

OM1 oncology & rare disease publications

1. Starzyk KA, Milberg K, Deshpande A, Swenson A, Curhan G. [An Evaluation of Real-World Use of Biologics in Rare Systemic Vasculitides During Routine Clinical Care in the US. Virtual ACR Convergence](#), November 2020.
2. Conant EF, Mortimer K, Friedler H, Behling M, Donadio G, Hitchcock C, Pohlman S, Sardiña A, Talley M, Alsheik N, [Effect of Breast Cancer Screening Modality Order on Recall, Cancer Detection Rates, and Positive Predictive Value 1 for Women with Multiple Screening Exams](#). Virtual RSNA 2020. Philadelphia, PA, October 2020.
3. Leavy MB, Starzyk K, Myers E, Curhan G, Gliklich R, [Using Real-World Evidence to Support a Changing Paradigm for Cancer Screening: A Commentary](#). Pharmacoepidemiology and Drug Safety, September 2020.
4. Alsheik N, Su Z, Lafontant A, Donadio G, Troeger K, Pohlman S, Talley M, Menon V, Conant E. [Disparities in Accessing Screening Mammography: Opportunities for Improving Diagnostic Outcomes](#). National Comprehensive Cancer Network Annual Conference, Orlando. March 21–23, 2019.
5. Alsheik NH, Dabbous F, Pohlman SK, Troeger KM, Gliklich RE, Donadio GM, Su Z, Menon V, Conant EF. [Comparison of Resource Utilization and Clinical Outcomes Following Screening with Digital Breast Tomosynthesis vs. Digital Mammography: Findings from a Learning Health System](#). Academic radiology, 2018 Jul 26.
6. Dabbous F, Su Z, Donadio G, Dolan J, Menon V, Alsheik N; [Towards Personalized Breast Imaging Pathways: Initial Findings from a Learning Health System](#). ACOG Annual Conference, March 2018. 27.
7. Alsheik N, Dabbous F, Donadio G, Su Z, Gliklich R, Pohlman S, Mortimer K, Menon V, Conant E. [Impact of Population Characteristic on Recall Rates: Initial Finding from a Learning Health System](#). NCCN Annual Conference, March 2018



RWF Co-publication (2018)

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Alsheik NH, Dabbous F, Pohlman SK, Troeger KM, Gliklich RE, Donadio GM, Su Z, Menon V, Conant EF. [Comparison of Resource Utilization and Clinical Outcomes Following Screening with Digital Breast Tomosynthesis vs. Digital Mammography: Findings from a Learning Health System.](#) Academic radiology, 2018 Jul 26.



Original Investigation

Comparison of Resource Utilization and Clinical Outcomes Following Screening with Digital Breast Tomosynthesis Versus Digital Mammography: Findings From a Learning Health System

Nila H. Alsheik, MD, Firas Dabbous, PhD, Scott K. Pohlman, Kathleen M. Troeger, Richard E. Gliklich, MD, Gregory M. Donadio, Zhaohui Su, PhD, Vandana Menon, MD PhD, Emily F. Conant, MD

Abstract

Background: This study was supported by Hologic Inc., Marlborough, Massachusetts. Declaration of interest: Nila H. Alsheik MD—employee of Advocate Health and is also on Hologic's scientific advisory panel; Firas Dabbous PhD—employee of Advocate Health; Scott K. Pohlman MD—employee of Hologic Inc.; Troeger KM—employee of Hologic Inc.; Richard E. Gliklich MD—employee of DBT Inc.; Gregory M. Donadio—employee of DBT Inc.; Zhaohui Su PhD—employee of OM1 Inc.; Vandana Menon MD PhD—employee of OM1 Inc.; Emily F. Conant MD—has grant from Hologic and is also on their scientific advisory panel.

