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Comparison of Abbreviated Breast MRI vs Digital Breast Tomosynthesis for Breast Cancer Detection Among Women With Dense Breasts Undergoing Screening

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5.6.22

Learning objectives

By the end of this journal club, participants will be able to:

1. Be familiar with breast anatomy
2. Recognize the categories of breast density
3. Recognize the various breast imaging modalities
4. Understand the pathophysiology of breast cancer
5. Compare the differences between abbreviated breast MRI (AB-MRI) and digital tomosynthesis (DBT)

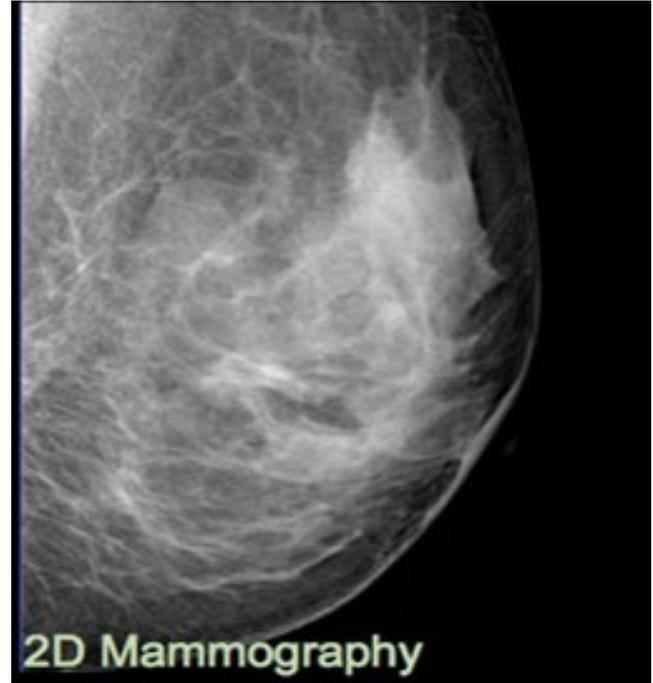
Module Outline

- I. Case
- II. Background
- III. Article Overview
- IV. Clinical Questions
- V. Key Points

Case

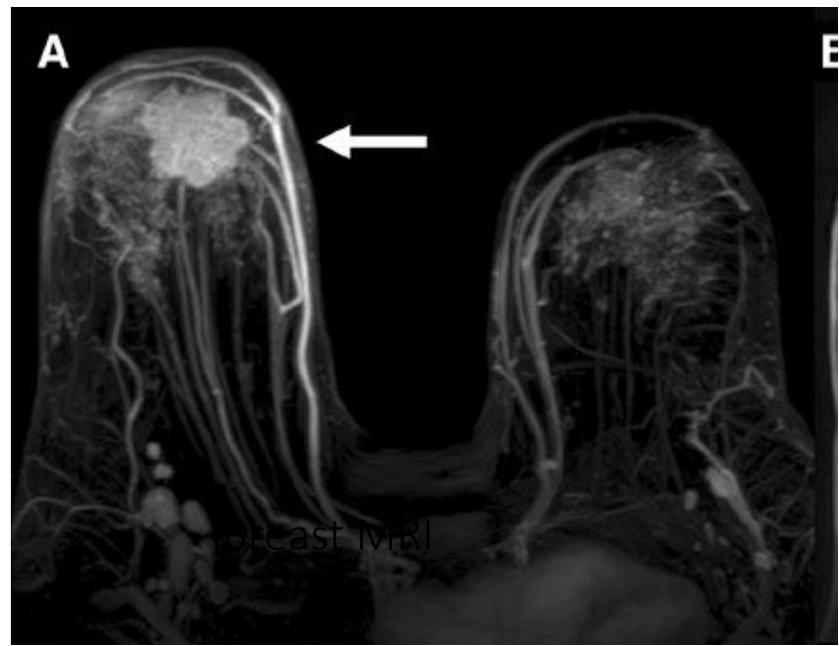
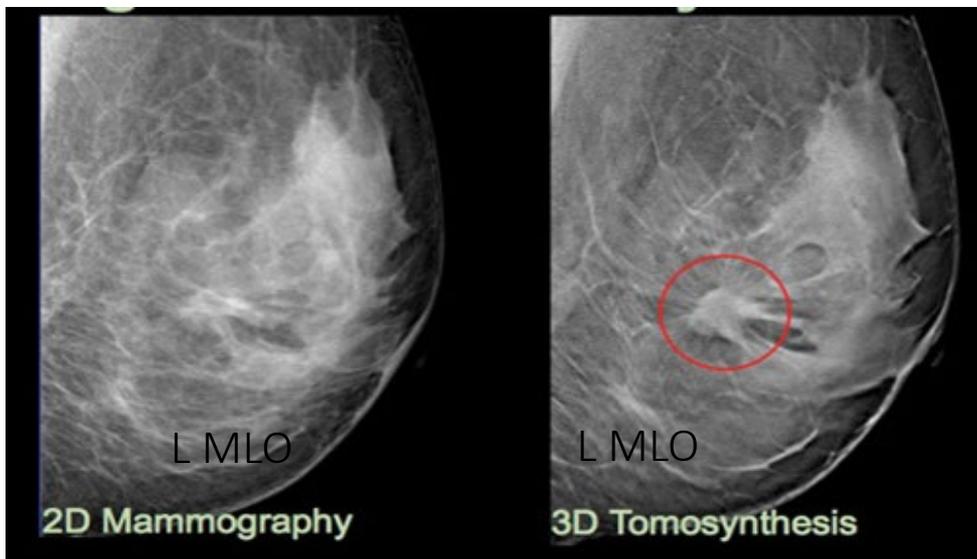
A 51-year-old asymptomatic woman presents to her PCP with a firm, palpable mass in her left breast. She says it has been there for around a year and reports no pain. Conventional mammography was ordered with the left MLO findings shown below:

