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Ductal Carcinoma in Situ on Digital Mammography versus Digital Breast Tomosynthesis: Rates and Predictors of Pathologic Upgrade

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We have submitted or previously published manuscripts in which there is overlap of patients with this study:

Noncalcified Ductal Carcinoma In Situ (DCIS): Rate and Predictors of Upgrade to Invasive Carcinoma (published in *Academic Radiology*). In this published study, we report on 53 of the patients included in the current study. The accepted study focuses on the upgrade rates of noncalcified DCIS detected on screening and diagnostic mammography and features associated with upgrade risk. Do Eligibility Criteria for Ductal Carcinoma in Situ (DCIS) Active Surveillance Trials Identify Patients at Low Risk for Upgrade to Invasive Carcinoma? (submitted, under review). In this submitted study, we report on 858 patients, 318 of whom are included in the current study. The purpose of the submitted study is to determine upgrade rates of DCIS at needle biopsy to invasive carcinoma at surgery among women who meet eligibility criteria for active surveillance trials.

Breast Cancer Characteristics Associated with 2D Digital Mammography versus Digital Breast Tomosynthesis for Screening-detected and Interval Cancers (published in *Radiology*). In this published study, we report on 948 breast cancers (Jan 2009-Feb 2011 and Jan 2013-Feb 2015), 184 of which are included in the current study. The purpose of the published study is to compare the rates and tumor characteristics of screening-detected and interval cancers with digital mammography (DM) versus digital breast tomosynthesis (DBT). We believe that the current manuscript is distinct with regard to its objectives, materials and methods, results, and conclusions. In this study, we compare upgrade rates of DCIS on DM versus DBT and identify features that are associated with upgrade risk. There are no published studies, to our knowledge, on upgrade rates of DCIS, characteristics of the upgraded cancers, or predictors of upgrade in the modern era of DBT.

Methodology:

- retrospective
- observational
- performed at one institution

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Abstract

Objectives: To compare upgrade rates of ductal carcinoma in situ (DCIS) on digital mammography (DM) versus digital breast tomosynthesis (DBT) and identify patient, imaging, and pathological features associated with upgrade risk.

Methods: A retrospective review was performed of 318 women (mean 59 years, range 37-89) with screening-detected DCIS from 2007-2011 (DM group) and 2013-2016 (DBT group). Comparisons made between DM and DBT groups using the unpaired *t*-test and chi-square tests include: detection rates of DCIS, upgrade rates to invasive cancer, and pathological features of DCIS and upgraded cases. Patient, imaging, and pathological features associated with upgrade were also determined. *p*-values<0.05 were considered significant.

Results: There was no significant difference in detection rates of DCIS between DM and DBT groups (0.9 versus 1.0 per 1000 examinations, *p*=0.45). Upgrade rates of DCIS to invasive cancer in DM and DBT groups were similar (17.3% versus 16.8%, *p*=0.90), despite significant differences in pathological features of DCIS between DM and DBT groups (including nuclear grade, comedonecrosis, and progesterone receptor status [*p* 0.01]). Among upgraded cases, a higher proportion were high-grade invasive cancers with DBT (36.7% versus 9.5%, *p*=0.03). In both groups, ultrasound-guided (versus stereotactic) biopsy was associated with higher upgrade risk (*p* 0.03).

Conclusions: There was no significant difference in detection rates or upgrade rates of DCIS on DM versus DBT; however, upgraded cases were more likely to be high-grade with DBT, suggesting possible differences in tumor biology between cancers with DM and DBT. In both DM and DBT groups, biopsy modality was associated with upgrade risk.

Keywords

Breast Cancer; Digital Breast Tomosynthesis; Digital Mammography; Ductal Carcinoma In Situ

Introduction

Ductal carcinoma in situ (DCIS), which accounts for approximately 20% of all breast cancer diagnoses, refers to abnormal epithelial cells that are morphologically similar to invasive cancers but are confined to the milk ducts [1; 2]. The current standard of care for DCIS includes surgery, radiation, and chemoprevention [2]. DCIS has the potential to be upgraded to invasive carcinoma at the time of surgery, with upgrade rates ranging from 10% to higher than 40% [3-12]. Because the surgical approach for invasive carcinoma includes sampling of lymph nodes, patients with DCIS at core needle biopsy who are subsequently upgraded to invasive carcinoma must then undergo a second surgery. Therefore, accurate diagnosis at the

time of core needle biopsy and improved assessment of upgrade risk would inform surgical decision-making. In addition, active surveillance trials for DCIS are currently underway, and accurate assessment of upgrade risk is necessary to determine patient eligibility for these trials [13-16].

