

BREAST IMAGING

ORIGINAL ARTICLE

Lesion characteristics, histopathologic results, and follow-up of breast lesions after MRI-guided biopsy

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PURPOSE

We aimed to assess the effectiveness of magnetic resonance imaging (MRI)-guided vacuum-assisted breast biopsy (VABB), evaluate and compare the characteristics and histopathologic findings of lesions, and overview the follow-up results of benign lesions.

METHODS

MRI findings and histopathologic results of breast lesions biopsied by MRI-guided VABB between 2013 and 2016 were retrospectively analyzed. MRI findings closely related with malignancy were investigated in particular. Follow-up results of benign lesions were evaluated.

RESULTS

MRI-guided VABB was applied to 116 lesions of 112 women. Of the lesions, 75 (65%) were benign, while 41 (35%) were malignant. Segmental (94%), clustered (89%), and clustered ring (67%) non-mass-like enhancement patterns were found to be more related with malignancy. False-negative rate of MRI-guided VABB was 12%, underestimation rate was 21%. One of the 54 followed-up benign lesions had a malignant result.

CONCLUSION

MRI-guided VABB is a reliable method for the diagnosis of breast lesions that are positive only on MRI. Follow-up results show that cancer detection rate is low for radio-pathologically concordant lesions. Further multicenter studies with larger patient population are needed to elucidate these results.

agnetic resonance imaging (MRI) is a widely used diagnostic tool for breast imaging in daily practice, with its high sensitivity to detect primary, recurrent, and residual breast cancer. Breast MRI serves as a reliable problem-solving tool in case of inconclusive mammography and ultrasonography (US) findings. It can be used to monitor the results of neoadjuvant chemotherapy and it may also contribute to preoperative evaluation of known lesions. With increasing use of MRI, number of breast lesions visible only on MRI and need for MRI-guided breast biopsy have increased (1). Second-look US can also be used for re-evaluation of these lesions; because US-guided biopsy is an easier, cheaper, and faster method if these lesions are visible on second-look US. According to a recently published meta-analysis, lesion detection rates with second-look US are variable in the literature (22.6%-82.1%). Mass lesions and malignant lesions were more likely to be detected at second-look US; average detection rates were 66% for masses, 29% for non-mass-like enhancement (NME) (2, 3). However, focal or NME lesions, which are less detectable than masses on second-look US, require MRI-guided biopsy in the majority of cases. According to the MRI-guided biopsy series in the literature, approximately 25%–35% of these lesions are diagnosed as malignant (4-9).

Within this context, the aim of the present study is to assess the effectiveness of MRI-guided 10 Gauge (G) vacuum-assisted breast biopsies (VABB) performed at our institution and to examine the relationship between lesion characteristics and histopathologic results.

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Methods

Patients

Institutional ethics committee approval and informed consent of the participants were obtained. Radiologic records of 121 lesions of 117 women, who had been referred for MRI-guided 10 G VABB for their MRI positive and second-look US negative lesions between 2013 and 2016, were retrospectively evaluated. Five lesions could not be seen on preparation sequences of MRI biopsy session, so these cases were excluded from the study. Finally, 116 lesions of remaining 112 patients constituted the study group. Average age of the patients was 51±12 years (32–68 years).

Patients in this cohort were evaluated with breast MRI due to the following indications: Preoperative staging of newly diagnosed breast cancer (47%), screening for high-risk women (37%), problem solving modality (14%), and suspicion of recurrence in the follow-up of breast conservation surgery (2%).

MRI acquisition parameters

Breast MRI examinations were carried out in a 1.5 T MRI unit (Achieva, Philips) with a 7-channel dedicated breast imaging coil on prone position. MRI protocol was as follows: T1-weighted axial spin echo sequence (TR/ TE, 454/10 ms; FOV, 300; matrix, 432; slice thickness, 3 mm); axial diffusion-weighted echo-planar imaging (DW-EPI) along the x, y, z axes (TR/TE, 7329/71 ms; slice thickness, 3 mm; b values of 50 and 800 s/mm²); and T2-weighted short tau inversion recovery (STIR: TR/TE, 2000/173 ms; FOV, 300; matrix, 432; slice thickness, 2 mm). For dynamic contrast enhancement evaluation, axial three-dimensional (3D) T1-weighted gradient echo seguence (THRIVE: TR/TE, 7/3.4 ms; matrix, 352; FOV, 340; flip angle, 10°; slice thickness, 1 mm) was used before and repeated 6 times after contrast administra-

Main points

- MRI-guided vacuum-assisted breast biopsy is a reliable method for diagnosis of MRI-only lesions with 11% false-negative rate.
- MRI follow-up is necessary for benign lesions even when radio-pathologic concordance is present.
- Segmental, clustered, and clustered ring nonmass-like enhancement patterns are closely related with malignancy.

tion. Following gadolinium contrast agents were used: gadoterate dimeglumine (Dotarem[®], Guerbet) for 57 cases, gadobutrol (Gadovist[®], Bayer Healthcare) for 31 cases and gadodiamide (Omniscan[®], GE Healthcare) for 28 cases. Contrast agents were infused with an automatic injector system (Medrad Spectris Solaris, Bayer Radiology Solutions) at a rate of 2 mL/s, then the lines were flushed with 10 mL of saline.