1. How would you characterize the breast density?
2. Where is the mass?
3. What should be the next step to confirm the diagnosis? Further imaging?



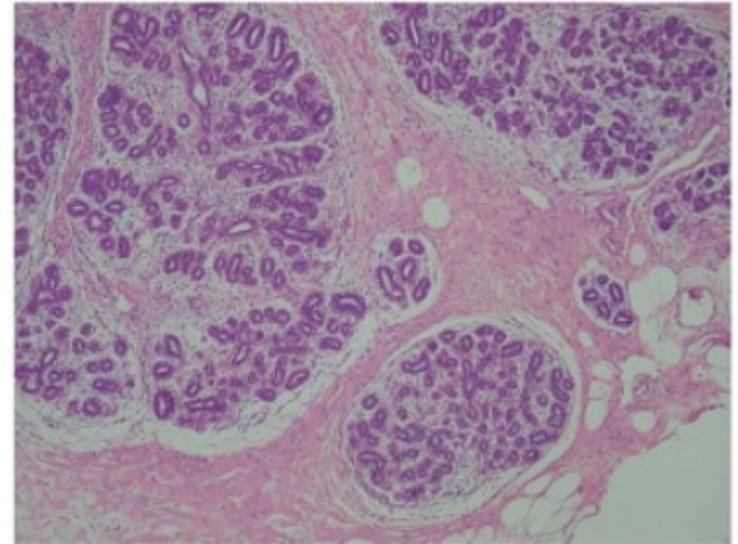
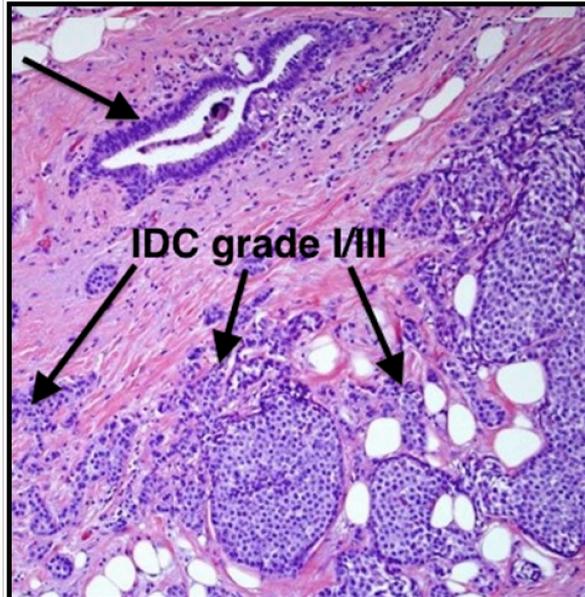
Case cont.

To better identify the mass radiologists inform the patient they would like to order a digital breast tomosynthesis (DBT) and breast MRI. The patient is worried about the costs but is reassured that both imaging studies are covered under her Medicare plan. Tests are ordered. Imaging results shown below:



Case cont.