Because most DCIS presents as calcifications, which are best detected by mammography, detection rates of DCIS increased dramatically as a result of screening mammography [17]. Recent research has shown that the integration of digital breast tomosynthesis (DBT) into the screening setting leads to higher detection rates of invasive cancer but not DCIS [18-20]. However, there are no published studies, to our knowledge, on upgrade rates of DCIS, characteristics of the upgraded cancers, or predictors of upgrade in the modern era of DBT.

Identification of patients diagnosed with DCIS at core needle biopsy who are at increased risk of upgrade to invasive carcinoma at surgery would allow for a more tailored treatment plan at the time of diagnosis. In addition, pre-operative determination of upgrade risk is critical to the success of the current active surveillance trials for DCIS. The purpose of this study was to compare the upgrade rates of DCIS on digital mammography (DM) versus DBT and identify patient, imaging, and pathologic features that are associated with upgrade risk.

Materials and Methods

Study Subjects

The institutional review board exempted this Health Insurance Portability and Accountability Act-compliant retrospective study from the requirement for written informed consent. We identified patients through our institution's mammography information system (MagView) who (1) presented from March 1, 2007, to February 28, 2011 (DM group), and from January 1, 2013, to December 31, 2016 (DBT group), for screening mammography, (2) were subsequently diagnosed with DCIS at image-guided core needle biopsy, and (3) underwent surgical excision. Patients who presented for screening mammography from March 1, 2011, to December 31, 2012, were excluded in order to avoid selection bias, since DM alone and combined DM and DBT were performed during this time period. The study cohort was therefore composed of 318 women with biopsy-proven DCIS (mean age 59 years, range 37-89 years) (Figure 1). The DM group was composed of 133 women (mean age 58 years, range 37-83 years), and the DBT group was composed of 185 women (mean age 59 years, range 38-89 years) (Figure 1).

Imaging Technique and Interpretation

Screening examinations were performed using full-field DM or DBT (Hologic Selenia Dimensions). DBT examinations included tomosynthesis and conventional DM images (without the use of synthetic images). Included patients underwent image-guided core needle biopsy under stereotactic, tomosynthesis, ultrasound, or MRI guidance, performed by dedicated breast imaging radiologists or supervised fellows or senior residents. Of note, our institution transitioned from stereotactic to tomosynthesis-guided biopsy in January 2016.

Histopathology slides were reviewed by dedicated breast pathologists, and all included patients had pure DCIS on core biopsy without evidence of invasion.

Data Collection and Statistical Analysis

Data about each case of DCIS were retrieved from the electronic medical record system (Table 1). The unpaired *t*-test (for continuous data), chi-square test (for categorical data), or Fisher's exact test (for categorical data when expected cell frequencies were less than 5) were used to make the following comparisons:

- a. Patient features and imaging features in the DM versus DBT groups (age, race, family history of breast cancer in a first-degree relative, personal history of breast cancer, detection of DCIS at baseline versus nonbaseline mammogram, breast density at mammography, finding type at mammography, and biopsy modality)
- b. Detection rates of DCIS and upgrade rates of DCIS to invasive cancer in the DM versus DBT groups
- c. Pathological features of DCIS and upgraded invasive cancers in the DM versus DBT groups (nuclear grade, presence of comedonecrosis, estrogen receptor status, and progesterone receptor status for DCIS; size at surgery, histologic grade, estrogen receptor status, human epidermal growth factor receptor 2 [HER2] status, and lymph node status for invasive cancers)
- d. Patient features, imaging features, and pathological features of DCIS associated with upgrade risk in the DM group
- e. Patient features, imaging features, and pathological features of DCIS associated with upgrade risk in the DBT group

For all comparisons, *p*-values less than 0.05 were considered statistically significant.

