

Are the initial benefits of digital breast tomosynthesis (DBT) sustained?

By Dr. M. Bahl

BENEFITS OF DIGITAL BREAST TOMOSYNTHESIS (DBT)

Multiple studies conducted in Europe and the United States have demonstrated the advantages of digital breast tomosynthesis (DBT) over two-dimensional digital mammography (DM) for screening purposes. Specifically, as compared to screening DM, screening DBT has led to higher rates of invasive cancer detection with a concurrent decline in false-positive examinations [1-6]. For example, in a prospective comparative study from Italy, the cancer detection rate was 5.3 per 1000 examinations with DM, compared to 8.1 per 1000 examinations with combined DBT and DM ($P < .0001$) [1]. The authors also reported that fewer false-positives resulted from combined DBT and DM compared to DM only.

The results of early investigations based on reader studies with cancer-enriched cases and single-site retrospective studies have been validated with subsequent prospective trials and multi-site studies. However, most studies report performance metrics that are based on the prevalent (or first) round of screening, and thus there are relatively scarce data with regard to whether or not the benefits of DBT are maintained over time and after multiple rounds of screening [7-9]. As a higher cancer detection rate can be seen when DBT (or other new imaging modality) is used to screen a population of women for the first time, emerging data provide insights into the performance of DBT beyond the first round.

“... there are relatively scarce data with regard to whether or not the benefits of DBT are maintained over time and after multiple rounds of screening...”

ARE THE INITIAL BENEFITS OF DBT SUSTAINED?

A retrospective study was performed of 304,630 screening mammograms obtained at Massachusetts General Hospital (Boston, Massachusetts, USA) from March 2008 to February 2011 (during which time all women were screened with DM only) and from January 2013 to December 2017

(during which time all women were screened with DBT and DM) [8]. Two analyses were performed: one at the population level that compared performance metrics over time (DM group versus DBT1 [year 2013], DBT2 [year 2014], DBT3 [year 2015], DBT4 [year 2016], and DBT5 [year 2017] groups) and one at the individual level that compared metrics based on screening round (0 previous DBT versus 1 previous DBT, 2 previous DBT, 3 previous DBT, and 4+ previous DBT). Performance metrics were compared using multivariable logistic regression models after adjustments were made for age, race, mammographic breast density, and interpreting radiologist.

No significant changes in cancer detection rates were observed between the DM and DBT1-5 groups (4.6 per 1000 examinations with DM versus 4.9-5.8 per 1000 examinations with DBT1-5 groups, $P = .08$ to $P = .95$) [8]. This finding suggests that higher cancer detection rates with DBT may not occur at practices that attain a high cancer detection rate with DM alone. Despite no significant changes in overall cancer detection rates, more cases of invasive cancer relative to ductal carcinoma in situ were observed with the DBT2, DBT3, and DBT5 groups, as compared to the DM group. This preferred ratio of invasive cancer relative to ductal carcinoma in situ may contribute to optimizing outcomes from mammography. The study also found that the highest rate of cancer detection was seen with the first round of screening (6.1 per 1000 examinations with the first DBT examination versus 4.4-5.7 per 1000 examinations with at least one previous DBT examination, $P = .001$ to $P = .054$), confirming the prevalence effect that is observed with baseline screening examinations.

A lower abnormal interpretation rate was seen in the DBT1 group compared to the DM group (6.6% versus 7.3%, $P < .001$), which continued to be lower in the DBT2, DBT3, and DBT5 groups ($P < .001$ to $P = .02$) [8]. The decrease in abnormal interpretation rate was also observed after the first round of screening ($P < .001$ to $P = .002$). Higher specificity was seen in the DBT1 group compared to the DM group (93.9% versus 93.1%, $P < .001$), which continued to be higher in the DBT2, DBT3, and DBT5 groups ($P < .001$ to $P = .004$). Higher specificity was also observed after the first round of screening ($P < .001$ to $P = .01$). Although the magnitude of differences observed was small (e.g., 0.4%-0.7% for abnormal interpretation rate), these

The Author

Manisha Bahl, MD, MPH

Massachusetts General Hospital
 Department of Radiology / Division of Breast Imaging
 55 Fruit Street, WAC 240
 Boston, Massachusetts, USA 02114
 Email: mbahl1@mgh.harvard.edu

results demonstrate that the advantages of lower abnormal interpretation rates and higher specificity with DBT are sustained over time and after the first round of screening.