A core needle biopsy was next done and showed the following histology:



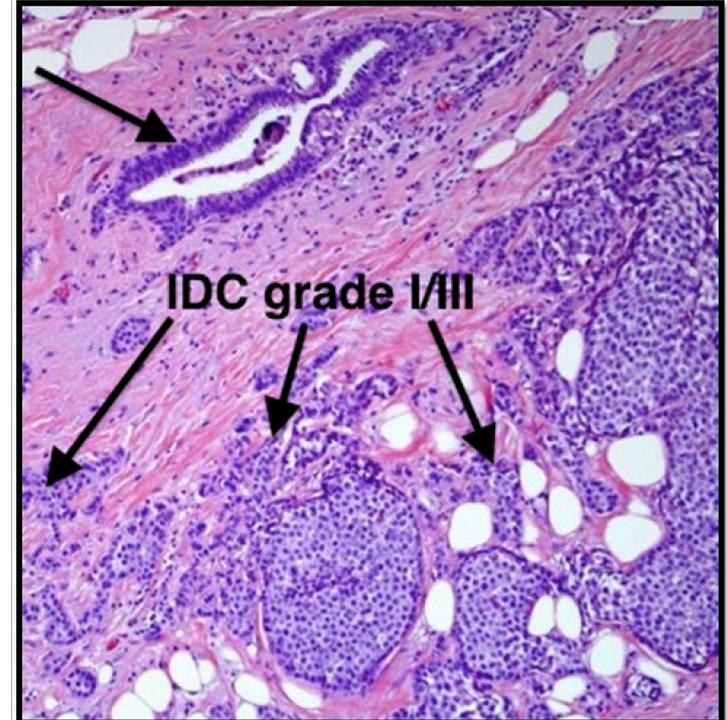
Normal

4. What is the differential diagnosis?

Case cont.

Diagnosis: **invasive ductal carcinoma**

- Most common type of invasive breast cancer
- DDx: invasive lobular carcinoma, DCIS, LCIS
- Treatment:
 - Adjuvant
 - Chemotherapy (i.e. Trastuzamab)
 - Tamoxifen
 - Radiation
 - Surgical: Lumpectomy vs Mastectomy



Duct cells invading the stroma

Case Questions to Consider

1. Which imaging modality should be used to detect breast cancers in women with dense breasts?
2. What is the breast cancer detection rate among the advanced forms of screening techniques (MRI, DBT)?
3. How can providers maintain cost-effectiveness without jeopardizing efficacy in breast imaging studies?

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Breast Density

- A measure of the amount of fibrous and glandular tissue in the breast, as compared to fat tissue
 - Not related to size or firmness
- 4 types of breast density
 - Breast Imaging Reporting and Data System (BI-RADS) categor

Category A

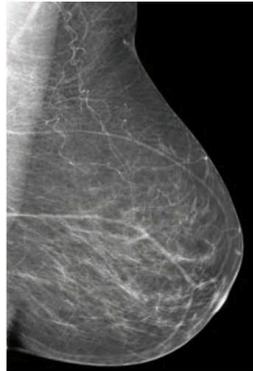
Category B

Category C

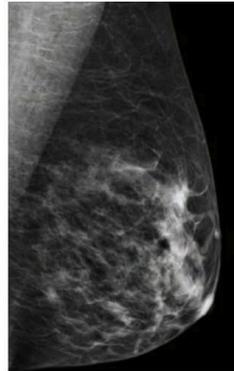
Category D



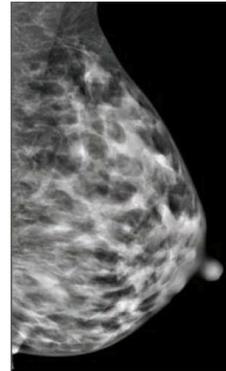
Almost entirely fat
($\leq 25\%$ fibroglandular)



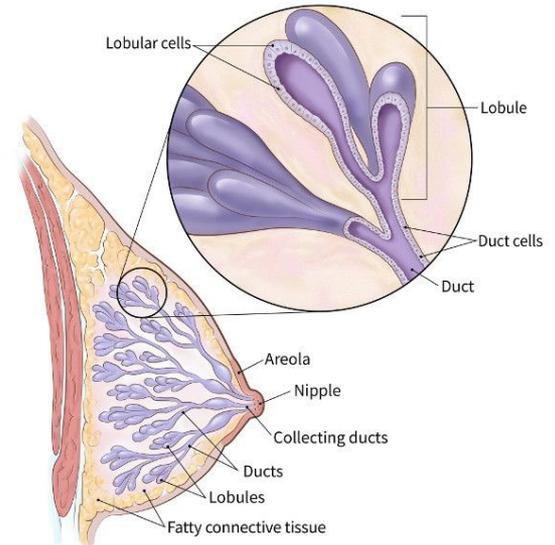
Scattered fibroglandular
densities
(25%–50% fibroglandular)



