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Radiological-Pathological Correlations

MRI-guided core needle biopsy of the breast: Radiology-pathology correlation and impact on clinical management

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ABSTRACT

Objective: Breast MRI is used to screen high-risk patients and determine extent of disease in breast cancer (BC) patients. The goal of this study was to determine the pathologic correlates of breast MRI abnormalities biopsied under MRI guidance.

Methods: We retrospectively identified 101 MRI-guided core needle biopsies (CNB) of the breast from 79 women over a 4-year period. MRI-detected lesions biopsied with ultrasound or stereotactic guidance were excluded. MRI studies and pathology were reviewed by breast radiologists and pathologists.

Results: Of the 79 patients, 72 (91%) had a history of prior (n = 13) or concurrent (n = 59) BC. There were 101 MRI abnormalities: 60 (59%) with non-mass enhancement (NME) and 41 (41%) with mass enhancement. Pathology was benign in 83/101 (82%), including in the majority of NME lesions (43/60, 72%). The most common benign findings were: fibrocystic changes (FCC) (49%), sclerosing lesions (13%), and fibroadenoma (FA) (9%). There were 18 (18%) malignant diagnoses: 8 (44%) invasive lobular carcinoma (ILC), 7 (39%) ductal carcinoma in situ (DCIS), and 3 (17%) invasive ductal carcinoma (IDC). Of the 18 malignant diagnoses, 16 (89%) occurred in 14 unique patients with concurrent BC. Based on the malignant MRI-guided CNB, 6 (46%) of these patients had additional (sentinel lymph node biopsy or contralateral breast surgery) or more extensive (wider lumpectomy) surgery.

Conclusion: In this series, most MRI-guided CNB of the breast were benign. The vast majority of malignant diagnoses occurred in patients with concurrent BC and frequently resulted in changes in clinical management.

1. Introduction

Breast magnetic resonance imaging (MRI) is a sensitive tool [1,2] that is recommended to be used to screen patients at an increased risk for the development of breast cancer [3-5]. However, it is also used to evaluate patients with newly diagnosed breast cancer in order to detect additional foci of disease in the ipsilateral breast [6] or occult disease in the contralateral breast [7].

Due to its high sensitivity and increased breast cancer detection rate, breast MRI has been widely adopted in clinical practice. However, this practice may come at a significant cost. Recent studies suggest that women screened with breast MRI are likely to have additional imaging studies and to undergo more frequent biopsies with a lower yield for malignancy [8]. Breast MRI is associated with an increased likelihood of ipsilateral mastectomy and contralateral prophylactic mastectomy without reducing the rates of positive margins or re-excisions in breast cancer patients or improving outcomes or survival [9,10].

A primary reason for the high sensitivity but low specificity of breast MRI is the limited understanding of the pathologic nature of MRI detected lesions. Prior studies correlating breast MRI findings with final pathologic diagnoses from MRI-guided CNB have shown a range of benign, atypical, and malignant lesions [11-14]. The primary aim of this study was radiologic-pathologic correlation in a series MRI-guided CNB of lesions that were not well-visualized with mammography or ultrasound. A secondary aim was to determine how often a malignant MRI-guided CNB diagnosis resulted in a change in clinical management.

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Table 1
Clinical and demographic features of MRI-guided core needle biopsies of the breast (n = 101).

Characteristic	Value
Age (range, mean)	24–77, 50
BMI (range, mean)	18–46.2, 26.1
Menopausal status (n)	
Pre-menopausal	51
Peri-menopausal	3
Post-menopausal	40
Unknown	7
Positive family history (n)	34
Prior cancer (n)	13
Ipsilateral	2
Contralateral	6
Both	5
Concurrent cancer (n)	59
Ipsilateral	28
Contralateral	27
Both	4
Race (n)	
Caucasian	51
African American	12
Other[a]	5
Unknown	33
Genetics (n)	
BRCA	10
Other[b]	3
None	41
Unknown	46
MRI indication	
High risk screening	34
Diagnostic	8
Extent of disease	59

[a] Native American (n = 2), Hispanic (n = 1), Indian (n = 1), Chinese (n = 1).
[b] Other genetic mutations: PALB2, MLH1, and CDH1.