Results

Patient Features and Imaging Features in the DM versus DBT Groups

There were no significant differences in patient features (age, race, family history of breast cancer in a first-degree relative, or personal history of breast cancer) between the DM and DBT groups (Table 2). Regarding imaging features, the majority of biopsies in the DM and DBT groups were performed for calcifications (93.7%, 298/318). The only difference observed in imaging features was that a lower proportion of women were diagnosed with DCIS based on findings at their baseline (rather than subsequent) mammogram in the DBT group than the DM group (Table 2).

Detection Rates of DCIS and Upgrade Rates of DCIS to Invasive Cancer in the DM versus DBT Groups

In the DM and DBT groups, the overall detection rate of DCIS was 1.0 per 1000 screening examinations (318 of 328,138). The screening detection rate of DCIS was 0.9 per 1000 examinations (133 of 144,091) in the DM group and 1.0 per 1000 examinations (185 of

184,047) in the DBT group ($p=0.45$) (Table 3). Of 318 cases of DCIS, 54 (17.0%) upgraded to invasive carcinoma at surgery. Fifty-two cases (96.3%) upgraded to invasive ductal carcinoma (IDC), and two cases (3.7%) upgraded to invasive lobular carcinoma (ILC). The upgrade rate was 17.3% (23/133) in the DM group and 16.8% (31/185) in the DBT group ($p=0.90$) (Table 3).

Pathological Features of DCIS and Upgraded Cases in the DM versus DBT Groups

Compared to the DM group, a higher proportion of women were diagnosed with grade 2 DCIS and a lower proportion were diagnosed with grade 3 DCIS in the DBT group (Table 3). A higher proportion had comedonecrosis at biopsy and a lower proportion were PR-positive in the DBT group (Table 3). A higher proportion of upgraded cases were high-grade invasive cancers in the DBT group than the DM group (Table 3). There were no other significant differences in pathological features of the invasive cancers in the DM versus DBT groups (Table 3). Of note, in the DM group, there were no cases with micrometastatic or macrometastatic lymph nodes, but three cases had isolated tumor cells in 1-3 lymph nodes. In the DBT group, one case had a micrometastatic lymph node, one case had macrometastatic lymph nodes, and four cases had isolated tumor cells in 1 lymph node.

Patient Features, Imaging Features, and Pathological Features of DCIS Associated with Upgrade in the DM Group

Among the upgraded cases in the DM group, biopsy modality was associated with risk of upgrade, with cases that underwent ultrasound-guided biopsy more likely to upgrade to invasive cancer (Table 4). There were no other significant differences in patient, imaging, and pathological features between cases in the DM era that did and did not upgrade to invasive cancer (Table 4).

Patient Features, Imaging Features, and Pathological Features of DCIS Associated with Upgrade in the DBT Group

Among the upgraded cases in the DBT group, biopsy modality was associated with risk of upgrade, with cases that underwent ultrasound-guided biopsy more likely to upgrade to invasive cancer (Table 5). There were no other significant differences in patient, imaging, and pathological features between cases in the DBT era that did and did not upgrade to invasive cancer (Table 5).

Discussion

We found that there are no significant differences in the detection rates and upgrade rates of DCIS in the DM versus DBT eras. Despite the equivalent upgrade rates, we did observe significant differences in the characteristics of DCIS cases that were detected with DM versus DBT, with a higher proportion of grade 2 DCIS, a lower proportion of grade 3 DCIS, a higher proportion of cases with comedonecrosis, and a lower proportion of cases that were PR-positive with DBT. In addition, of the cases that upgraded to invasive cancer at surgery, a higher proportion were high-grade invasive cancers in the DBT versus DM groups. In both DM and DBT groups, biopsy modality was the only feature associated with risk of upgrade.

These results provide insight into the characteristics of screening-detected breast cancers in the modern era of DBT.

In our study, the two cohorts (that is, DM and DBT groups) were similar with regard to patient and imaging features. With regard to imaging, more than 90% of biopsies leading to the diagnosis of DCIS were performed for calcifications with DM and DBT, as expected [21]. The only difference in imaging features that we observed is that a lower proportion of women were diagnosed with DCIS based on findings at their baseline mammogram in the DBT group than the DM group. The reason for this difference is not known but could reflect a higher proportion of baseline (versus nonbaseline) mammographic examinations among the entire DM population or could reflect changes in the utilization of the Breast Imaging Data and Reporting System (BI-RADS) final categories over time, with possibly less recalls for calcifications at baseline mammography or increased use of the probably benign assessment (BI-RADS Category 3) for calcifications at baseline mammography (and thus less recommendations for biopsies) [22; 23].