Heterogeneous fibroglandular
densities
(51%–75% fibroglandular)



Extremely dense
($> 75\%$ fibroglandular)



Breast Cancer: Overview

- Most common cancer diagnosed in women (1 in 10 each year)
- Risk factors:
 - Age
 - Gender
 - Family history
 - Genetic (BRCA1/A2 mutations)
 - Estrogen exposure
- Epidemiology:
 - Invasive breast cancer affects 1 in 8 women in the U.S during their lifetime
 - 95% of new cases occur in women aged 40 years or older
 - Approximately 1 in 1000 men will have breast cancer in their lifetime

Breast Cancer: Pathology

- Due to DNA damage and genetic mutations that can be influenced by exposure to estrogen or an inheritance of DNA defects or pro-cancerous genes like *BRCA1* and *BRCA2*
- Types:
 - Noninvasive
 - Ductal carcinoma in-situ (DCIS)
 - Lobular carcinoma in-situ (LCIS)
 - Invasive
 - Invasive ductal carcinoma
 - Invasive lobular carcinoma

- Histology:

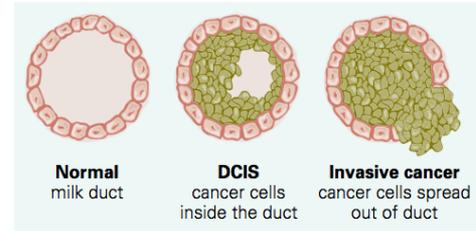
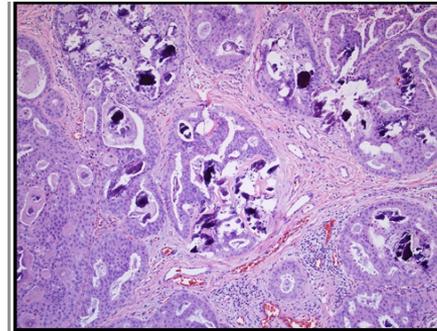
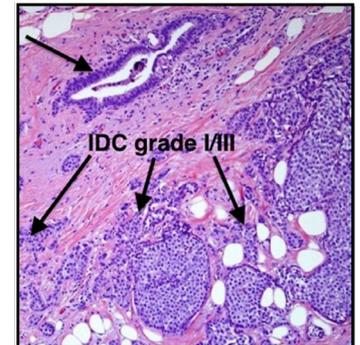


Fig 2: Normal cells lining a milk duct may develop into DCIS; sometimes this will progress to invasive cancer.



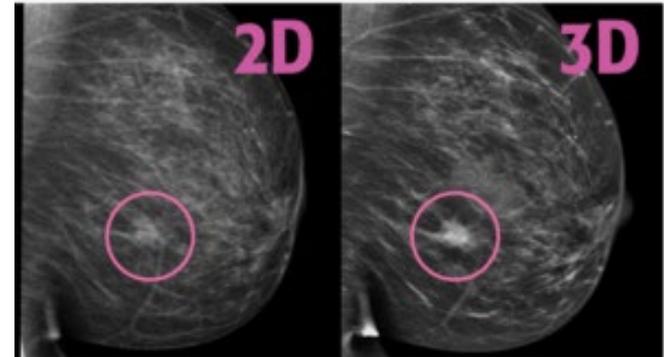
DCIS



Invasive ductal carcinoma

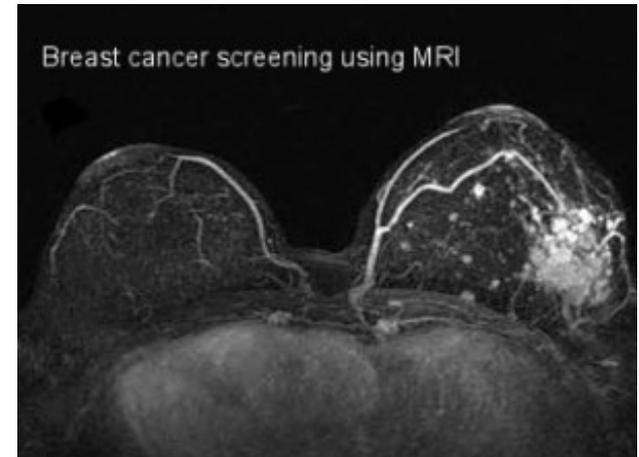
Breast Cancer: Imaging Modalities

- 1. Breast Ultrasound (U/S)
 - High frequency sound waves
 - Pros: inexpensive, flexible
 - Cons: false-positive breast cancer rates in dense breasts
- 2. Digital Mammography
 - Ionizing radiation
 - Types:
 - Conventional Digital Mammography
 - 2D image
 - Digital Breast Tomosynthesis (DBT)
 - 3D image
 - Evaluates dense tissue compared to conventional



Breast Cancer: Imaging Modalities cont.