MRI-guided biopsy

All interventions were performed by the same staff radiologist who had 12 years of experience on breast imaging. All procedures were conducted with the same MRI equipment described above. Dedicated breast coil and grid-localization system was used for obtaining samples on prone position. Breast was compressed at mediolateral direction with a perforated compression plate. Breast skin was marked with a vitamin E capsule according to the possible lesion site. Without using a localization software, the lesion was detected and localized with the contrast-enhanced sagittal 3D T1-weighted gradient echo seguence (THRIVE: TR/TE, 7/3.4 ms; matrix, 352; FOV, 340; flip angle, 10°; slice thickness, 1 mm). Best fitting entry hole was determined and the lesion depth was calculated. After local anesthetic infiltration, introducer needle with an inner stylet was placed. Then an obturator was placed instead of the stylet and a verification image set was obtained. Finally, MRI compatible 10 G vacuum needle (Encor, Bard Biopsy Systems) was inserted instead of the obturator and VABB was performed. At least 6 and maximum 18 cores were obtained. MRI compatible markers (Senomark UltraCor, Bard Biopsy Systems) were deployed to biopsy sites. Marker localization was verified with a single mammogram. Histopathologic results were followed up by the performing radiologist and the radio-pathologic concordance was assessed. Most of the cases were also evaluated for radio-pathologic concordance at multidisciplinary meetings of our institution. Concordant benign lesions were re-evaluated 6 months after biopsy and then they were followed up annually.

Data collection

Age, menopause status, risk factors, and clinical findings of all MRI-guided breast biopsy cases in the last 3 years were retrospectively recorded. Breast MRI indications were noted. Breast MRI examinations were re-evaluated. Two experienced radiologists, with 12 years (F.T.) and 3 years (A.U.) of experience in breast imaging, re-evaluated the imaging findings of breast biopsy cases in consensus. The lesions detected with MRI were classified according to the BI-RADS MR lexicon (10). Lesions were classified as mass, NME, or focus. The widest single diameter of the lesions was noted. Visibility and dimensional or structural alterations of the lesions after biopsy procedures were recorded.

All biopsy and surgical excision results, as well as breast conservation surgery or mastectomy results were recorded. Cases with radio-pathologic discordance and those with high-risk benign lesions were noted in particular. Follow-up imaging findings of benign lesions were evaluated.

Statistical analysis

Chi-square test was used to compare lesion characteristics and histopathologic results. For NME lesion distribution, findings were aggregated and compared as focal, linear, and segmental NME vs. other three patterns. SPSS version 15.0 (IBM Corp.) was used. P < 0.05 was set as the limit of statistical significance.

Results

Median lesion size was 16 mm (range, 4–81 mm). No major complications occurred during or after biopsy. Localized minor hematomas (size range, 1–4 cm) were seen in 7 patients.

Nine of 116 lesions (8%) were masses, 28 (24%) were foci and the remaining 79 (68%) were NME lesions. Of mass lesions, 3 were malignant and 6 were benign. Of 28 foci, 6 were malignant and 22 were benign. Thirty-two NME lesions were malignant and the remaining 47 were benign. Distribution of MRI findings according to histopathologic diagnosis is summarized in Table 1. Of three malignant masses, one was wellcircumscribed and two were ill-defined. Morphologic features of mass lesions are summarized in Table 2. Distribution of 79 NME lesions was as following: 21 focal, 17 segmental, 17 regional, 14 linear, 9 multiple, 1 diffuse. Contrast enhancement pattern of NME lesions was homogeneous (n=18), heterogeneous (n=28), clustered (n=24), and clustered-ring type (n=9). Lesion distribution characteristics and histopathologic results of NME lesions are summarized in Table 3.

Overall, 75 of 116 lesions were benign (65%) and 41 were malignant (35%). Of malignant lesions, 26 were invasive cancer

Table 1. Distribution of MRI findings according to histopathologic results						
	Histopathologic diagnosis					
MRI finding	Benign	High risk	DCIS	Invasive cancer	Total	
Mass	5 (56)	1 (11)	0 (0)	3 (33)	9	
Focus	20 (72)	2 (7)	4 (14)	2 (7)	28	
NME	36 (46)	11 (14)	11 (14)	21 (26)	79	
Total	61 (53)	14 (12)	15 (13)	26 (22)	116	
Data are presented as n (%).						

