Pathologic Findings of Breast Lesions Detected on Magnetic Resonance Imaging

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During the last 20 years, magnetic resonance imaging (MRI) has emerged as the most sensitive imaging technique for detecting breast cancers. Currently it is used for evaluation of extent of disease in patients with newly diagnosed breast cancer, screening of high-risk patients for early diagnosis of cancer, additional evaluation of indeterminate breast abnormalities identified by mammography or sonography, and evaluation of response to neoadjuvant systemic therapy.1-4 In breast MRI, a lesion’s level of suspicion is based on whether or not it displays contrast enhancement, the speed and pattern of enhancement (ie, kinetics), and the morphologic characteristics of the lesion. Magnetic resonance imaging-guided biopsy is performed when a suspicious finding cannot be adequately detected by mammographic or ultrasound evaluation. The increase in the number of MRI-guided breast biopsies within the last 5 years parallels the increase in the total number of breast MRI studies performed for all indications. Since a large number of these lesions are benign, it has become apparent that the high sensitivity of this imaging modality is challenged by its low specificity. This, in turn, has sparked controversies regarding the increasing use of breast MRI with increased rates of unnecessary mastectomy, increased workups, delay to definitive surgery, and limited evidence of improved clinical outcomes even with the added costs.5-7

Radiology-pathology correlation has helped to improve patient care.8,9 Previous radiologic-pathologic correlation studies have involved mostly ultrasound-guided core needle and some stereotactic-guided core biopsies.10-14 Of the correlation studies pertaining to MRI, most are found within the radiology literature, but a few studies appear in pathology sources.15-20 It is important for pathologists to understand this imaging technique and be familiar with the entities that can present as an abnormal enhancing lesion on MRI. The purpose of this study is to identify the spectrum of pathologic changes that present as abnormal enhancing lesions and to determine if any specific MRI pattern correlates with malignant lesions.

MATERIALS AND METHODS

Study Population

The institutional review board approved the study and granted a waiver of informed consent. The pathology and radiology databases at University of Texas Southwestern Medical Center (Dallas) were searched to identify all MRI-guided breast biopsies. Cases from October 2007 through September 2012 were included in the study. Radiology and pathology reports were correlated for...
finding that would have correlated with the radiologic findings of mass, nonmass, or focus enhancements. Each core biopsy was examined by hematoxylin-eosin–stained slides cut at 3 different levels per paraffin block. The slides were reviewed by 3 breast pathologists. The malignant lesions were categorized as invasive carcinomas or ductal carcinoma in situ (DCIS). Biopsies that showed atypical ductal hyperplasia, atypical lobular hyperplasia, lobular carcinoma in situ, or flat epithelial atypia were grouped as atypical epithelial lesions. The lesions in the benign category were subcategorized into benign breast diagnoses and unremarkable/normal breast tissue. The benign breast diagnoses included proliferative and nonproliferative breast diseases, miscellaneous benign findings such as intramammary lymph node, fat necrosis, and hemangiomata. The breast tissue that did not reveal any specific pathologic abnormality other than normal glandular elements with or without dense stroma was categorized as normal breast tissue for the study. Lesions were classified as fibrocystic change with or without epithelial hyperplasia if the lesion had apocrine metaplasia, nodular adenosis, sclerosing adenosis, papillomatosis, and usual ductal hyperplasia. Lesions labeled as columnar cell lesions included columnar cell change and/or columnar cell hyperplasia. Some of the columnar cell lesions had associated pseudoangiomatous stromal hyperplasia or concomitant fibrocystic change. The miscellaneous lesions were specific findings and were recorded as such.