- 3. Breast MRI
 - Nuclear magnetic resonance
 - Uses 8 pulse sequences
 - 1st choice in screening for high-risk women
 - Pros: Very high sensitivity (99%)
 - Cons: cost; IV contrast
- 4. Abbreviated Breast MRI (AB-MRI)
 - Shortened version of MRI (1st 2 pulse sequences)
 - Differences:
 - Shorter acquisition time (< 10 min)
 - Decreased cost
- 5. Others: CT, Molecular breast imaging



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Article Nuts & Bolts

- **Purpose:** to compare the screening performance of abbreviated breast magnetic resonance imaging (AB-MRI) and digital breast tomosynthesis (DBT) in women with dense breasts
- **Journal:** Journal of American Medical Association (JAMA), 2020
- **Study type:** Cross-sectional study at 48 academic, community hospital, and private practice sites in the United States and Germany between Dec 2016-Nov 2017 with longitudinal follow-up through Sep 2019
- **Number of cases:** 1444 women who underwent both abbreviated breast MRI and DBT
- **Data:** imaging examinations, primary end point (cancer detection rate) and secondary end points (sensitivity, specificity, additional imaging rate, PPV of biopsy)

Study Cohort

- Asymptomatic women aged 40 to 75 years (average risk) who were scheduled to undergo routine breast cancer screening with DBT reported as **having dense breasts from most recent screening mammogram**
- Exclusion Criteria:
 - a screening breast U/S within the past 12 months
 - a previous breast MRI, a molecular breast imaging study, or a contrast-enhanced mammogram
 - they qualified for full-protocol breast MRI based on the ACS guidelines

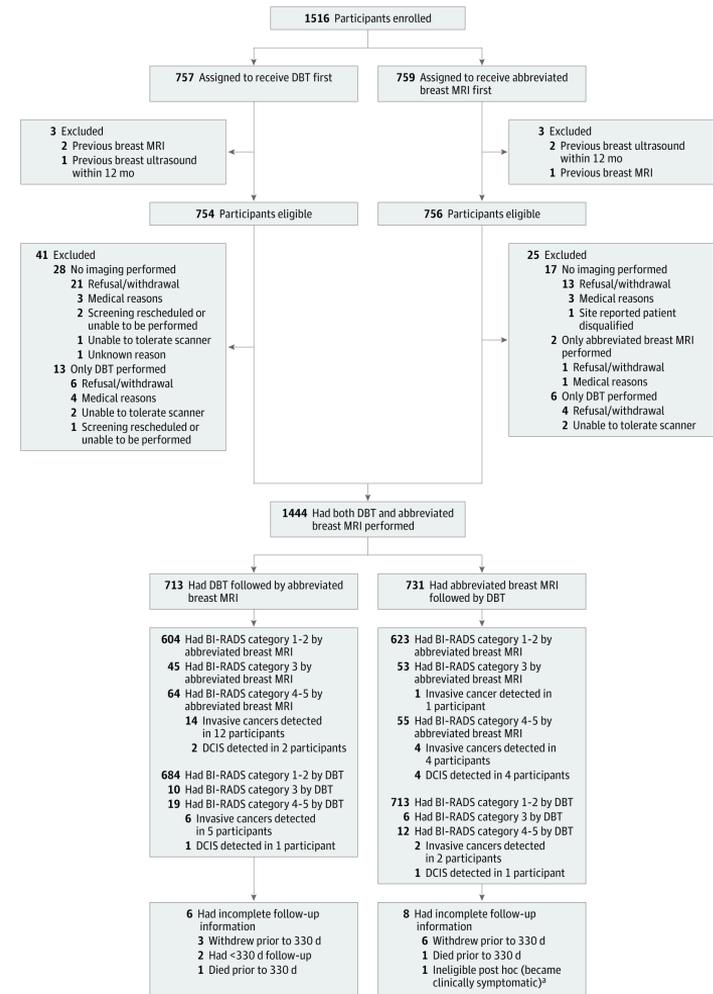


Figure 1: Study Flow Chart

Table 1. Baseline Demographics and Risk Characteristics of Participants Completing Both DBT and Abbreviated Breast MRI (N = 1444)