ADDITIONAL EVIDENCE IN SUPPORT OF THE SUSTAINED BENEFITS OF DBT

Further evidence in support of the sustained benefits of DBT comes from a retrospective study of 67,350 screening mammograms obtained at the Hospital of the University of Pennsylvania (Philadelphia, Pennsylvania, USA) from September 2010 to August 2011 (during which time all women underwent screening with DM) and from October 2011 to September 2016 (during which time all women underwent screening with DBT and DM) [9]. Similar to the aforementioned study, analyses were performed at the population and individual levels. In the population-level analysis, nonsignificant increases in cancer detection rate were seen with DBT (5.0 per 1000 women screened with DM versus 5.3-6.6 per 1000 women screened with DBT, $P = .25$). Of note, the results from the study suggest that more poor-prognosis cancers are detected with DBT than DM, although this finding requires validation with larger studies with long-term follow-up. The study also found a lower abnormal interpretation rate for the combined DBT groups than the DM group (8.0% versus 10.4%, $P < .001$), and this reduction in abnormal interpretation rate was sustained over several years and multiple rounds of screening examinations. Sustained improvements were also seen with specificity, positive predictive value 1, and positive predictive value 3.

Two-year data from a European study add to the growing body of evidence in support of the sustained impact of DBT

[7]. In a retrospective review that analyzed data from Breast-Screen Norway, 35,736 women underwent two consecutive screening mammographic examinations – DM after DBT, DM after DM, DBT after DBT, and DBT after DM. In the second round of screening, cancer detection rates were 4.3 per 1000 for DM after DBT, 4.6 per 1000 for DM after DM, 8.3 per 1000 for DBT after DBT, and 9.9 per 1000 for DBT after DM. Abnormal interpretation rate was 3.6% for DM after DM and was lower than 3.6% for all other groups ($P < .001$). The lowest abnormal interpretation rate (1.9%) was seen among women who underwent DBT after DBT.

IMPLICATIONS FOR THE FUTURE

The studies thus far demonstrate that the advantages of lower abnormal interpretation rates and higher specificity with DBT are sustained at the population and individual levels. The resultant reduction in diagnostic imaging may lead to savings in health care costs, resources, and time, while reducing the ensuing anxiety for patients [10]. In addition, the resources and time saved by decreasing abnormal interpretation rates may offset the additional time that is needed to interpret DBT examinations as compared to DM examinations [11]. In fact, a study of 450 breast conservation therapy patients with follow-up DM ($n=288$) or DBT ($n=162$) found that the estimated cost per patient, including downstream workup, was \$237.83 in the DM group and \$216.14 in the DBT group [12].

However, the findings with regard to cancer detection with DBT are mixed. The increase in cancer detection seen with a woman's first DBT examination may not be sustained over time, but findings do suggest that differences exist in the biology of

