assessment following symptomatic mammography. Both used the Hologic [Selenia] Dimensions DBT system. These two studies are discussed in more detail below.

The first study (Morel *et al*, 2014) compared ‘coned compression magnification mammography’ (CCMM) with DBT in the assessment of abnormalities found on screening mammography or symptomatic screening (n=354)<sup>18</sup>. The study was retrospective, and the authors stated that follow-up of the cases was from 2–3 years and no false-negative assessments were recorded. The study was one of the largest in terms of the number of cases, although only one reader reviewed each case. The CCMM and DBT images were reviewed alongside two-view mammograms, 2 weeks apart to reduce the effects of reader recall. Of the lesions, 279 were soft tissue lesions and 75 were microcalcifications. The authors reported that DBT plus screening mammography showed improved accuracy compared to CCMM plus screening mammography (AUC 0.93 versus 0.87; difference 0.06; p=0.0014). The authors also presented the results separately for the soft-tissue lesions and microcalcifications. They reported greater significance for the subset of soft-tissue lesions compared to the whole data set. For the subset of microcalcifications there was no statistical difference between DBT and CCMM, but the authors noted the small number of cases. Based on the results of this study, and on a study from 2012 (Michell *et al* 2012 – which did not meet inclusion criteria for this evidence note), the authors stated that they had revised their imaging protocol to ‘...include two-view DBT imaging in place of CCMM examination for all soft-tissue lesions requiring further mammographic assessment. For the further mammographic assessment of microcalcification, fine-focus magnification views in the CC [craniocaudal] and lateral projections are still required’<sup>18</sup>.

The aim of the second study (Zuley *et al*, 2013) was to compare the diagnostic performance of two-view DBT with ‘supplemental diagnostic mammographic views’ in the classification of masses, distortions, and asymmetries (but not lesions that were only a calcification). The women were younger than in the study by Morel *et al*, ranging from 31 to 60 years old. Histopathologic examination established diagnosis in 191 lesions, ultrasound revealed a cyst in 12 lesions, and 14 lesions had a normal follow-up (217 lesions in total). The results suggested that the use of DBT as a replacement for standard supplemental views improved accuracy in women with soft-tissue-based breast findings. The authors reported that DBT resulted in fewer benign masses categorised as BI-RADS category 3, 4, or 5 without loss of sensitivity. In addition, more malignant lesions were rated as highly suggestive of malignancy. The authors concluded that the use of DBT in this population is likely to result in fewer biopsies in women with benign lesions.

However, the authors also caution that because they included only noncalcified lesions in the study, and because their study participants were on average younger than women who would normally attend screening, the results may not be applicable to the entire population of diagnostic cases<sup>20</sup>.

### Other outcomes

Beyond the standard measures of diagnostic accuracy, a number of other outcomes were reported.

One Irish study described an assessment unit's experience following the introduction of DBT (Hologic [Selenia] Dimensions) in the work-up of screen-detected masses, asymmetries and architectural distortion (Ni Mhuirheartaigh *et al*, 2017)<sup>16</sup>. In the first 6 months, spot compression (coned view) was performed in recalled women in addition to DBT; the study involved three readers retrospectively reviewing the images to ascertain whether spot compression provided any additional diagnostic information. In the 6 month period, 548 women with 565 lesions, were recalled. Of these lesions, 341 were assessed by spot compression and DBT. The authors reported that spot compression was only considered helpful (in that it provided additional diagnostic information not obtained from DBT) in one woman whose breast had been inadequately positioned for DBT. They also stated that three additional cancers were detected by DBT that had not been identified by the two-view screening mammograms. The authors noted that only seven calcifications were imaged with both spot compression and DBT, and so were unable to draw any conclusions on the assessment of calcifications<sup>16</sup>.

Another study, from America, evaluated DBT as an alternative to conventional diagnostic mammography in the work-up of noncalcified findings in women recalled from screening mammography (Brandt *et al*, 2013)<sup>19</sup>. This retrospective study of 146 women (with 158 abnormalities detected at breast screening) involved three radiologists reviewing abnormal screening mammograms, comparison mammograms and DBT images before recording a DBT BI-RADS category and confidence score (3-point scale) for each finding. The three readers DBT BI-RADS categories were compared to the original BI-RADS scores based on the diagnostic mammograms. In addition to reporting no significant difference between DBT and diagnostic mammography with respect to sensitivity, specificity or accuracy for any of the readers, the authors reported that the agreement between DBT BI-RADS and clinical diagnostic mammography BI-RADS was excellent for two of the readers, and good for a third. The results of this study suggested that the use of DBT would not reduce the number of ultrasounds requested. This is at odds with Hakim *et al*<sup>23</sup> who reported that the availability of DBT would have eliminated the need for ultrasound in 12% of cases retrospectively reviewed. Brandt *et al* suggested that the higher than expected request for ultrasounds in their study may be partly explained by the fact that their readers had limited clinical experience with DBT, and that as experience grew, the perceived need for ultrasounds may decrease in some cases<sup>19</sup>.