Characteristics	Value
Age, y	
Mean (SD)	54.9 (8.5)
Median (range)	54 (40-75)
Race, No. (%)	n = 1361
White	1233 (91)
Black/African American	61 (4)
Asian	57 (4)
Mixed race	5 (<1)
American Indian/Alaskan Native	3 (<1)
Native Hawaiian/Pacific Islander	2 (<1)
Hispanic or Latino, No./total (%)	39/1356 (3)
Menopausal status, No. (%)	n = 1443
Premenopausal	440 (30)
Perimenopausal	94 (7)
Naturally postmenopausal	669 (46)
Surgically postmenopausal	240 (17)
ACR category of breast density from year 0 DBT, No. (%) ^a	
A: Almost entirely fat	2 (<1)
B: Scattered fibroglandular densities	115 (8)
C: Heterogeneously dense	1108 (77)
D: Extremely dense	219 (15)
History of ≥ 1 first-degree relative, No. (%)	n = 1438
With breast cancer	271 (19)
With ovarian cancer	30 (2)
Prior benign biopsy with atypias, No./total (%)	10/1423 (1)
Breast Cancer Surveillance Consortium risk score, % ^b	n = 1385
5-y risk	
Mean (SD)	1.8 (0.8)
Median (range)	1.6 (0.3-7.8)
10-y risk	
Mean (SD)	3.7 (1.6)
Median (range)	3.5 (0.9-14.2)

Materials & Methods

- Screening examinations: DBT and AB-MRI performed at baseline and at 1 year; both within a single 24-hr period
- Interpretation of positive findings:
 - If made on screening mammography or DBT, women were invited to return for additional imaging workup (callback)
 - BI-RADS category 3 on DBT or AB-MRI underwent short-term follow-up imaging after 6 months
 - All suspicious findings on DBT or AB-MRI were biopsied regardless of the final interpretation of the other modality
- *For multiple comparisons of the primary and 4 secondary end points $P < .01$ was considered statistically significant*

BI-RADS Screening Categories

BI-RADS® ASSESSMENT CATEGORIES

includes PPV for
malignancy and
suggested
verbiage for the
accompanying
Recommendation

- Category 0: INCOMPLETE - NEED ADDITIONAL IMAGING EVALUATION AND/OR PRIOR MAMMOGRAMS FOR COMPARISON
Recall for additional imaging and/or comparison with prior examinations
- Category 1: NEGATIVE (0% risk)
Routine mammography screening
- Category 2: BENIGN (0% risk)
Routine mammography screening
- Category 3: PROBABLY BENIGN (<2% risk)
Short interval 6 month follow-up *OR continued surveillance*
- Category 4: SUSPICIOUS (2-95% risk)
Biopsy should be performed in the absence of clinical contraindications
- Category 5: HIGHLY SUGGESTIVE OF MALIGNANCY (>95% risk)
Biopsy should be performed in the absence of clinical contraindications
- Category 6: KNOWN BIOPSY-PROVEN MALIGNANCY (100% risk)
Surgical excision when clinically appropriate

Materials & Methods cont.

- Breast cancers:
 - Invasive: Invasive ductal carcinoma, Invasive lobular carcinoma
 - DCIS
- Diagnostic examinations: pathology of core or surgical biopsy was the reference standard for cancer detection rate and PPV of biopsy
- End points:
 - Primary: rate of invasive cancer detection at baseline screening
 - verified by pathology (core biopsy or surgical excision) and a positive test result (BI-RADS 3 or more)
 - Secondary: sensitivity, specificity, additional imaging recommendation rate (ie. callback plus recommendation for short-term follow-up), and PPV of biopsy

Results

- 77% had heterogeneously dense breasts and 15% had extremely dense breasts (out of 1444 women)
- 17 women were detected to have invasive cancers at baseline screening
 - AB-MRI detected invasive cancer in all 17 women
 - invasive cancer detection rate: 11.8 (95% CI, 7.4-18.8) per 1000 women
 - DBT detected in 7 women
 - invasive cancer detection rate: 4.8 (95% CI, 2.4-10.0) per 1000 women