Table 2
MRI lesion characteristics.

Mass (n = 41)		NME (n = 60)	
Characteristic	Value	Characteristic	Value
Size (cm; range, mean)	0.4–2.6, 0.98	Size (cm; range, mean)	0.5–15, 3.14
Shape (n)		Distribution (n)	
Round	19	Focal	16
Oval	2	Linear	22
Irregular	20	Segmental	15
Margin (n)		Regional	4
Circumscribed	18	Multiple regions	0
Non-circumscribed	23	Diffuse	3
Enhancement (n)		Enhancement (n)	
Homogeneous	28	Homogeneous	11
Heterogeneous	10	Heterogeneous	26
Rim	3	Clumped	22
Dark internal	0	Clustered Ring	1
Kinetics (n)		Kinetics (n)	
Persistent	22	Persistent	23
Plateau	13	Plateau	21
Washout	3	Washout	5
Not available	3	Not available	11

2. Materials and methods

This study is an IRB-approved single institution, retrospective review of MRI-guided core needle biopsies performed from January 1, 2014 to December 31, 2017. All MRI-guided core needle biopsies were included. Lesions detected by MRI but biopsied with different modalities were excluded. A total of 101 MRI-guided core needle biopsies (CNB) for lesions visualized only on MRI from 79 women met these inclusion criteria.

Table 3
Primary diagnoses and final biopsy designations after accounting for clinically significant secondary diagnoses in MRI-guided core needle biopsy specimens.

Diagnostic category[a]	Primary	Final[b]
Normal breast tissue	6	6
Benign lesion	73	68
Fibrocystic changes	41	37
Sclerosing adenosis	8	8
Fibroadenoma	8	8
UDH	5	5
PASH	3	3
Radial scar	3	3
Granulomatous mastitis	2	2
Columnar cell change	1	0
Fat necrosis	1	1
Intraductal papilloma	1	1
Atypical lesion	5	9
ADH	3	4
ALH	2	3
Both	0	1
LCIS	0	1
DCIS	6	7
Invasive carcinoma	11	11
IDC	3	3
ILC	8	8

[a] UDH = usual ductal hyperplasia, PASH = pseudoangiomatous hyperplasia, ADH = atypical ductal hyperplasia, ALH = atypical lobular hyperplasia, LCIS = lobular carcinoma in situ, IDC = invasive ductal carcinoma, ILC = invasive lobular carcinoma.
[b] The final diagnosis varied from the primary diagnosis in five lesions biopsied in five unique patients. Four were re-categorized to atypical and one was re-categorized to malignant based on secondary diagnoses.

MRI studies were reviewed and verified by two breast radiologists (CMK, MJ). The studies were evaluated for the following features: background breast enhancement, lesion enhancement pattern [mass, non-mass enhancement (NME), focus], lesion size, lesion morphology (including margins and distribution), and enhancement kinetics [Type 1 (persistent), Type 2 (plateau), or Type 3 (washout)]. The indication for MRI was recorded as one of three categories: [1] screening in high-risk patients, [2] diagnostic study of an equivocal lesion, and [3] extent of disease in patients with a current diagnosis of breast cancer. MRI-guided core needle biopsies were obtained using a 9-gauge vacuum-assisted needle (ATEC, Suros Surgical Systems, Hologic, Inc., Marlborough, Massachusetts) with a dedicated breast coil (Invivo 7-Channel, Invivo Corporation, Gainesville, Florida), DynaCad software (Version 4.0.0.0, Invivo Corporation, Gainesville, Florida) with a 1.5 T magnet (Avanto, Siemens Healthineers, Munich, Germany) and Multihance (0.1 mmol/kg, Bracco Diagnositics Inc., Monroe Township, NJ) as the IV contrast. For each procedure, a marker was placed at the time of biopsy and post-biopsy mammograms were performed.