We observed no significant difference in the detection rates of DCIS in the DM versus DBT eras, which is in agreement with prior studies [18; 19]. Given that the majority of cases of DCIS present as calcifications that are detected on DM, the integration of DBT into the screening setting would not be expected to affect detection rates of DCIS. Although detection rates of DCIS with DM versus DBT have been previously reported, there are no published studies, to our knowledge, on upgrade rates of DCIS with DM versus DBT. In this study, we report no significant difference in upgrade rates in the DM versus DBT eras. The upgrade rates we report (17.3% and 16.8%) are in keeping with the results of other studies based on DM data [4; 7; 8; 10].

Despite similar DCIS detection rates and upgrade rates, we did observe significant differences in the pathological features of DCIS between the DM and DBT groups and also in the pathological features of the upgraded invasive cancers. For example, the DBT group had a higher proportion of DCIS cases with comedonecrosis at biopsy. Previous studies have reported an association between comedonecrosis and upgrade risk [24; 25]. In our study cohort, however, the increased proportion of DCIS cases with comedonecrosis in the DBT group did not lead to a higher upgrade rate. Although upgrade rates to invasive cancer were similar in the DM and DBT groups, a higher proportion of upgraded cancers in the DBT group were high-grade invasive cancers. None of the patients with upgraded invasive cancers in the DM group had metastatic axillary lymph nodes, but two patients in the DBT group were found to have metastatic disease. Prior studies on screening mammography have demonstrated a higher proportion of invasive versus in situ histologies of screening-detected cancers with DBT versus DM and a higher likelihood of upgrade of high-risk breast lesions to invasive cancer at surgical excision with DBT than DM [18-20; 26; 27]. Taken together with our results, these findings suggest possible differences in tumor biology between cancers that are detected with DM versus DBT, which merits further investigation. The current Tomosynthesis Mammographic Imaging Screening Trial (TMIST), which is a randomized trial comparing DM and DBT, may shed light on differences in the types of cancers detected with these imaging modalities [28].

Although there was no significant difference in finding type (calcifications, asymmetry, architectural distortion, or mass) between cases that did and did not upgrade to invasive cancer in the DM or DBT groups, we found that biopsy modality was associated with risk of upgrade, with cases that underwent ultrasound-guided biopsy associated with a higher risk of upgrade. Suspicious microcalcifications are not commonly visualized on sonography; however, when detected, these calcifications are more likely to represent cancer and more likely to represent invasive cancer rather than DCIS [29]. Of note, we found no other features associated with risk of upgrade in the DM or DBT groups. The current active surveillance trials for DCIS in the United States, Europe, and Japan use low nuclear grade, absence of comedonecrosis, and positive ER status as some of the inclusion criteria and thus as surrogate markers for “low-risk” DCIS; however, our results suggest that these criteria may not reliably exclude patients with biopsy-proven DCIS who also harbor invasive carcinoma [13-16].

Our study has several limitations. First, it was conducted at a single institution, where the majority of patients identify themselves as white, thereby limiting the generalizability of these results to a non-white population. Second, although pathology slides were reviewed at point of care by dedicated breast pathologists, a central review process was not conducted, and nuclear grading may not be consistent among pathologists. Third, the comparisons made between the DM and DBT groups may be influenced by other factors that changed over time; however, a strength of our study is that we avoided the possibility of selection bias that can occur within practices that perform DM alone and combined DM and DBT for screening purposes. Fourth, our institution transitioned from stereotactic to tomosynthesis-guided biopsies in January 2016, and thus a small proportion of biopsies performed in the DBT group were performed under tomosynthesis rather than stereotactic guidance. Of note, similar upgrade rates have been reported with stereotactic versus tomosynthesis-guided biopsies [30].

We observed no significant difference in the detection rate of DCIS in the DM and DBT eras. Despite significant differences in DCIS characteristics between the DM and DBT groups (such as nuclear grade and presence of comedonecrosis), the upgrade rates to invasive cancer between the two groups were similar. Among the upgraded cases, a higher proportion was high-grade invasive cancers in the DBT group. In both the DM and DBT groups, biopsy modality was the only feature associated with risk of upgrade. These results provide insight into the characteristics of screening-detected breast cancers in the modern era of DBT and also have implications for the current DCIS active surveillance trials.