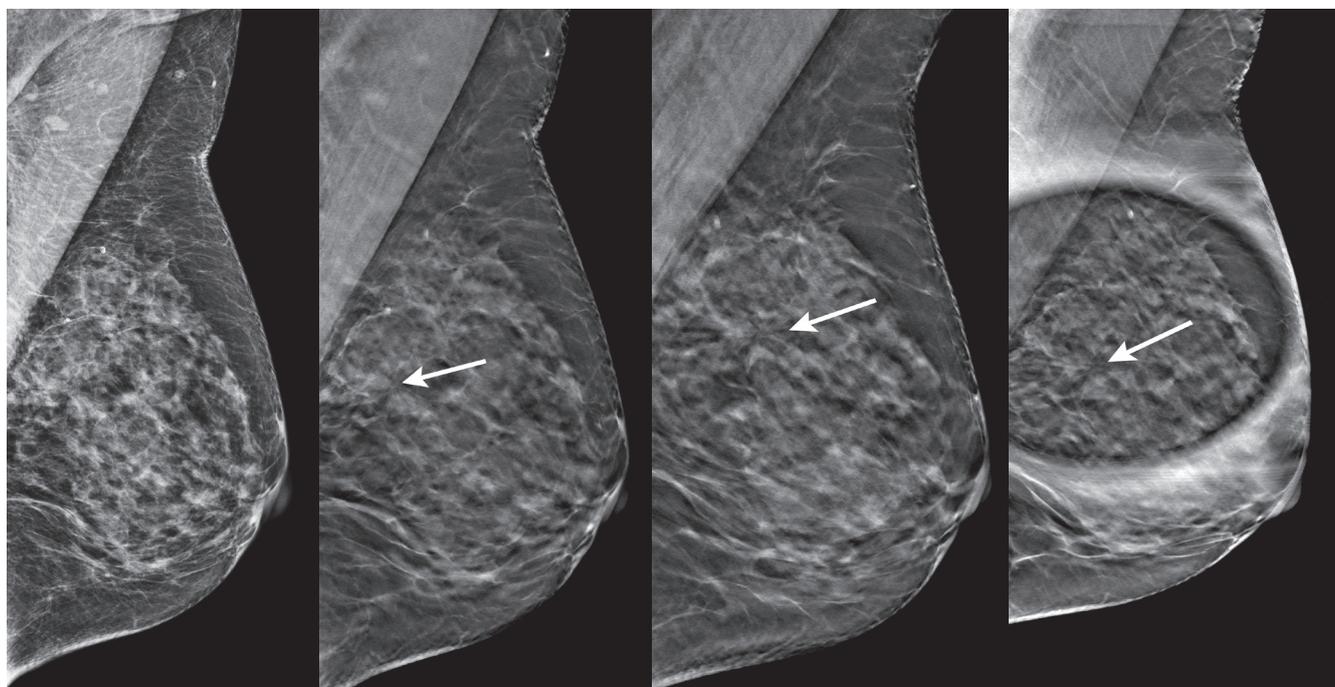


Figure 1. 82 year old female presented for screening mammography. Left Panel: Left mediolateral oblique 2D view. Second Panel from left: Left mediolateral oblique tomosynthesis image. Second Panel from right: Left mediolateral tomosynthesis image. There is architectural distortion in the superior aspect of the left breast at posterior depth, best seen on the tomosynthesis views (arrows). Right Panel: The finding persisted on the left oblique mediolateral spot compression tomosynthesis view (arrow). No correlate was seen on the craniocaudal view nor on ultrasound. Tomosynthesis-guided core needle biopsy was subsequently performed, which yielded grade 2 invasive ductal carcinoma.

DM- and DBT-detected tumors. Future studies will shed light on the characteristics of screening-detected cancers – that is, does DBT identify larger numbers of indolent cancers than DM? Or, does DBT lead to increased detection of poor-prognosis cancers, for which earlier detection would be beneficial?

The ongoing Tomosynthesis Mammographic Imaging Screening Trial (TMIST), which is a National Institutes of Health (NIH)-funded randomized trial that compares DM and DBT, may provide insight into the differences in the biology of tumors detected by these two imaging modalities [13]. In addition, further research on cancers not detected by DBT (i.e., false negatives or interval cancers) is warranted. Ultimately, these metrics – cancer detection rates, types of cancers detected, and interval cancer rates – are surrogates for the most critical metric: the impact of DBT on mortality.