The CNB slides and subsequent resection pathology, where applicable, were reviewed by two breast pathologists (BCC, AJL). The dominant (primary) histopathologic finding in the CNB and additional significant findings (secondary) were recorded. The primary diagnosis was the pathologic finding that represented the majority of the core biopsy tissue and correlated with imaging findings (i.e. targeted findings). The secondary diagnoses were any additional pathologic findings identified in the tissue (i.e. incidental findings). The final categorization of the core biopsy pathology was based on the most clinically significant diagnosis, whether primary or secondary. For statistical purposes, pathologic diagnoses were categorized as benign or malignant. The benign diagnoses included normal breast tissue, as well as benign and atypical lesions, including atypical ductal hyperplasia (ADH), atypical lobular hyperplasia (ALH), and lobular carcinoma in situ (LCIS). The relationship between categorical variables was assessed using the chi square test, and a p-value of < 0.05 was considered significant.

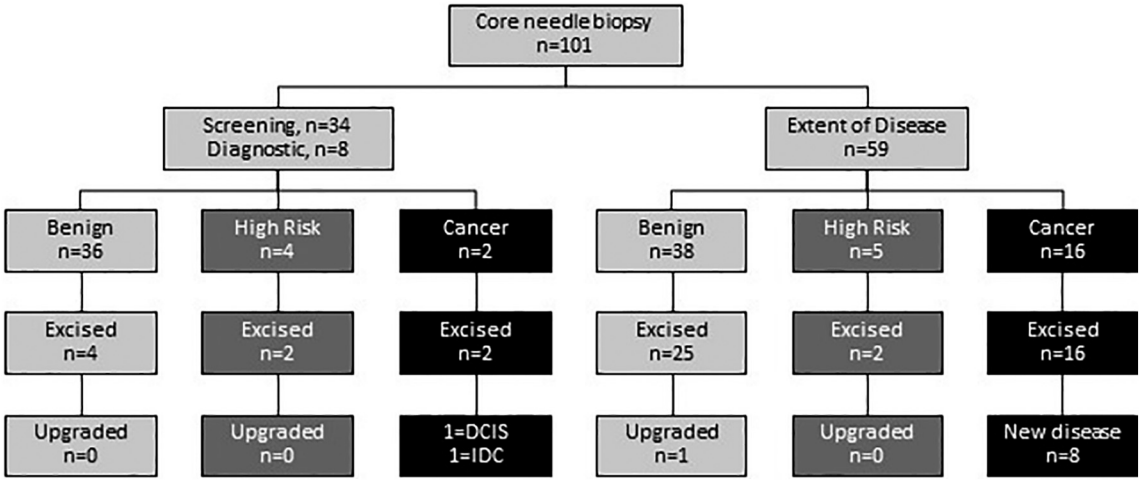

Fig. 1. MRI-guided core needle biopsy specimens sorted by indication for MRI and final pathology.

Table 4
Clinical impact of malignancies detected in breast cancer patients with MRI for extent of disease.[a]

Patient	Original diagnosis	MRI	Biopsy	New primary?	Change in management?	Excision diagnosis[b]
1	ILC (L)	NME (L)	ILC	No	No	ILC
2	IDC (L)	NME (L)	DCIS	No	No	IDC, DCIS
3	DCIS (R)	NME (R)	DCIS	No	No	DCIS
4	IDC (R)	Mass (R)	IDC	No	No	No residual
5	IDC (R)	NME (R)	DCIS	No	No	No residual
6	ILC (L)	NME (L)	ILC	No	No	mc ILC
		Mass (L)	ILC	No	No	
7	ILC (R)	Mass (R)	ILC	Ipsi	Yes[c]	mc ILC
8	IDC (R)	NME (R)	IDC	Ipsi	No	mf IDC
9	IDC (R)	Mass (R)	IDC/DCIS	Ipsi	Yes[c]	mc IDC
10	ILC (L)	Mass (L)	ILC	Ipsi	Yes[d]	mf ILC
11	IDC, DCIS (R)	NME (R)	IDC	Ipsi	Yes[c]	mf IDC
		Mass (R)	IDC	Ipsi		
12	DCIS (R)	NME (R)	DCIS	Ipsi	Yes[c]	IDC, DCIS
13	DCIS (R)	NME (L)	ILC	Contra	Yes[e]	DCIS (R), ILC (L)