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Abbreviations:

DBT	Digital breast tomosynthesis
DCIS	Ductal carcinoma in situ
DM	Digital mammography
ER	Estrogen receptor
HER2	Human epidermal growth factor receptor 2
IDC	Invasive ductal carcinoma
ILC	Invasive lobular carcinoma
PR	Progesterone receptor

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Key Points:

- Detection rates and upgrade rates of ductal carcinoma in situ (DCIS) on digital mammography (DM) versus digital breast tomosynthesis (DBT) are similar.
- A higher proportion of upgraded cases were high-grade invasive cancers with DBT than DM, suggesting possible differences in tumor biology between cancers that are detected with DM and DBT.
- With both DM and DBT, ultrasound-guided biopsy (versus stereotactic biopsy) was associated with higher risk of upgrade.

Figure 1.

Flow diagram of screening mammograms. DBT = digital breast tomosynthesis, DM = digital two-dimensional mammogram.

Table 1.

List of patient features, imaging features, pathological features of DCIS, and pathological features of invasive cancers.

PATIENT FEATURES
Age
Race
Family history of breast cancer in a first-degree relative
Personal history of breast cancer
IMAGING FEATURES
Screening mammogram modality (DM or DBT)
Baseline or nonbaseline mammogram
Breast density (assessed by interpreting radiologist)
Finding type at mammography (calcifications, asymmetry, architectural distortion, or mass)
Biopsy modality (stereotactic / tomosynthesis, ultrasound, or MRI)
PATHOLOGICAL FEATURES OF DCIS
Nuclear grade
Presence of comedonecrosis
Estrogen receptor status
Progesterone receptor status
PATHOLOGICAL FEATURES OF INVASIVE CANCERS
Size at surgery
Histologic grade
Estrogen receptor status
Progesterone receptor status
HER2 status
Lymph node status

DBT = digital breast tomosynthesis, DCIS = ductal carcinoma in situ, DM = digital mammography, HER2 = human epidermal growth factor receptor 2.

Table 2.

Comparison of patient features and imaging features between the digital two-dimensional mammography (DM) and digital breast tomosynthesis (DBT) groups.

Feature	DM group (n=133)	DBT group (n=185)	p-value
PATIENT FEATURES			
Age (SD)	58.2 (11.0)	59.2 (10.7)	0.39
Race			
White	88.7% (118/133)	85.9% (159/185)	0.76
African American	3.8% (5/133)	4.3% (8/185)	
Other	7.5% (10/133)	9.7% (18/185)	
Family history of breast cancer in a first-degree relative	24.8% (33/133)	30.8% (57/185)	0.24
Personal history of breast cancer	14.3% (19/133)	15.7% (29/185)	0.73
IMAGING FEATURES			
Baseline mammography	9.0% (12/133)	0.5% (1/185)	<0.001 *
Breast density			
Almost entirely fatty	3.0% (4/133)	3.2% (6/185)	0.85
Scattered areas of fibroglandular density	43.6% (58/133)	44.3% (82/185)	
Heterogeneously dense	50.4% (67/133)	47.6% (88/185)	
Extremely dense	3.0% (4/133)	4.9% (9/185)	
Finding type at mammography			
Calcifications	95.5% (127/133)	92.4% (171/185)	0.54
Asymmetry	2.3% (3/133)	1.6% (3/185)	
Architectural distortion	0	0.5% (1/185)	
Mass	2.3% (3/133)	5.4% (10/185)	
Biopsy modality			
Stereotactic / tomosynthesis	94.0% (125/133)	92.4% (171/185)	0.38
Ultrasound	4.5% (6/133)	7.6% (14/185)	
MRI	1.5% (2/133)	0	

DBT = digital breast tomosynthesis, DM = digital mammography.

* Statistically significant result.

Table 3.

Comparison of pathological features of ductal carcinoma in situ (DCIS) and pathological features of upgraded invasive cancers between the digital two-dimensional mammography (DM) and digital breast tomosynthesis (DBT) groups.