### RESULTS

Table 1 summarizes the patient population, indications for MRI evaluation, and the number of patients in each category. We identified 177 MRI-guided biopsies in 152 patients. Patient age ranged from 27 to 83 years, with a mean of 52 years. The most common indication for MRI was to determine the extent of disease (43%; 66 of 152), followed by screening for high-risk women (39%; 59 of 152), which included those with a strong family history or carriers of BRCA1 or BRCA2 mutations or other rare gene mutations that increased breast cancer risk. The remaining biopsies (18%; 27 of 152) were performed to follow up an incomplete evaluation or indeterminate lesion. The median and mean sizes of MRI lesions were 10 and 14 mm, respectively (range, 5–80 mm). The mass lesions ranged from 5 to 40 mm (median, 8 mm), and the nonmass lesions ranged from 5 to 80 mm (median, 15 mm). All focus lesions measured 5 mm or less.

The vast majority (82%; 145 of 177) of biopsied lesions were BI-RADS 4, followed by BI-RADS 3 (8%; 13 of 177), BI-RADS 5 and 6 constituted 8% of cases. Only 2% (4 of 177) of the lesions did not have a completed evaluation for BI-RADS assessment. The lesions targeted via MRI were mostly mass lesions (54%; 95 of 177), followed by nonmass lesions (44%; 76 of 177). The largest number of biopsied lesions (42%; 74 of 177) showed persistent kinetics, followed by plateau (25%; 44 of 177) and washout kinetics (17%; 30 of 177). Due to imaging protocol limitations, kinetic assessment was not available for 16% (29 of 177) of lesions, most of which were performed in 2007 and early 2008 (Table 1).

Table 2 summarizes the different categories of pathologic diagnosis in different patient populations based on the MRI indication. Of all the malignant cases in our study, the majority (61%; 19 of 31) were identified in the group undergoing MRI evaluation for extent of disease, followed by those undergoing high-risk screening (23%; 7 of 31). Malignancy was identified in 14% (5 of 35) of indeterminate lesions.

Overall, 18% (31 of 177) of biopsies were malignant, of which 61% (19 of 31) were invasive carcinoma and 39% (12 of 31) were DCIS (Table 3). The remaining 82% (146 of 177) of MRI-guided biopsies were nonmalignant, of which 71%...
(126 of 177) revealed benign changes (or no pathologic findings) and 11% (20 of 177) showed epithelial atypia, which includes 17 cases of lobular neoplasia and 3 cases of atypical ductal hyperplasia. Some of the atypical epithelial changes were identified in a background of benign changes. All 3 atypical ductal hyperplasia were focal. One did not reveal additional atypia on excision, one was lost to follow-up, and the last one revealed DCIS on excision.

Figure 1 demonstrates the percentages of benign, atypical, and malignant diagnosis in the different categories of MRI lesions. Sixty-five percent (62 of 95) of the mass lesions and 76% (58 of 76) of nonmass enhancing lesions were benign. All 6 MRI focus lesions were benign. Only 21% (20 of 95) of the mass lesions and 14% (11 of 76) of nonmass lesions were malignant.

Dynamic contrast-enhanced MRI kinetics were compared in the benign, atypical, and malignant categories (Figure 2). Of the MRI lesions with persistent kinetics, the vast majority (84%; 62 of 74) were benign (Figure 3, A through C). Lesions with plateau kinetics portend an indeterminate level of suspicion. The majority (70%; 31 of 44) of lesions with this kinetic pattern were benign (Figure 4, A through C). Out of 30 lesions with washout kinetics, 57% (17 of 30) were benign and 30% (9 of 30) were malignant (Figure 5, A through C).

Figure 6 describes the distribution of different kinetic patterns in all malignant lesions. Most of the malignant mass lesions (40%; 8 of 20) showed washout kinetics (Figure 7, A through C), whereas the majority of nonmass lesions exhibited persistent or plateau kinetics (Figures 6 and 8, A through C). Fifteen of the 19 invasive carcinomas were mass lesions, and the remaining 4 showed nonmass enhancements (3 invasive lobular carcinomas, 1 invasive ductal carcinoma). The invasive lesions did not show a specific kinetic pattern (5 with washout kinetics, 4 showing persistent kinetics, and 4 with plateau kinetics). The size of the lesions ranged from 5 to 70 mm (median, 9 mm). Seven DCIS cases presented as nonmass enhancements and