[a] One patient with a CNB identifying known disease was lost to follow up and not included in this table.
[b] Mf = multi-focal disease; mc = multi-centric disease.
[c] Breast conservation therapy converted to total mastectomy. Patient #12 also had sentinel lymph node biopsy.
[d] Continued with breast conservation therapy, however a wider lumpectomy was performed.
[e] Unilateral mastectomy converted to bilateral mastectomy.

3. Results

3.1. Patient characteristics, MRI findings, and pathologic findings

A total of 79 patients underwent MRI-guided CNB of 101 clinically, mammographically, and sonographically occult lesions. The clinical and demographic features are summarized in Table 1. The most common indication for MRI was to determine extent of disease in patients with a current diagnosis of BC (58%). Of the 34 patients in the high-risk screening group, 19 (56%) either had a family history of BC (n = 13) and/or predisposing genetic mutation (n = 10) and 15 (44%) had a prior history of BC (n = 14) or ADH (n = 1).

On imaging, the majority of lesions were categorized as BI-RADS 4, suspicious of malignancy (n = 93, 92%), with the remaining lesions being BI-RADS 5, highly suggestive of malignancy (n = 3), BI-RADS 6, known biopsy proven malignancy (n = 4), or undocumented (n = 1) [15]. Of the 101 MRI-detected lesions, 60 (59%) were designated as non-mass enhancement (NME), 38 (38%) as a mass, and 3 (3%) as a focus. For this study, the focus lesions were grouped with the mass lesions. The features of these lesions are summarized in Table 2.

The final pathologic diagnoses for the MRI-guided CNB, summarized in Table 3, were benign in 83 (82%) CNB followed by breast cancer in 18 (18%). The most common benign findings were: fibrocystic changes (FCC) (37%), sclerosing lesions including sclerosing adenosis and radial scars (10%), and fibroadenoma (FA) (8%). All of the sclerosing lesions showed NME and all of the FA showed mass enhancement. Of the 18 breast cancer cases, 8 (44%) were invasive lobular carcinoma (ILC), 7 (39%) DCIS, and 3 (17%) invasive ductal carcinoma (IDC). All of the DCIS cases showed NME.

Analysis of the 60 NME lesions showed a final pathologic diagnosis of benign in 43 (72%) CNB followed by BC in 12 (20%) and atypia in 5 (8%). Of the NME BC cases, 7 (58%) were DCIS, 4 (33%) were ILC, and 1 (8%) was IDC. The DCIS cases were primarily grade 3 (71%) and solid (86%) type. Of the atypical lesions, 3 (60%) were ADH and 2 (40%) were ALH. The most common benign findings in MRI-guided CNB of NME lesions were fibrocystic changes in 21 (35%) and sclerosing lesions in 10 (17%) CNB.

Analysis of the 41 mass lesions showed a final pathologic diagnosis of benign in 31 (75%), BC in 6 (15%) and atypia in 4 (10%). Of the BC cases detected as a mass on MRI, 4 (67%) were ILC and 2 (33%) were IDC. Of the atypical lesions, there was one each of ADH, ALH, LCIS, and both ADH and ALH. The most common benign findings in MRI-guided CNB of mass lesions were fibrocystic changes in 18 (58%) and fibroadenomas in 8 (26%).