REFERENCES

- Ciatto S, Houssami N, Bernardi D, Caumo F, Pellegrini M, Brunelli S, Tuttobene P, Bricolo P, Fanto C, Valentini M, Montemezzi S, Macaskill P. Integration of 3D digital mammography with tomosynthesis for population breast-cancer screening (STORM): a prospective comparison study. *Lancet Oncol* 2013;14(7):583-589. doi: 10.1016/S1473-2045(13)70134-7
- Rose SL, Tidwell AL, Bujnoch LJ, Kushwaha AC, Nordmann AS, Sexton R, Jr. Implementation of breast tomosynthesis in a routine screening practice: an observational study. *AJR Am J Roentgenol* 2013;200(6):1401-1408. doi: 10.2214/AJR.12.9672
- Skaane P, Bandos AI, Gullien R, Eben EB, Ekseth U, Haakenaasen U, Izadi M, Jepsen IN, Jahr G, Krager M, Niklason LT, Hofvind S, Gur D. Comparison of digital mammography alone and digital mammography plus tomosynthesis in a population-based screening program. *Radiology* 2013;267(1):47-56. doi: 10.1148/radiol.12121373
- Bernardi D, Caumo F, Macaskill P, Ciatto S, Pellegrini M, Brunelli S, Tuttobene P, Bricolo P, Fanto C, Valentini M, Montemezzi S, Houssami N. Effect of integrating 3D-mammography (digital breast tomosynthesis) with 2D-mammography on radiologists' true-positive and false-positive detection in a population breast screening trial. *Eur J Cancer* 2014;50(7):1232-1238. doi: 10.1016/j.ejca.2014.02.004
- Friedewald SM, Rafferty EA, Rose SL, Durand MA, Plecha DM, Greenberg JS, Hayes MK, Copit DS, Carlson KL, Cink TM, Barke LD, Greer LN, Miller DP, Conant EF. Breast cancer screening using tomosynthesis in combination with digital mammography. *JAMA* 2014;311(24):2499-2507. doi: 10.1001/jama.2014.6095
- Greenberg JS, Javitt MC, Katzen J, Michael S, Holland AE. Clinical performance metrics of 3D digital breast tomosynthesis compared with 2D digital mammography for breast cancer screening in community practice. *AJR Am J Roentgenol* 2014;203(3):687-693. doi: 10.2214/AJR.14.12642
- Hovda T, Brandal SHB, Sebuodegard S, Holen AS, Bjørndal H, Skaane P, Hofvind S. Screening outcome for consecutive examinations with digital breast tomosynthesis versus standard digital mammography in a population-based screening program. *Eur Radiol* 2019;29(12):6991-6999. doi: 10.1007/s00330-019-06264-y
- Bahl M, Mercaido S, Dang PA, McCarthy AM, Lowry KP, Lehman CD. Breast cancer screening with digital breast tomosynthesis: are initial benefits sustained? *Radiology* 2020;295(3):529-539. doi: 10.1148/radiol.2020191030
- Conant EF, Zuckerman SP, McDonald ES, Weinstein SP, Korhonen KE, Birnbaum JA, Tobey JD, Schnall MD, Hubbard RA. Five consecutive years of screening with digital breast tomosynthesis: outcomes by screening year and round. *Radiology* 2020;295(2):285-293. doi: 10.1148/radiol.2020191751
- Mullen LA, Panigrahi B, Hollada J, Panigrahi B, Falomo ET, Harvey SC. Strategies for decreasing screening mammography recall rates while maintaining performance metrics. *Acad Radiol* 2017;24(12):1556-1560. doi: 10.1016/j.acra.2017.06.009
- Dang PA, Freer PE, Humphrey KL, Halpern EF, Rafferty EA. Addition of tomosynthesis to conventional digital mammography: effect on image interpretation time of screening examinations. *Radiology* 2014;270(1):49-56. doi: 10.1148/radiol.13130765
- Hasan S, Gresswell S, Colosimo B, Weinberger K, Anderson S, Abel S, Bigbee M, Shindel B, Hilton C, Julian T, Trombetta M. Surveillance mammography after breast conservation therapy: is tomosynthesis worth it? *Am J Clin Oncol* 2019;42(8):682-686. doi: 10.1097/COC.0000000000000568
- National Cancer Institute. TMIST (Tomosynthesis Mammographic Imaging Screening Trial), 2019. Available via <https://www.cancer.gov/about%20cancer/treatment/clinical-trials/nci-supported/tmist.%20Accessed%2015%20September%202020>. Accessed 15 September 2020.

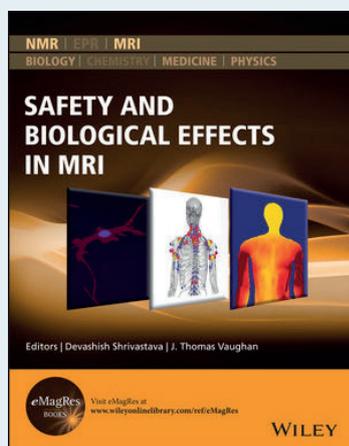
“... the advantages of lower abnormal interpretation rates and higher specificity with DBT are sustained at the population and individual levels. ...”

Book Review

Safety and Biological Effects in MRI

Ed by D Shrivastava & J TVaughan

Pub By Wiley Blackwell Dec 2020; 536 Pages Hardcover \$190



In vivo magnetic resonance imaging (MRI) has evolved into a versatile and critical, if not ‘gold standard’, imaging tool with applications ranging from the physical sciences to the clinical ‘-ology’. In addition, there is a vast amount of accumulated but unpublished inside knowledge on what is needed to perform a safe, in vivo MRI. The goal of this comprehensive text, written by an outstanding group of world experts, is to present information about the effect of the MRI

environment on the human body, and tools and methods to quantify such effects. By presenting such information all in one place, the expectation is that this book will help everyone interested in the Safety and Biological Effects in MRI find relevant information relatively quickly and know where we stand as a community. The information is expected to improve patient safety in the MR scanners of today, and facilitate developing faster, more powerful, yet safer MR scanners of tomorrow.