From the Advocate Breast Cancer Center, Advocate Lutheran General Hospital, 1700 Luthan Lane, Park Ridge, IL 60069 (N.H.A.); James R. & Helen D. Russell Institute for Research & Innovation, Advocate Lutheran General—Center for Advanced Care, 1700 Luthan Lane, Suite 1410, Park Ridge, IL 60069 (F.D.); Hologic Inc., 240 Campus Drive, Marlborough, MA 01752 (B.K.P., K.M.T.); OM1 Inc., 800 Boylston Street, Suite 1410, Boston, MA 02116 (R.E.G., G.M.D., Z.S., V.M.); Department of Radiology, 3400 Spruce Street, Hospital of the University of Pennsylvania, Philadelphia, PA 19104 (E.F.C.). Received May 3, 2018; revised May 28, 2018; accepted May 30, 2018. Address correspondence to E.F.C. e-mail: emily.conant@upenn.edu

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Figure 1. Most common diagnostic pathways within 90 days following a positive screening digital mammography (DM) or digital breast tomosynthesis (DBT) examination.

Table 4. Present data on the clinical characteristics of the cancers identified by each screening modality. Histopathologic, stage, and receptor data were available for 807 women with cancer in the study cohort. There were no differences in tumor size, nodal status, or estrogen and progesterone status between women in the DBT or DM groups. The cancer detection rates per 1,000 exams by tumor grade for DBT by Grade I, II, III, or IV, and Unknown were 1.3, 1.4, 0.7, and 1.4, respectively. In comparison, the cancer detection rates by tumor grade for DM were 0.8, 1.5, 0.9, and 0.6 for the same groups. A larger proportion of cancers in the DBT group were categorized as Grade I and human epidermal growth factor receptor 2 (HER2) negative compared to DM.

DISCUSSION

This study utilized a learning health system to examine clinical outcomes and downstream imaging after screening with DBT or DM in two large, geographically and clinically diverse U.S. health care networks. The results of this study confirm previous reports of recall rate reduction achieved with DBT with the clinical benefits of improved PPV-1, specificity, and cancer detection rate (7,9). Recall rate reduction was most significant in the 60–79 year old age group, while increased cancer detection was most significant in the 60–79 year old age group and the heterogeneously dense breast subtype. This study builds upon prior studies by demonstrating overall reduction in recall rate as well as reduction across demographic (age, race, ethnicity), and clinical (breast risk profile and density) strata, and facilities. Further, our data suggest DBT may provide a more efficient diagnostic work-up at recall and a faster time to biopsy and ultimate diagnosis. There were significant differences in the risk profile of women who received DBT versus DM; the former group was more likely to have dense breasts and higher calculated risk scores for breast cancer. This finding underscores the importance of adequately controlling for these population differences in comparative analysis. Our data demonstrate that recall rates are lower with DBT overall, across all age groups, all races, non-Hispanic ethnicity, all breast density categories, and in women with elevated lifetime Tyrer-Cuzick risk score. These findings may assist clinical decision making for specific groups of women who are the most likely to be recalled such as those with dense breasts. The observation that African American women and women of Hispanic ethnicity were less likely to receive DBT raises concerns related to DBT access and potential health care disparities. As recommendations for screening mammography are increasingly delayed past the original cut point of 40 years of age, DBT may be of value in younger women, particularly those at higher lifetime risk of breast cancer. Facility level data from our study indicate that those facilities which fully transitioned to DBT exhibit lower DBT recall rates than hybrid and predominantly DM screen environments. The finding that women in the DBT group were more likely to receive ultrasound alone as their diagnostic test is in line with Loane et al. who reported that 28.3% in the DBT recall cohort proceeded to ultrasound alone for diagnostic evaluation versus 2.6% in the DM recall cohort, in a single center study (15). A potential explanation for this is that superior lesion localization, characterization and complexity on the index screening DBT provides higher diagnostic confidence and the more direct route to ultrasound alone. Time to biopsy and time to final diagnosis was significantly shorter in the DBT group after adjustment for institution and race. This may be, in part, because those institutions with greater DBT utilization represent tertiary referral centers within their health care systems, thereby implicitly having the most interdisciplinary resources by which to shorten ultimate time to biopsy, time to final diagnosis, and time to treatment. Within our cohort, however, those institutions with greater DBT screen utilization also exhibit proportionately higher DBT diagnostic utilization at recall suggesting that these findings may be due to improved diagnostic confidence in biopsy recommendations arising from DBT diagnostic examinations. This is further supported by our finding that in subgroup analyses within hybrid sites, time to biopsy, and diagnosis were shorter with DBT than DM. In line with these findings, Raghu et al. reported a decrease in the proportion of lesions characterized as probably benign (BI-RADS 3) and an increase in the proportion of examinations characterized as benign (BI-RADS 1 or 2) DBT versus DM cohorts (11). In our study, there was a 22% higher cancer detection rate for DBT compared to DM. The majority of screen detected cancers were early stage for both DBT and DM with no significant differences in nodal status between the two groups. There were significant differences in the distribution of tumor size and grade with a larger proportion of Grade 1 tumors in the DBT group. There was a trend for DBT-detected cancers to be human epidermal growth factor negative. Similar results were also reported by Kim et al., demonstrating a benign A-like subtype (estrogen receptor positive or progesterone receptor positive or both, human epidermal growth factor receptor 2 negative, and Ki-67 expression <1%) were more often associated with DBT screening than DM alone screening on multivariate analysis (2). Further investigation is warranted to evaluate whether DBT screening detects earlier stage, less advanced, and aggressive breast cancers. The strengths of this study include the large, geographically, ethnically, and racially diverse screening cohort from multiple academic and community health care networks. Linkage with either RIS and/or local tumor registry allowed analysis of the histopathologic characteristics of the breast cancer detected as well as the false negative rates. Limitations include linkage for some of the data with only local tumor registry from one institution versus complete matching with state or larger population-based tumor registry, which may affect sensitivity and specificity calculations. Additionally, while we adjusted for facility and several patient factors associated with screening outcomes when comparing DBT and DM outcomes, it is possible that other factors not included in the adjustment may affect the results. Our data demonstrate a streamlined diagnostic imaging evaluation in the DBT cohort and sustained recall rate reduction across all patient strata. Improved imaging efficiency, decreases