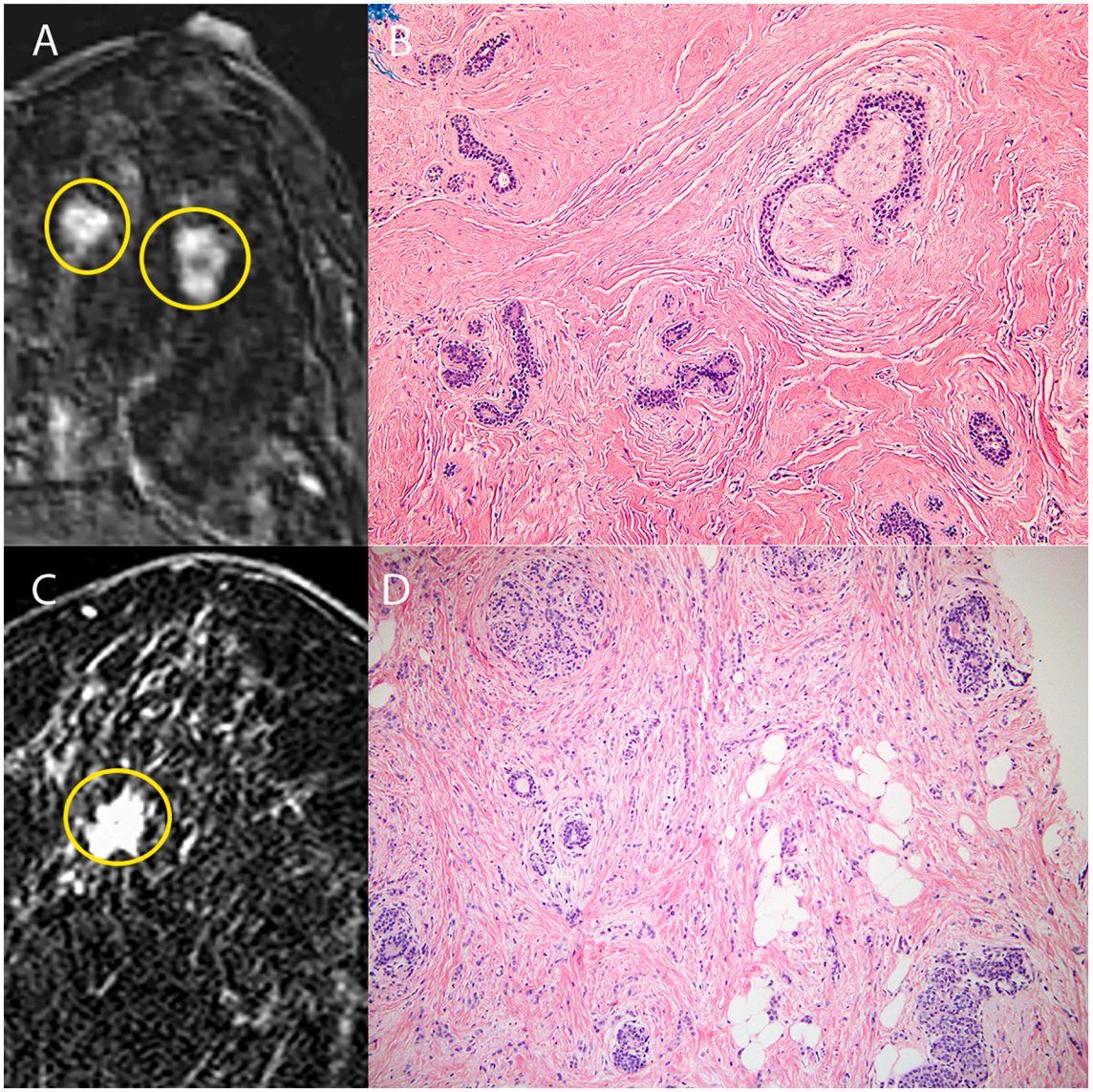

Fig. 2. Comparison of similar appearing homogeneously enhancing irregular MRI mass lesions (circled) with benign and malignant pathology. Representative MRI and histologic images of fibroadenomas (A, B) and invasive lobular carcinoma (C, D).