The study by Hakim *et al* was small (n=25)<sup>23</sup>. The aim of the study was to subjectively compare additional mammographic views to DBT in the characterising of known masses, architectural distortions, or asymmetries. The study included four readers, and the authors reported their perceptions of DBT. In addition to the perceived reduction in the need for ultrasound, the authors stated that FFDM plus DBT were thought to be better for diagnosis in 50% (50/100) of cases, compared with FDDM plus additional diagnostic views. The methods were considered equivalent in 31% of cases, and DBT was perceived as worse for diagnosis in 19% of cases. The authors also noted that for all readers, 92% of ratings for biopsy-verified cancer cases and 50% of the ratings for high-risk cases were rated as BI-RADS 4 or 5.

Finally, a small study by Noroozian *et al* (n=67) aimed to determine if the performance of DBT was comparable to mammographic spot views in characterising breast masses as benign or malignant<sup>21</sup>. One outcome that was unique to this study was 'mean mass visibility ratings' (whereby mass visibility was

rated on a 10-point scale, with one being the easiest to visualise and 10 being the most difficult). The authors reported that the mean mass visibility rating was slightly better with DBT (range 3.2 to 4.4) than with spot views (range 3.8 to 4.8), based on information from the four readers in the study. However, only one reader achieved a statistically significant difference ( $p=0.001$ ).

### Microcalcifications

For the assessment of microcalcifications, the existing evidence base is not clear on whether the comparable/improved accuracy for DBT still applies.

Morel *et al* concluded that fine-focus magnification views in the craniocaudal and lateral projections are still required for the assessment of microcalcifications<sup>18</sup>. Likewise, Heywang-Köbrunner *et al* stated that 'DBT was most helpful for architectural distortions and densities but did not contribute significant information over AV [Additional Views] for microcalcifications or for the few cases of global asymmetry'<sup>15</sup>.

### Breast density/stage and type of cancer

The studies did not explore in detail how breast density, and stage and type of cancer influences the performance of DBT. This issue was discussed by Whelehan *et al* who noted that: 'In common with other studies of DBT in the assessment context, the number of actual cancers was too low to justify any sub-analysis by lesion type, grade, age of participants, or breast density'<sup>5</sup>.

No further evidence was identified to answer this question.

### Clinical Guidelines

#### NHS Public Health England: Clinical guidance for breast cancer screening assessment<sup>14</sup>

The literature search for secondary evidence highlighted guidance from NHS Public Health England on breast cancer screening assessment (2016). In the guidance, DBT is listed as an option in women who have been recalled for assessment. It is not clear from the guidance whether it is based on a systematic review of the literature. Based on the references, the evidence supporting this appears to come from five primary studies, four of which have been discussed under 'Primary studies' above<sup>17, 18, 20, 21</sup> (the fifth, Michell *et al*, did not meet the inclusion criteria for this evidence note).

Furthermore, an associated NHS England position paper states: 'there is sufficient evidence to justify the use of the Hologic [Selenia] Dimensions tomosynthesis system and the GE Healthcare Essential (SenoClaire) tomosynthesis system in assessment in the NHS Breast Screening Programme'<sup>24</sup>.

### Safety

Most of the included studies did not detail the radiation doses for DBT and SMV, with only two providing figures (Zuley *et al* and Tagliafico *et al*). Where mentioned, studies generally noted that the radiation dose from coned or magnified mammographic views is similar to, or slightly higher than DBT.

Zuley *et al* provided figures, stating that the radiation dose per view for the tomosynthesis image sets and the corresponding two-dimensional mammograms was, on average, 257 mGy  $\pm$  73 and 230 mGy  $\pm$  76, respectively<sup>20</sup>.

