Breast Tomosynthesis
Clinical Evidence

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KEYWORDS

• Digital breast tomosynthesis • Diagnostic evaluation • Trial outcomes

KEY POINTS

- The data on the efficacy and effectiveness that has accumulated in the last 20 years is consistent and compelling.
- Most published outcomes suggest that screening with DBT improves cancer detection and reduces false positive recalls.
- Diagnostic imaging with DBT of non-calcified findings has equivalent or superior performance compared to digital mammography.

INTRODUCTION

In January 2016, the United States Preventive Services Task Force updated their breast cancer screening recommendations and classified digital breast tomosynthesis (DBT), concluding that "the current evidence is insufficient to assess the benefits and harms of digital breast tomosynthesis (DBT) as a primary screening method for breast cancer."[1] This was primarily based on the absence of randomized controlled trials of DBT. In sharp contrast to this conclusion, nearly 20 years of scientific and service data have accumulated that clearly confirm the efficacy of the DBT technology and strongly suggest its effectiveness in both screening and diagnostic applications. Beginning in 1997 with the first scientific publication on DBT[2] and continuing with the ongoing results reporting of a wide variety of clinical trials, the data supporting the use of DBT are both consistent and compelling. This article catalogs the scientific and clinical evidence of DBT, highlighting some of the most important studies that have been reported to date.

EARLY OBSERVATIONAL STUDIES: 1997 TO 2008

Modern DBT was first introduced into the peer reviewed literature in 1997 by Niklason and colleagues[2] in a proof of principle experiment conducted at the Massachusetts General Hospital (MGH) using a prototype modification of the senographe DMR (GE Medical Systems, Milwaukee, WI). Three radiologists with mammography expertise rated lesion and margin visibility and diagnostic confidence of DBT images (at the slice of interest) and film mammography (FM) images of 6 abnormalities contained within 4 mastectomy specimens. Images were viewed side by side on a high luminance view box. The abnormalities included subtle findings (irregular mass, calcifications, round mass), a discrete round mass, architectural distortion, and an obvious 3 cm mass. DBT was superior to FM in the evaluation of all of the subtle abnormalities and the area of architectural distortion. Only the obvious mass had comparable ratings. The investigators concluded that DBT is "capable of producing high-quality breast images that may contain information that is currently not visible with conventional imaging" and that the value of DBT was most evident in the setting of radiographically dense tissue.

After a 10 year hiatus, Poplack and colleagues,[3] described the first in vivo DBT experience in a consecutive series of clinical subjects. The study was intended to evaluate the efficacy of DBT in the setting of diagnostic imaging. Ninety-eight women with 99 abnormalities recalled from digital

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mammography (DM) screening were enrolled. Current practice at that time included screening with DM and diagnostic work up with FM; therefore, subjects underwent FM diagnostic evaluation per usual clinical protocol. DBT full-field images were obtained with a prototype unit, Genesis (Hologic Inc), and matched to the FM diagnostic views, Lorad MIV (Hologic Inc, Danbury, CT), in up to 3 projections. One mm DBT slices were viewed on a prototype workstation. One radiologist specializing in breast imaging subjectively compared the diagnostic image quality of DBT with FM based on lesion conspicuity and feature analysis. At a separate session, the radiologist reviewed the DM screening examination with the additional DBT images to determine recall status, providing a reason for no recall.

The results for both diagnostic and screening DBT applications were remarkable. For the diagnostic imaging comparison, DBT was superior to FM in 37 out of 99 (37%), equivalent in 51 out of 99 (52%), and inferior in 11 out of 99 (11%) of the cases based on subjective image quality. Eight of the 11 (73%) inferior ratings involved calcifications. The adjunctive use of DBT for screening led to a 40% (37/92) reduction in false positive (FP) recalls. The study provided insight into the nature of DBT recall reduction. Most, 71% (32/45), came under the heading of no abnormality seen and were thought to reflect superimposition of normal fibroglandular tissues. The remainder of the recalls, 27% (12/45), reflected definitive lesion characterization (7/12) and detection of multiple benign masses (5/12).

A third important pilot observational study evaluated the cancer detection potential of DBT. In this study, Andersson and colleagues[4] assessed the conspicuity of subtle breast malignancy defined as questionably visible or occult on DM. DBT was performed on a modified DM unit, Mammomat Novation (Siemens Medical, Erlangen, Germany). Two experienced breast radiologists compared single-view (1v) DBT with 1v DM and 2-view (2v) DM on a prototype workstation and rendered a nonblinded consensus opinion. The DBT projection was selected to correspond with the DM view in which the cancer was judged to be least well seen, and defaulted to the mediolateral oblique (MLO) projection when the cancer was occult on DM. The readers rated each case by modality on a 4-point visibility scale, reported final Breast Imaging Reporting and Data System (BIRADS), overall breast density, breast density within 1 cm of the cancer, and mammographic finding type.

There were 40 breast cancers in 36 women, with an average subject age of 59 years and median tumor size of 11 mm. Almost all, 39 out of 40 (98%) were invasive cancer with only a single case of pure ductal carcinoma in situ (DCIS). Both invasive lobular carcinoma, 10 out of 39 (26%), and tubular carcinoma, 3 out of 39 (8%), were over-represented relative to a typical invasive cancer distribution. Two-thirds (24/36) of breasts had dense composition (heterogeneously dense or extremely dense). Cancer was significantly ($P<.01$) more visible with DBT than with either 1v DM or 2v DM. Visibility was rated higher with 1v DBT than 2v DM in 11 out of 40 (28%) cancers. BIRADS assessment was upgraded by DBT in 11 subjects compared with 2v DM. The investigators concluded that 1v DBT was better than DM in visualizing and classifying mammographically subtle cancer.

Summary

- Early studies showed a decrease in recall with DBT, primarily because of the ability to discount superimposed tissue.
- Increase in cancer conspicuity was appreciated with DBT when the malignancies were either mammographically subtle or occult.
- Calcifications were not as well characterized on DBT, possibly due to long exposure times.

READER STUDIES: 2008 TO 2012

Over the course of the next 5 years, 16 small to intermediate-scale DBT reader studies were published in the English language in peer reviewed journals from the United States and Europe.[5–20] For the most part, these studies consisted of small-scale rating trials that evaluated the efficacy of DBT in different clinical settings (ie, screening or diagnostic breast imaging) or in the assessment of distinct mammographic finding types (eg, calcifications or masses). Studies ranged from 30 to 376 subjects and involved up to 20 mammography readers with varying levels of mammography expertise, although none of the readers had a high-volume experience with DBT due to its novelty. Highlights from some of those studies are noted here.

SCREENING STUDIES: 2008 TO 2012

Under the leadership of David Gur, researchers from the University of Pittsburgh Medical Center (UPMC) published 2 pilot performance studies using a common image data set of 125 unilateral examinations enriched with 35 cancers. Eight breast radiologist specialists compared DM alone with the combination of DM and 2v DBT. In the first study,[6] the readers also evaluated DBT source images and 2v DBT only. DM was acquired using the Selenia (Hologic Inc) and DBT with the Genesis (Hologic Inc). Unilateral examinations were viewed