**Table 2. Pathologic Findings Based on the Magnetic Resonance Imaging Indication**

| Extent, No. | HRS, No. | F/U-IL, No. | Total, No. (%) |
|------------|----------|-------------|----------------|
| Malignant  | 19       | 7           | 5              | 31 (18) |
| Atypical   | 8        | 11          | 1              | 20 (11) |
| Benign     | 50       | 47          | 29             | 126 (71) |
| Total      | 77       | 65          | 35             | 177     |

Abbreviations: F/U-IL, follow-up of indeterminate lesion; HRS, high-risk screening.

**Table 3. Pathologic Diagnosis Category**

| Category                                      | No. |
|-----------------------------------------------|-----|
| Malignant (18%; 31/177)                      |     |
| Invasive ductal carcinoma                     | 13  |
| Invasive lobular carcinoma                    | 4   |
| Ductal carcinoma in situ                      | 12  |
| Invasive mixed carcinoma                      | 1   |
| Tubular carcinoma                             | 1   |
| Atypical epithelial hyperplasia (11%; 20/177) |     |
| Atypical ductal hyperplasia                   | 3   |
| Lobular neoplasia (12 ALH, 5 LCIS)           | 17  |
| Benign (71%; 126/177)                        |     |
| Benign breast diagnoses (105/126)            |     |
| Fibrocystic changes with/without epipleelial hyperplasia | 31  |
| Columnar cell lesions                         | 30  |
| Fibroadenoma and fibroadenomatoid change      | 14  |
| Ductal ectasia                                | 7   |
| Radial sclerosing lesion                      | 6   |
| Papilloma                                     | 7   |
| PASH                                          | 5   |
| Intramammary lymph node                       | 3   |
| Fat necrosis                                  | 1   |
| Hemangiomal                                   | 1   |
| Normal breast tissue (21/126)                 |     |

Abbreviations: ALH, atypical lobular hyperplasia; LCIS, lobular carcinoma in situ; PASH, pseudoangiomatous stromal hyperplasia.

**Figure 1.** Magnetic resonance imaging lesion type and corresponding pathology diagnosis.

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5 as mass enhancements. Most DCIS cases (9 of 12) showed plateau or washout kinetics. These lesions ranged in size from 7 to 46 mm (median, 12.5 mm). The majority of the DCIS cases were high-grade type (8 of 12).

Magnetic resonance imaging features and kinetics were also examined in all benign lesions (Figure 9). These lesions were most commonly masses (49%; 62 of 126), closely followed by nonmass lesions (46%; 58 of 126). Although...
nearly half (62 of 126; 49%) of these lesions had persistent kinetics, 13% (17 of 126) of benign lesions showed washout kinetics.

Table 3 lists different benign lesions and “unremarkable/normal” breast tissue (71% of all MRI-guided biopsies; 126 of 177). Fibrocystic changes comprised the largest number of the benign breast cases, closely followed by columnar cell lesions. The remaining lesions included fibroadenomas, hemangioma, duct ectasia, pseudoangiomatous stromal hyperplasia, fat necrosis, and intramammary lymph nodes.

Follow-up of the 20 patients (21 biopsies) who had unremarkable/normal breast tissue on MRI-guided biopsy revealed the following: 11 patients had resolution of the initial lesion on follow-up MRI, 1 patient had a prophylactic mastectomy with concordant benign pathology at the 2 MRI biopsy sites, 4 women underwent rebiopsy that yielded benign breast tissue or fibrocystic changes, 3 women were lost to follow-up, and 1 had a follow-up ultrasound guided biopsy that revealed focal lobular carcinoma in situ in a background of columnar cell change.