Table 2. Characteristics of Screen-Detected Cancers

Observed Cancer ^a	Case ^a	Lesion Detected by Abbreviated Breast MRI	Lesion Detected by DBT	ACR Breast Density ^b	Age, y	Type of Cancer ^c	Largest Diameter, mm ^c	Maximum Reported Grade ^c	Estrogen Receptor Status ^c	Progesterone Receptor Status ^c	ERBB2 Status ^c	Breast Cancer Surveillance Consortium Risk Score, %	
												5-Year Risk	10-Year Risk
1	1	Yes	Yes	C	62	DCIS	15	2	Positive	Positive	Not performed	2.79	5.62
2	2	Yes		C	69	DCIS	20	2	Positive	Positive	Not performed	3.24	6.17
3	3	Yes		C	68	DCIS	10	2	Positive	Negative	Not performed	4.64	8.82
4	4	Yes		C	71	DCIS	10	3	Positive	Negative	Not performed	2.10	3.95
5	5	Yes		C	68	DCIS	5	3	Not performed	Not performed	Not performed	2.08	4.02
6	6a	Yes		D	63	DCIS	30	2	Positive	Not performed	Not performed	3.40	6.77
7	7		Yes ^d	D	40	DCIS	70	3	Positive	Positive	Not performed	1.25	3.13
8	8	Yes		B	62	IDC	4	1	Positive	Positive	Negative	2.04	4.13
9	9	Yes		B	65	ILC	16	2	Positive	Negative	Negative	1.50	2.97
10	10a	Yes	Yes	C	62	IDC	11	1	Positive	Positive	Negative	1.92	3.88
11	10b	Yes	Yes	C	62	IDC	9	2	Positive	Positive	Negative	1.92	3.88
12	11	Yes		C	72	IDC	8	2	Positive	Positive	Negative	NA ^e	NA ^e
13	12	Yes		C	67	ILC	14	2	Positive	Positive	Negative	3.14	6.08
14	13a	Yes	Yes	C	56	ILC	25	2	Positive	Positive	Negative	2.41	5.07
15	13b	Yes		C	56	ILC	25	2	NA	NA	NA	2.41	5.07
16	14	Yes	Yes	C	64	IDC	18	2	Negative	Negative	Negative	2.89	5.73
17	15	Yes	Yes	C	48	IDC	10	1	Positive	Positive	Negative	1.07	2.43
18	16	Yes		C	47	IDC	10	1	Positive	Positive	Negative	0.99	2.21
19	17	Yes	Yes	C	44	IDC	NA ^f	2	Positive	Positive	Negative	1.39	3.28
20	18	Yes		C	52	IDC	24	3	Negative	Negative	Positive	1.92	4.19
21	19	Yes	Yes	C	46	Mixed IDC/ILC	48	1	Positive	Positive	Negative	0.93	2.16
22	20	Yes		C	51	IDC	10	3	Positive	Negative	Negative	2.01	4.41
23	21	Yes		C	70	IDC	10	2	Positive	Negative	Negative	4.80	8.96
24	22	Yes	Yes	C	41	IDC	10	1	Positive	Positive	Negative	0.61	1.50
25	23	Yes		D	53	IDC	10	1	Positive	Positive	Negative	4.83	10.21
26	6b	Yes		D	63	IDC	14	3	Positive	Positive	Negative	3.40	6.77

Abbreviations: DBT, digital breast tomosynthesis; DCIS, ductal carcinoma in situ; ERBB2, Erb-B2 receptor tyrosine kinase 2; IDC, invasive ductal cancer; ILC, invasive lobular cancer; MRI, magnetic resonance imaging; NA, not available.

^a Observed numbers signify sequentially numbered individual cancers, and cases signify unique participants. Participants with more than 1 cancer have separate cancers distinguished by "a" and "b."

^b See Table 1, footnote a, for description of American College of Radiology (ACR) categorization of breast density.

^c Grade is the highest reported grade across core and surgical biopsies. For estrogen receptor, progesterone receptor, and ERBB2 status, if either the core biopsy or surgical biopsy had positive findings, value is reported as positive. Largest diameter, ductal carcinoma pattern, and invasive pattern are taken from surgical pathology.

In 1 participant (case 9), the histologic description of a lobular invasive cancer corresponded to intermediate grade, although no specific grading information was provided.

^d Digital breast tomosynthesis reported 2 lesions that were the same pathological lesion (a single 70-mm DCIS).

^e Breast Cancer Surveillance Consortium risk scores were not computed because of a previous diagnosis of breast cancer.

^f This participant had invasive disease by vacuum-assisted core biopsy, but there was no residual cancer in the surgical biopsy specimen which showed only benign changes with atypia. Thus, tumor size data from surgical pathology are not available; however, the lesion size was 11 mm by abbreviated breast MRI and 9 mm by DBT.

Results cont.