Table 3. Cancer Outcomes by Screening Modality in Women with At Least 12 months of Follow-up After a Positive Screening Examination

Cancer Outcomes	DBT n = 86,379	DM n = 99,660	P Value	Unadjusted		Adjusted*	
				Odds Ratio	95% CI	Odds Ratio	95% CI
Total cancers (n)	497	429					
Invasive cancers (n)	350	328					
Cancer rate per 1000	4.2	4.3	0.004	1.21 (0.7–1.38)	1.16 (0.91–1.35)		
Invasive cancer rate per 1000†	3.17	3.3	0.16	1.16 (0.81–1.50)	1.19 (0.91–1.49)		
Cancer detection rate per 1000	5.8	5.8	0.001	1.27 (1.11–1.45)	1.22 (1.05–1.42)		
Invasive cancer detection rate per 1000†	2.3	2.5	0.19	1.14 (0.91–1.46)	1.22 (0.91–1.62)		
False negative rate per 1000	0.42	0.52	0.30	0.80 (0.53–1.21)	0.76 (0.48–1.19)		
PPV1 (sensitivity), %	5.4	3.5	<0.001	1.57 (1.26–1.90)	1.44 (1.24–1.68)		
PPV2 (specificity), %	23.8%	24.9%	0.47	0.94 (0.79–1.11)	0.94 (0.78–1.13)		
Sensitivity %	92.0%	87.9%	0.039	1.58 (1.02–2.43)	1.64 (1.01–2.64)		
Specificity %	81.2%	88.5%	<0.001	1.20 (1.12–1.28)	1.25 (1.12–1.38)		

* Adjusted for institution, age categories (40–44, 45–49, 50–59, 60–79 years), breast density the four BI-RADS density categories, and first exam.