Feature	DM group (n=133)	DBT group (n=185)	p-value
PATHOLOGICAL FEATURES OF DCIS			
Detection rate of DCIS	0.9 per 1000 exams (113/144,091)	1.0 per 1000 exams (185/184,047)	0.45
Nuclear grade of DCIS ^a			
1	20.9% (19/91)	15.1% (28/185)	<0.01 [*]
2	37.4% (34/91)	57.8% (107/185)	
3	41.8% (38/91)	27.0% (50/185)	
Comedonecrosis at biopsy	20.3% (27/133)	34.6% (64/185)	<0.01 [*]
Estrogen receptor status at biopsy ^b			
Positive	91.5% (118/129)	92.3% (167/181)	0.80
Negative	8.5% (11/129)	7.7% (14/181)	
Progesterone receptor status at biopsy ^c			
Positive	89.0% (113/127)	77.9% (127/163)	0.01 [*]
Negative	11.0% (14/127)	22.1% (36/163)	
PATHOLOGICAL FEATURES OF INVASIVE CANCERS			
Upgrade rate of DCIS to invasive cancer	17.3% (23/133)	16.8% (31/185)	0.90
Size (SD) of invasive cancer in mm	3.6 (3.0)	5.4 (4.7)	0.14
Histologic grade of invasive cancer ^d			
Low/intermediate	90.5% (19/21)	63.3% (19/30)	0.03 [*]
High	9.5% (2/21)	36.7% (11/30)	
Estrogen receptor status of invasive cancer ^e			
Positive	90.5% (19/21)	74.1% (20/27)	0.15
Negative	9.5% (2/21)	25.9% (7/27)	
Progesterone receptor status of invasive cancer ^f			
Positive	81.0% (17/21)	63.0% (17/27)	0.17
Negative	19.0% (4/21)	37.0% (10/27)	
HER2 status of invasive cancer ^g			
Positive	20.0% (4/20)	25.9% (7/27)	0.64
Negative	80.0% (16/20)	74.1% (20/27)	
Lymph node status of invasive cancer ^h			
Positive	0	8.3% (2/24)	0.23
Negative	100.0% (20/20)	91.7% (22/24)	

DBT = digital breast tomosynthesis, DCIS = ductal carcinoma in situ, DM = digital mammography, HER2 = human epidermal growth factor receptor 2, SD = standard deviation.

* Statistically significant result.

^a Nuclear grade of DCIS not reported in 42 cases.

^b Estrogen receptor status of DCIS not reported in 8 cases.

^c Progesterone receptor status of DCIS not reported in 28 cases.

^d Histologic grade of invasive carcinoma not reported in 3 cases.

^e Estrogen receptor status of invasive carcinoma not reported in 6 cases.

^f Progesterone receptor status of invasive carcinoma not reported in 6 cases.

^g HER2 status of invasive carcinoma not reported in 7 cases.

^h Lymph nodes not tested in 10 cases.

Table 4.

Comparison of patient features, imaging features, and pathological features of ductal carcinoma in situ (DCIS) between digital two-dimensional mammography (DM) cases that did and did not upgrade to invasive cancer.

Feature	DM cases upgraded to invasive carcinoma (n=23)	DM cases not upgraded to invasive carcinoma (n=110)	p-value
PATIENT FEATURES			
Age (SD)	59.8 (11.7)	57.8 (10.9)	0.42
Race			
White	87.0% (20/23)	89.1% (98/110)	0.96
African American	4.3% (1/23)	3.6% (4/110)	
Other	8.7% (2/23)	7.3% (8/110)	
Family history of breast cancer in a first-degree relative	30.4% (7/23)	23.6% (26/110)	0.49
Personal history of breast cancer	13.0% (3/23)	14.5% (16/110)	0.85
IMAGING FEATURES			
Baseline mammography	4.3% (1/23)	10.0% (11/110)	0.39
Breast density			
Almost entirely fatty	4.3% (1/23)	2.7% (3/110)	0.87
Scattered areas of fibroglandular density	47.8% (11/23)	42.7% (47/110)	
Heterogeneously dense	43.5% (10/23)	51.8% (57/110)	
Extremely dense	4.3% (1/23)	2.7% (3/110)	
Finding type at mammography			
Calcifications	95.7% (22/23)	95.5% (105/110)	0.57
Asymmetry	0	2.7% (3/110)	
Architectural distortion	0	0	
Mass	4.3% (1/23)	1.8% (2/110)	
Biopsy modality ^a			
Stereotactic	87.0% (20/23)	97.2% (105/108)	0.03 [*]
Ultrasound	13.0% (3/23)	2.8% (3/108)	
PATHOLOGICAL FEATURES OF DCIS			
Nuclear grade ^b			
1	12.5% (2/16)	22.7% (17/75)	0.22
2	56.3% (9/16)	33.3% (25/75)	
3	31.3% (5/16)	44.0% (33/75)	
Comedonecrosis	13.0% (3/23)	21.8% (24/110)	0.34
Estrogen receptor status ^c			
Positive	100.0% (22/22)	89.7% (96/107)	0.37
Negative	0	10.3% (11/107)	
Progesterone receptor status ^d			