- Secondary end points:
 - 23 women had cancer (invasive or DCIS) at the study baseline screen
 - 1) Sensitivity
 - AB-MRI for invasive cancer or DCIS was **significantly higher** at 95.7% (95% CI, 79.0%-99.2%; 22 of 23 women) vs 39.1% (95% CI, 22.2%-59.2%; 9 of 23 women) for DBT ($P=.001$)
 - 2) Specificity
 - AB-MRI was **significantly lower** than that of DBT, at 86.7% (95% CI, 84.8%-88.4%; 1220 of 1407 women) vs 97.4% (95% CI, 96.5%-98.1%; 1371 of 1407 women) ($P<.001$)
 - 3) PPV of biopsy
 - AB-MRI was 19.6% (95% CI, 13.2%-28.2%; 21 of 107 women), which was **not statistically significantly** different compared with DBT at 31.0% (95% CI, 17.0%-49.7%; 9 of 29 women) ($P=.15$)
 - 4) Additional imaging recommendation rate (callback)
 - additional imaging (either callback or short-term follow-up) was required in 7.5% (95% CI, 6.2%-9.0%; 108 of 1444 women) for AB-MRI and in 10.1% (95% CI, 8.7%-11.8%; 146 of 1444 women) for DBT; this difference was **not statistically significant** after Bonferroni adjustment ($P=.02$)

Figure 2. Summary of Relevant Study Findings

Diagnostic accuracy of detection of invasive cancer or DCIS						
Imaging modality	DBT			AB-MRI		
Invasive cancer or DCIS	Absent	Present	Total	Absent	Present	Total
Negative test result	1371	14	1385	1220	1	1221
Positive test result	36	9	45 ^a	187	22	209 ^a
Total	1407	23	1430	1407	23	1430

Rate of detection of invasive cancer and DCIS		
Imaging modality	DBT	AB-MRI
Total participants	1444	1444
Invasive cancer detected	7	17
DCIS detected	2	6 ^b
Invasive cancer or DCIS detected	9	22 ^b
Sensitivity (95% CI) ^c	39.1% (22.2%-59.2%) [9/23]	95.7% (79.0%-99.2%) [22/23]
Specificity (95% CI) ^c	97.4% (96.5%-98.1%) [1371/1407]	86.7% (84.8%-88.4%) [1220/1407]
PPV of biopsy (95% CI) ^c	31.0% (17.0%-49.7%) [9/29]	19.6% (13.2%-28.2%) [21/107]
Additional imaging recommendation (95% CI) ^c	10.1% (8.7%-11.8%) [146/1444]	7.5% (6.2%-9.0%) [108/1444]

DBT indicates digital breast tomosynthesis; DCIS, ductal carcinoma in situ; ER, estrogen receptor; ERBB2, Erb-B2 receptor tyrosine kinase 2; AB-MRI, abbreviated breast magnetic resonance imaging.

^aMore women had a Breast Imaging Reporting and Data System (BI-RADS) category of 3 to 5 by abbreviated breast MRI than by DBT.

^bOne participant had both invasive cancer and DCIS.

^cEstimated at the participant level and including callback and recommendation for short-term follow-up.

Characteristics of detected invasive cancer and DCIS			
Imaging modality	Detected by DBT alone	Detected by AB-MRI alone	Detected by both DBT and AB-MRI
Participants with invasive cancer (with or without DCIS)	0	10	7
Low grade	-	3	3
Intermediate grade	-	4	4
High grade	-	3	0
ER positive	-	9	6
ER negative	-	1	1
ERBB2 positive	-	1	0
ERBB2 negative	-	9	7
Participants with DCIS only	1	4	1
Low grade	0	0	0
Intermediate grade	0	2	1
High grade	1	2	0
ER positive	1	3	1
ER negative	0	0	0
ER status unknown	0	1	0

Discussion

- AB-MRI improved breast cancer detection in women with dense breasts
- No interval cancers were observed during follow-up
- DBT may require further imaging after initial screen-detected abnormalities
 - DBT alone detected no invasive cancers
- Contribution of mammography in women undergoing AB-MRI screening is limited

Study Limitations

- Mortality or degree of overdiagnosis
- Systematic bias
- Cost effectiveness
- Practicality of AB-MRI implementation
- Comparison of incidence DBT screen to a prevalence AB-MRI screen
- Sample size estimation
 - AB-MRI detected an additional 7 invasive cancers per 1000 women rather than 9 per 1000

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Clinical Questions

- Is it practical to implement AB-MRI as part of breast cancer screening?
- Should AB-MRI be indicated for non-dense women?
- What is the current protocol at UNC for MRI and DBT implementation?
- Should mammography and/or DBT always be followed-up with an MRI?
- Are there long term risks associated with IV contrast administration?
- How could such studies highlight the disproportionally in invasive cancers seen in minority women?

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Key Points

- Always report breast density
- Dense breasts can obscure malignancy detection on imaging and may increase risk of malignancy
- Be mindful of cost-effective imaging tools that can benefit patients
- AB-MRI has been found to have a higher invasive cancer detection rate in women with dense breasts compared to DBT however no conclusion can be made about mortality benefits

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