3.2. Correlation of breast MRI findings with malignant pathology

The majority of malignant MRI-guided CNB diagnoses were in the extent of disease group: 16 of 18 (89%) total malignancies diagnosed in 14 unique patients (Fig. 1). One of these patients was lost to follow up. The MRI findings and the impact of the malignant diagnoses on clinical management for the remaining 13 patients (corresponding to 15 of 16 malignancies in the extent of disease group) are summarized in Table 4. Of these 15 malignancies, 7 (47%) represented additional sampling of the patient's known disease, 7 (47%) represented a new diagnosis of BC in the ipsilateral breast and 1 (6%) represented a new diagnosis of BC in the contralateral breast. Based on the malignant MRI-guided CNB, 6/13 (46%) patients had additional (i.e., sentinel lymph node biopsy or contralateral breast surgery) or more extensive (i.e., wider lumpectomy) surgery. The MRI findings and impact on clinical management for the 2 remaining patients with malignant CNB are summarized in Supplemental Table 1. Both patients had a personal history of breast cancer, NME on breast MRI and DCIS in the MRI-guided CNB.

Malignancy rates were correlated with MRI morphology, MRI kinetics, and background parenchymal enhancement (BPE) (Supplemental Tables 2 and 3). There was no significant difference in the malignancy rate for NME (20%) lesions compared to mass lesions (15%) ($p = 0.4$). For the malignancies presenting as mass lesions (Fig. 2), 100% (6/6) were irregular in shape and 83% (5/6) had non-circumscribed margins. For the NME lesions (Fig. 3), segmental distribution was associated with a higher malignancy rate as compared to focal or linear distribution ($p < 0.001$). The malignancy rate was not significantly different for NME lesions with persistent, plateau, or washout kinetics ($p = 0.88$). However, for mass lesions, MRI kinetic parameters were associated with malignancy rate ($p < 0.001$). Among patients with minimal, moderate or marked background parenchymal enhancement (BPE), the highest malignancy rate was in the minimal BPE group (37%) while none of the lesions identified in women with moderate or marked BPE showed malignant pathology (0%) ($p < 0.001$).

Two false negative MRI-guided CNB were detected in this study. Both occurred in patients in the extent of disease group who had MRI-guided CNB of lesions in the breast contralateral to their known malignancies. The first patient had a moderate degree of BPE and MRI-guided CNB of an area of NME showed sclerosing adenosis and fibrocystic changes. In the excision specimen there was an unexpected small focus of IDC, distant from the area corresponding to the NME on