Feature	DM cases upgraded to invasive carcinoma (n=23)	DM cases not upgraded to invasive carcinoma (n=110)	p-value
Positive	95.5% (21/22)	87.6% (92/105)	0.29
Negative	4.5% (1/22)	12.4% (13/105)	

DBT = digital breast tomosynthesis, DCIS = ductal carcinoma in situ, DM = digital mammography, SD = standard deviation.

* Statistically significant result.

^a Two biopsies were performed under MRI guidance.

^b Nuclear grade not reported in 42 cases.

^c Estrogen receptor status not reported in 4 cases.

^d Progesterone receptor status not reported in 6 cases.

Table 5.

Comparison of patient features, imaging features, and pathological features of ductal carcinoma in situ (DCIS) between digital breast tomosynthesis (DBT) cases that did and did not upgrade to invasive cancer.

Feature	DBT cases upgraded to invasive carcinoma (n=31)	DBT cases not upgraded to invasive carcinoma (n=154)	p-value
PATIENT FEATURES			
Age (SD)	59.6 (11.0)	59.1 (10.7)	0.81
Race			
White	90.3% (28/31)	85.1% (131/154)	0.74
African American	3.2% (1/31)	4.5% (7/154)	
Other	6.5% (2/31)	10.4% (16/154)	
Family history of breast cancer in a first-degree relative	38.7% (12/31)	29.2% (45/154)	0.30
Personal history of breast cancer	12.9% (4/31)	16.2% (25/154)	0.64
IMAGING FEATURES			
Baseline mammography	0	0.6% (1/154)	0.21
Breast density			
Almost entirely fatty	0	3.9% (6/154)	0.73
Scattered areas of fibroglandular density	38.7% (12/31)	45.5% (70/154)	
Heterogeneously dense	58.1% (18/31)	45.5% (70/154)	
Extremely dense	3.2% (1/31)	5.2% (8/154)	
Finding type at mammography			
Calcifications	90.3% (28/31)	92.9% (143/154)	0.42
Asymmetry	0	1.9% (3/154)	
Architectural distortion	0	0.6% (1/154)	
Mass	9.7% (3/31)	4.5% (7/154)	
Biopsy modality			
Stereotactic / tomosynthesis	80.6% (25/31)	94.8% (146/154)	<0.01 [*]
Ultrasound	19.4% (6/31)	5.2% (8/154)	
PATHOLOGICAL FEATURES OF DCIS			
Nuclear grade			
1	9.7% (3/31)	16.2% (25/154)	0.59
2	64.5% (20/31)	56.5% (87/154)	
3	25.8% (8/31)	27.3% (42/154)	
Comedonecrosis	41.9% (13/31)	33.1% (51/154)	0.35
Estrogen receptor status ^a			
Positive	86.7% (26/30)	93.4% (141/151)	0.21
Negative	13.3% (4/30)	6.6% (10/151)	
Progesterone receptor status ^b			

Feature	DBT cases upgraded to invasive carcinoma (n=31)	DBT cases not upgraded to invasive carcinoma (n=154)	p-value
Positive	84.6% (22/26)	76.6% (105/137)	0.37
Negative	15.4% (4/26)	23.4% (32/137)	

DBT = digital breast tomosynthesis, DCIS = ductal carcinoma in situ, DM = digital mammography, SD = standard deviation.

* Statistically significant result.

^a Estrogen receptor status not reported in 4 cases.

^b Progesterone receptor status not reported in 22 cases.