† 15 women with cancer did not have information on whether the cancer was invasive and were therefore excluded from this analysis.

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Figure 2. Cancer detection rates by age (A) and breast density (B), and screening modality in women with at least 12 months follow-up after a positive screening.

importance of adequately controlling for these population differences in comparative analysis. Our data demonstrate that recall rates are lower with DBT overall, across all age groups, all races, non-Hispanic ethnicity, all breast density categories, and in women with elevated lifetime Tyrer-Cuzick risk score. These findings may assist clinical decision making for specific groups of women who are the most likely to be recalled such as those with dense breasts. The observation that African American women and women of Hispanic ethnicity were less likely to receive DBT raises concerns related to DBT access and potential health care disparities. As recommendations for screening mammography are increasingly delayed past the original cut point of 40 years of age, DBT may be of value in younger women, particularly those at higher lifetime risk of breast cancer. Facility level data from our study indicate that those facilities which fully transitioned to DBT exhibit lower DBT recall rates than hybrid and predominantly DM screen environments. The finding that women in the DBT group were more likely to receive ultrasound alone as their diagnostic test is in line with Loane et al. who reported that 28.3% in the DBT recall cohort proceeded to ultrasound alone for diagnostic evaluation versus 2.6% in the DM recall cohort, in a single center study (15). A potential explanation for this is that superior lesion localization, characterization and complexity on the index screening DBT provides higher diagnostic confidence and the more direct route to ultrasound alone. Time to biopsy and time to final diagnosis was significantly shorter in the DBT group after adjustment for institution and race. This may be, in part, because those institutions with greater DBT utilization represent tertiary referral centers within their health care systems, thereby implicitly having the most interdisciplinary resources by which to shorten ultimate time to biopsy, time to final diagnosis, and time to treatment. Within our cohort, however, those institutions with greater DBT screen utilization also exhibit proportionately higher DBT diagnostic utilization at recall suggesting that these findings may be due to improved diagnostic confidence in biopsy recommendations arising from DBT diagnostic examinations. This is further supported by our finding that in subgroup analyses within hybrid sites, time to biopsy, and diagnosis were shorter with DBT than DM. In line with these findings, Raghu et al. reported a decrease in the proportion of lesions characterized as probably benign (BI-RADS 3) and an increase in the proportion of examinations characterized as benign (BI-RADS 1 or 2) DBT versus DM cohorts (11). In our study, there was a 22% higher cancer detection rate for DBT compared to DM. The majority of screen detected cancers were early stage for both DBT and DM with no significant differences in nodal status between the two groups. There were significant differences in the distribution of tumor size and grade with a larger proportion of Grade 1 tumors in the DBT group. There was a trend for DBT-detected cancers to be human epidermal growth factor negative. Similar results were also reported by Kim et al., demonstrating a benign A-like subtype (estrogen receptor positive or progesterone receptor positive or both, human epidermal growth factor receptor 2 negative, and Ki-67 expression <1%) were more often associated with DBT screening than DM alone screening on multivariate analysis (2). Further investigation is warranted to evaluate whether DBT screening detects earlier stage, less advanced, and aggressive breast cancers. The strengths of this study include the large, geographically, ethnically, and racially diverse screening cohort from multiple academic and community health care networks. Linkage with either RIS and/or local tumor registry allowed analysis of the histopathologic characteristics of the breast cancer detected as well as the false negative rates. Limitations include linkage for some of the data with only local tumor registry from one institution versus complete matching with state or larger population-based tumor registry, which may affect sensitivity and specificity calculations. Additionally, while we adjusted for facility and several patient factors associated with screening outcomes when comparing DBT and DM outcomes, it is possible that other factors not included in the adjustment may affect the results. Our data demonstrate a streamlined diagnostic imaging evaluation in the DBT cohort and sustained recall rate reduction across all patient strata. Improved imaging efficiency, decreases