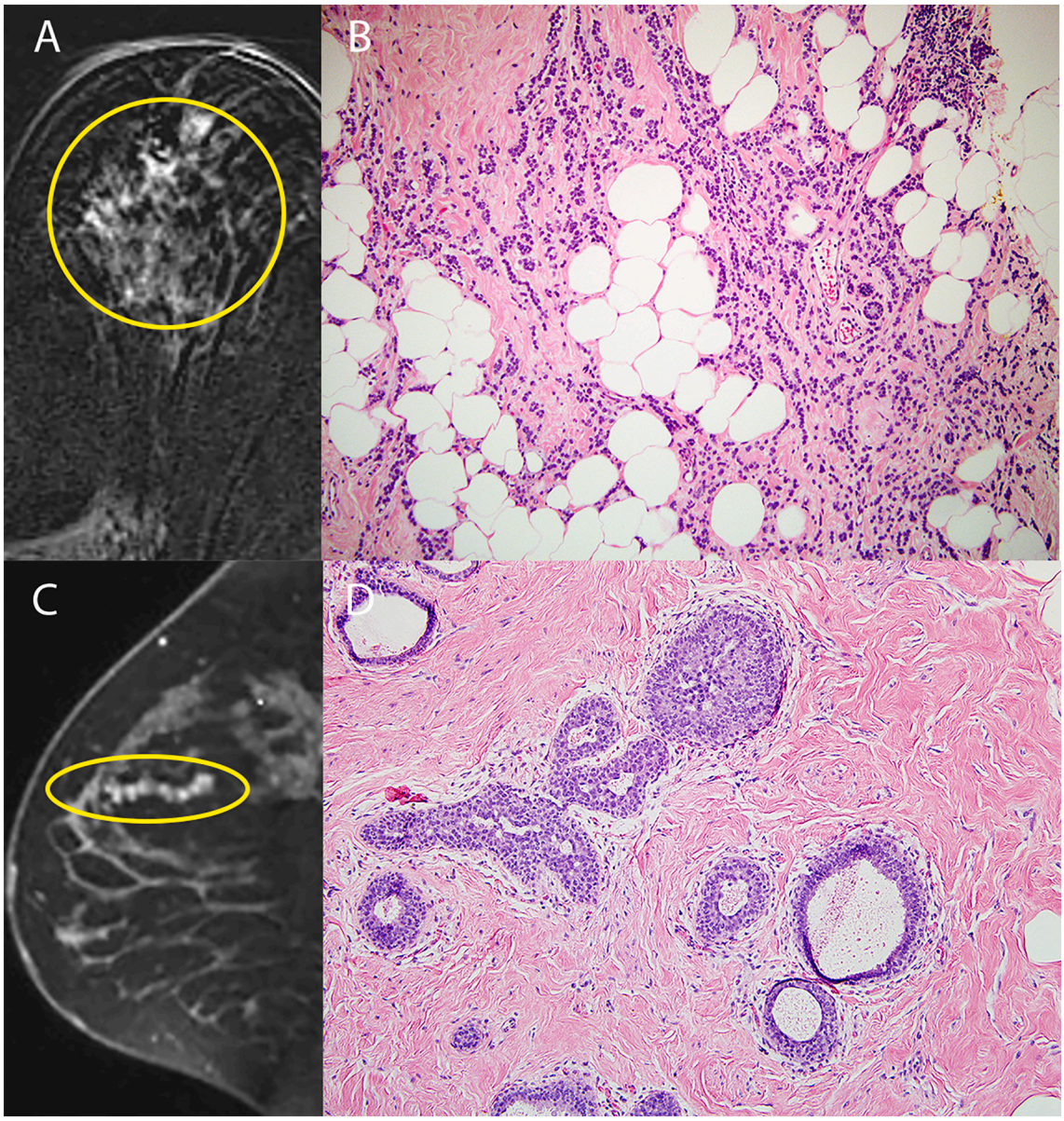

Fig. 3. Comparison of similar appearing non-mass enhancing (NME) lesions (circled) with benign and malignant pathology. Representative MRI and histologic images of invasive lobular carcinoma (A, B) and fibrocystic changes with usual ductal hyperplasia and pseudoangiomatous hyperplasia (PASH) (C, D).

preoperative MRI. On re-review of the preoperative MRI, no lesion was identified in the area with malignant pathology. The second patient had minimal BPE and MRI-guided CNB of a mass showed dense stromal fibrosis. Final excision showed DCIS with microinvasive IDC in tissue adjacent to the biopsy site. On re-review of the pre-operative MRI, the biopsy targeted a 0.3 cm mass with associated, characteristic of DCIS.

4. Discussion

Due to its high sensitivity [1,2] MRI has been established as a valuable clinical tool for detecting BC in high-risk patients. However, it is also highly sensitive at detecting benign lesions. As a result, widespread adoption of breast MRI in clinical practice has led to increased biopsy rates but diminished diagnostic yield [8]. Recent studies have shown that the large majority (65–74%) of suspicious breast MRI lesions investigated with MRI-guided CNB are benign (65–74%) [16-18] with the most common pathologic diagnosis being FCC.