**DISCUSSION**

Dynamic contrast-enhanced MRI has emerged as a highly sensitive (88%–92%) technique for evaluation of breast lesions, but the specificity associated with this method ranges from 67% to 77%. In breast MRI, lesions are characterized based on their morphologic features and dynamic contrast enhancement and kinetic pattern such as signal intensity or speed of enhancement combined with morphologic patterns. The initial upslope (early phase enhancement) equates to signal intensity during the first 2 minutes following contrast administration. It is described as slow, medium, or rapid depending on the steepness of the curve (enhancement velocity). The delayed phase begins after peak enhancement, usually within 2 minutes, and is characterized as persistent if it continues to rise, plateau if it levels off, and washout if it drops off (Figure 10). Persistent kinetics is generally aligned more with benign lesions, washout kinetics is generally regarded as suspicious for malignancy, and plateau kinetics are considered indeterminate.

Morphologically, lesions are separated into enhancing masses, nonmass enhancements, and foci. Masses are 3-dimensional space-occupying lesions, which are further characterized by shape, margin, and internal enhancement characteristics. Nonmass enhancements have an absence of distinct 3-dimensional or masslike features, and are characterized by distribution, internal patterns, and symmetry or asymmetry between breasts. A focus lesion...
Figure 5. A 33-year-old woman presented for high-risk screening magnetic resonance imaging (MRI). A, An axial postcontrast subtraction image shows a 5-cm regional clumped area of enhancement in the right breast. B, This area exhibits washout kinetics. C, An MRI-guided biopsy of nonmass enhancement shows columnar cell lesion (hematoxylin-eosin, original magnification ×10).

Figure 6. Magnetic resonance imaging kinetics of malignant lesions (n = 31).
measures less than 5 mm and cannot be further characterized by shape or margin status.\textsuperscript{22,23} Example descriptions of suspicious MRI lesions would include “irregular spiculated mass with rim enhancement” or “linear clumped nonmass enhancement.”

The BI-RADS lexicon, now in its fifth edition, standardizes the reporting of MRI-detected lesions. The lexicon standardizes the approach to assigning morphology and enhancement characteristics for lesions and has overall improved the diagnostic specificity of the lesions detected by MRI.\textsuperscript{22,23} Although combining these features has improved the overall diagnostic specificity of MRI, in our study only 18% (31 of 177) of the biopsied lesions revealed malignancy.

Lesions that show washout kinetics favor a malignant process, whereas those that show persistent kinetics favor a benign process. As expected, the majority of benign lesions in our study showed persistent (49%; 62 of 126) or plateau (25%; 31 of 126) kinetics, but interestingly, 13% (17 of 126) of the benign lesions exhibited more suspicious washout kinetics. Of the benign lesions, 49% (62 of 126) were described as mass lesions, of which 21% (13 of 62) had washout kinetics. Only one focus lesion showed washout kinetics. Among the benign lesions that showed a washout kinetic pattern, fibrocystic changes comprised 35% (6 of 17), closely followed by normal breast tissue (24%; 4 of 17) and columnar cell lesions (12%; 2 of 17). The remaining lesions with this kinetic pattern were radial scars, intraductal papilloma, fibroadenoma, and duct ectasia. Most malignant lesions showed either washout or plateau kinetics (29% in each category; 9 of 31), as expected, but 16% (5 of 31) of malignant lesions demonstrated persistent kinetics (2 invasive duct carcinomas, 2 invasive lobular carcinomas, and 1 DCIS). These results highlight the overlap in MRI features between benign and malignant lesions. It is important to note that malignant lesions such as invasive lobular carcinoma and some DCIS may not present as mass lesions or show washout kinetics. This is further compounded by the fact that many lesions that present as a mass with washout kinetics (21% in our study; 13 of 62) can be benign, making it difficult to determine how suspicious a lesion is for malignancy.