Tagliafico *et al* reported that DBT has a lower radiation dose than the combination of dual-view mammography and digital spot compression. The mean glandular dose reported was  $4.69 \pm 1.7$  mGy for the FFDM system (the two projections of FFDM added to the spot compression view) and  $2.39 \pm 0.6$  mGy for DBT<sup>22</sup>.

Furthermore, repeat views with standard supplementary diagnostic views are not uncommon (for example, due to incorrect positioning of the breast). In the study by Cornford *et al*, repeat spot compression (coned) views were requested in 15.2% of assessment work-ups<sup>17</sup>. Therefore, in some instances DBT may result in a lower dose of overall radiation.

## Cost effectiveness

No cost effectiveness evidence was identified. However, a number of cost issues for consideration are described below.

DBT is currently available, but switched off, on most mammography machines in NHSScotland. Enabling DBT capability on the Hologic [Selenia] Dimensions system requires a software upgrade and purchase of a license (£50,000 per unit, with discounts for multi-license purchases). Other costs to consider include increased servicing costs and the cost associated with PACS (Picture Archiving and Communication System).

DBT involves taking an image of the whole breast and therefore obtaining DBT images should take the same amount of (or less) time than coned views - which requires placement of special paddles and sometimes repositioning of the woman. DBT images take longer to read than spot compression and magnified mammographic views (though time taken may reduce with experience). Furthermore, there may be a requirement for additional quality assurance. These are important considerations given the existing demands on the radiology workforce.

The file size of DBT images are larger than SMVs, and so the use of DBT may result in increased data storage requirements. However, women who have been recalled for assessment may have more than one SMV, and possibly an additional mammogram, and so the impact on data storage would not be as great as if DBT was used in initial screening.

While not reported in the literature, a peer reviewer for this evidence note commented that there are rare occasions where appearances on DBT images may be equivocal, and a spot compression view may still be helpful.

DBT is already in use in some Scottish centres, and so there already exists a knowledge base amongst some Scottish breast radiologists. However, if DBT was introduced in the assessment setting, an initial period of training would be required, and radiologists would need to gain experience in order to become familiar with and skilled at interpretation of DBT images. One peer reviewer for this evidence note suggested that there should be a low threshold for discussing cases with colleagues in the assessment clinic.

There is also potential for resource savings. Sometimes supplementary coned mammographic views have to be repeated due to incorrect positioning of the breast. In addition if - as some of the studies suggest - the diagnostic accuracy of DBT is superior to SMVs, it may reduce the number of women who require biopsies. However, further research would be needed to establish this.

## Conclusion

This rapid review of the literature highlighted ten studies which consistently reported that DBT can be used in place of SMVs in women who have been recalled from initial breast screening for further assessment. With regards to diagnostic accuracy, six concluded that DBT demonstrated comparable diagnostic accuracy when used in place of SMVs, and two concluded that the diagnostic accuracy of DBT was superior. However, this comparable/improved accuracy of DBT in the assessment of screen-detected abnormalities only applies to soft-tissue abnormalities, not to microcalcifications.

It is worth noting the second question that this evidence note sought to answer: how breast density and type/stage of cancer influence the performance of DBT. Unfortunately, no studies were identified that were able to help answer this question.

No studies on cost effectiveness were identified. Although the use of DBT in women who have been recalled from breast screening for further assessment would require some additional resource, there is the potential for cost savings; for example if DBT increased diagnostic confidence for benign finding, this may lead to a reduction in biopsies (although this is not demonstrated within the existing evidence).

Based on evidence that has been included in this rapid review, guidance from Public Health England has listed DBT as an option in women who have been recalled for assessment.

## Identified research gaps

- There is a need to establish the cost-effectiveness and resource implications of replacing additional coned views with DBT in women who have been recalled from breast screening.
- The existing evidence does not report the influence of breast density and type/stage of cancer on DBT performance.
- More information on the difference in radiation dose between coned views and DBT would aid decision making. Of the included studies some noted that the dose is similar, but only two provide figures.

## Equality and diversity

Healthcare Improvement Scotland is committed to equality and diversity in respect of the nine equality groups defined by age, disability, gender reassignment, marriage and civil partnership, pregnancy and maternity, race, religion, sex, and sexual orientation.

The process for producing evidence notes has been assessed and no adverse impact across any of these groups is expected. The completed equality and diversity checklist is available on [www.healthcareimprovementscotland.org](http://www.healthcareimprovementscotland.org)

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A glossary of commonly used terms in Health Technology Assessment is available from [htaglossary.net](http://htaglossary.net).

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