In this series of MRI-guided CNB, there were 18 malignant diagnoses, 16 (89%) of which occurred in 14 patients with concurrent BC. Almost half (46%) of the patients with available follow up data had additional or more extensive surgery based on the malignant MRI-guided CNB diagnosis. The remaining 2 malignant CNB diagnoses were in patients who had a personal history of BC but no concurrent diagnosis of BC. There were 8 ILC among the 18 malignant MRI-guided CNB, consistent with prior studies of breast MRI and increased detection of clinically and mammographically occult ILC [19]. No malignant CNB diagnoses were made in the diagnostic (n = 8) or high-risk screening but breast cancer naïve (n = 19) groups. Similar to prior studies [18], there was minimal-to-no association between enhancement kinetics and malignancy in the mass and NME lesions, respectively. There was no significant difference in the rate of malignancy in mass-enhancing versus NME lesions, a finding that could be related to sample size and selection bias in the patients referred to our institution.

All 6 (100%) of the malignant mass lesions had one or more characteristics associated with malignancy. However, an even greater number (n = 17) of MRI-detected lesions with benign pathologic diagnoses had concerning MRI features. A similar pattern was seen with the 12 malignant NME lesions. While, the majority (75%) had one or

more MRI features associated with malignancy, there was a greater number ($n = 25$) of benign cases with similar morphology. The highest malignancy rate was identified in women with minimal BPE (37%, $n = 35$) and no malignancies were identified in women with moderate to marked degrees of BPE ($n = 26$), suggesting that increased BPE may increase the false positive rate of MRI and MRI-guided CNB. However, there were only two false negative MRI-guided CNBs in this series. One was due to lack of detection on MRI and one was due to under sampling of a field of DCIS during the biopsy procedure.

The limitations of this study include the sample size and single-institution retrospective design. The strengths of the study include the focus on MRI-guided CNB with exclusion of MRI lesions that could be visualized and biopsied with ultrasound or stereotactic guidance. The study included detailed review of the pathologic and radiologic findings by breast pathologists and breast radiologists, providing thorough radiological-pathological correlation. Furthermore, this study reflects contemporary practice with the use of MRI (and subsequent MRI-guided CNB) outside of a clinical trial and protocols for BC screening with MRI.

There are important differences between our study and most prior studies of breast MRI. One difference is that the patients in this series were selected solely on the basis of having had an MRI-guided CNB of the breast. As our study demonstrates, this is not the same as the patient population for whom screening MRI is recommended [3-5]. It is also not exactly the same as the patient population in larger studies and meta-analyses of patient who had breast MRI [9,10]. Those studies did not select patients based on the type of guidance used for core needle biopsy procedures after detection of an MRI abnormality. Additionally, those studies showed no significant improvement in patient outcomes (e.g., local control, rates of reoperation) based on the use of breast MRI [9,10]. The outcomes analyzed in this study were the MRI-guided CNB diagnoses (benign versus malignant) and changes in clinical management based on those diagnoses. The limited sample size and short follow-up in this series precluded correlation of the observed changes in clinical management (additional/more extensive surgery) with other endpoints. However, our findings appear to be consistent with at least one recent study of BC patients staged with multimodality imaging, including MRI [20]. In a series of 1547 patients, Mariscotti et al. [20] reported that use of preoperative digital breast tomosynthesis and/or MRI was associated with more extensive surgery and lower reoperation rates.

In conclusion, the data from this series of MRI-guided CNB indicate that most diagnoses were benign, including the majority of NME lesions. False-negative MRI-guided CNB were uncommon. The majority of malignant diagnoses on MRI-guided CNB occurred in patients with concurrent BC and frequently led to changes in clinical management.

Prior presentation

Preliminary data were presented at the Annual Meeting of the United States and Canadian Academy of Pathology, March 16–22, 2019, in National Harbor, MD.

Ethical approval

This study was approved by the Institutional Review Board of the University of North Carolina with a waiver of consent.

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Declaration of competing interest

Dr. Calhoun is a member of the Oncology Advisory Board for Luminex Corporation. The other authors have no conflicts of interest or financial disclosures.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.anndiagpath.2020.151563.

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