A variety of benign breast conditions have been previously described to mimic malignancy on MRI. Some of these entities include radial scar, sclerosing adenosis, fibroadenoma, fat necrosis, and pseudoangiomatous stromal hyperplasia.\textsuperscript{24} In our study, more than half of the benign lesions were fibrocystic change with or without epithelial hyperplasia, followed by columnar cell lesions. Interestingly, one-
fourth of all the benign biopsies had columnar cell lesions, alone or associated with pseudoangiomatous stromal hyperplasia or other proliferative changes such as usual ductal hyperplasia. Apocrine metaplasia was described as a frequent biopsy finding in MRI-guided biopsies in one study (38%; 11 of 29 cases). However, in our study, 10 cases showed cystic apocrine metaplasia, mostly as one of the findings in the fibrocystic change category, with the exception of 1 case where apocrine metaplasia was the only finding. A recent study showed that increased microvascular density in select benign breast lesions, notably cystic apocrine metaplasia when compared with normal fibro-glandular tissue, led to their detection on MRI as an enhancing focus or small mass. In our study, a large spectrum of benign changes showed abnormal enhancement. Most of the benign lesions had some form of proliferative change, inflammatory reaction, or reactive changes; the associated increased vascularity and the localized nature of the abnormality led to their detection on MRI.

Atypical hyperplasia, both ductal and lobular type, may be the most significant lesion found on MRI-guided biopsy, but may not necessarily be the lesion being targeted by imaging, as it is usually incidental or quantitatively too small. However, in certain instances these lesions represent a dominant finding, as in lobular carcinoma in situ.

Normal breast tissue can show significant enhancement depending on the phase of the menstrual cycle, further complicating image interpretation. Twenty-one of our biopsies showed normal breast tissue, of which 11 patients had follow-up imaging studies documenting resolution of the initial lesion, 4 patients had repeat biopsies showing either benign breast tissue or fibrocystic changes, and 1 patient underwent total mastectomy with concordant results. This finding confirms that morphologically normal-appearing breast tissue can show segmental or focal enhancement. However, on rare occasions, there may be sampling error, which occurred in one case in our study where a subsequent ultrasound guided biopsy of the area revealed focal lobular carcinoma in situ in a background of columnar cell lesion. Excluding 3 cases that were lost to follow-up, there were no cases in our series that revealed a missed malignancy on follow-up examination or repeat biopsy. In summary, finding normal-appearing breast tissue on an MRI-guided biopsy should not automatically raise the possibility of sampling error, but should be correlated with other findings and follow-up. However, any growth of a...
sampled lesion showing normal tissue should prompt rebiopsy and further histologic confirmation.

The rate of detecting malignancy on MRI is variable and depends on the study design and the patient population being evaluated. Prior studies have shown overall malignancy rates of 22% to 29%. The overall rate of malignancy identified in our study was slightly lower (18%; 31 of 177). The highest percentage of malignancy was identified in patients who were being evaluated for extent of disease in our study (25%; 19 of 77), a finding similar to those of other studies. In our study, 11% (7 of 65) of biopsies were classified as malignant in this particular population (4 invasive carcinomas, including 1 tubular carcinoma and 3 DCIS). Lastly, follow-up of 35 indeterminate lesions found malignancy in 14% (5 of 35) of cases.

In summary, the likelihood of discovering an undetected malignancy on MRI is higher in those with a new cancer diagnosis compared with those undergoing screening or further workup for indeterminate lesions. The specificity of MRI is significantly lower than that of screening mammography. However, when MRI or ultrasound is used in conjunction with traditional mammography, it yields a higher rate of cancer detection. Nevertheless, the increased sensitivity of MRI leads to detection of a large number of benign lesions, thus increasing the number of biopsy procedures and added cost. This may change in the future if significant improvement occurs in MRI techniques to increase specificity, thereby reducing the number of false-positive MRI findings.

In conclusion, MRI detects a wide spectrum of benign findings as suspicious lesions. Many benign lesions show morphologic and kinetic features similar to malignant lesions on MRI. Because MRI is highly sensitive but not specific, pathologists will continue to play an important role in the final diagnosis of these lesions. It is important that we understand the strengths and weaknesses of this imaging modality and ensure adequate communication regarding radiologic-pathologic correlation of these biopsies for optimal patient care.
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