DCIS, ductal carcinoma in situ; NME, non-mass-like enhancement.

 Table 2. Distribution of morphologic characteristics of masses according to histopathologic diagnosis

	Histopathol	ogic diagnosis	
Mass lesions (n=9)	Benign	Malignant	Total
Shape			
Round	2	1	3
Oval-lobulated	4	0	4
Irregular	0	2	2
Margin			
Circumscribed	5	1	6
Not circumscribed	1	2	3

Table 3. Morphologic characteristics of NME according to histopathologic results

	Benign		Malignant		
NME morphology (n=79)	Benign	High risk	DCIS	Invasive cancer	Total
Distribution					
Focal	11 (52)	3 (14)	1 (5)	6 (29)	21
Linear	7 (50)	3 (21.5)	1 (7)	3 (21.5)	14
Segmental	0 (0)	1 (6)	5 (29)	11 (65)	17
Regional	10 (59)	3 (17.5)	4 (23.5)	0 (0)	17
Multiple	7 (78)	1 (11)	1 (11)	0 (0)	9
Diffuse	1(100)	0 (0)	0 (0)	0 (0)	1
NME type					
Homogeneous	16 (89)	0 (0)	0 (0)	2 (11)	18
Heterogeneous	16 (57)	6 (21)	1 (4)	5 (18)	28
Clustered	4 (16.5)	4 (16.5)	6 (25)	10 (42)	24
Clustered ring	1 (11)	0 (0)	5 (56)	3 (33)	9
Data are presented as n (%).					

DCIS, ductal carcinoma in situ; NME, non-mass-like enhancement.

(20 invasive ductal and 6 invasive lobular cancers) and 15 were ductal carcinoma in situ (DCIS). Fourteen (19%) of the 55 benign lesions were high risk (5 atypical ductal hyperplasia [ADH], 6 papillary lesions, 2 lobular neoplasia, and 1 flat epithelial atypia). These high-risk lesions had undergone

surgical excision after wire localization of markers with mammography.

Two of 6 DCIS lesions were upgraded to invasive ductal cancer after surgical excision. In addition, 14 high-risk lesions were evaluated with surgical excision after wire localization. Two of 5 ADH lesions and 1 of 6 papillary lesions were upgraded to DCIS. One of the ADH lesions that upgraded to DCIS showed linear clustered enhancement (Fig. 1), the other lesion was 2.5 cm in diameter and showed clustered ring enhancement. The papillary lesion with atypia that upgraded to DCIS had a linear clustered NME pattern. The final diagnosis did not change in one case of flat epithelial atypia, in 2 cases of NME LCIS, 2 cases of masses and 3 NME lesions diagnosed as papillary lesion and 3 cases of NME lesions diagnosed as ADH after surgical excision. Underestimation rate of MRI-guided VABB for high-risk patients was 21.4% (3/14). Underestimation rate for ADH was 40% (2/5), and for papillary lesions was 17% (1/6). One focal NME lesion with a biopsy diagnosis of fibrosis underwent wire localized surgical excision due to radio-pathologic discordance, and had a final diagnosis of invasive ductal cancer (Fig. 2). Three lesions with a concordant benign diagnosis were excised during simultaneous cancer surgery and the diagnosis did not change. Histopathologic results of high-risk benign lesions after surgical excision are summarized in Table 4.

Average follow-up period was 17±10 months (range, 7-37 months). Three cases left follow-up. Remaining 54 concordant benign cases had short-term (6-month) MRI follow-up. One of these cases was directed to surgical excision after 7 months because of shape alteration (development of spicules) on MRI. This lesion was detected as a 4 mm focus in previous examination and diagnosed as fibrocystic changes at VABB. After surgical excision, the final diagnosis was invasive ductal cancer. Including this case, the total number of false-negative cases were 5 and false-negative rate of 10 G VABB was 11%. Size and morphologic features of false-negative lesions are summarized in Table 5.

No suspicious alterations occurred in the remaining 53 lesions. Histopathologic diagnosis of concordant benign lesions were as follows: fibrocystic changes (27/53), fibrosis (10/53), inflammation (5/53), fibroadenoma (4/53), normal breast tissue (3/53), other benign lesions (4/53).

Segmental distribution (P < 0.001) and clustered enhancement pattern (P < 0.001) had a statistically significant association with malignancy among NME lesions. Malignancy was detected in 94% of segmentally distributed lesions, 89% of clustered ring enhanced lesions and 67% of clustered enhanced lesions. There was no statistically significant relationship between focal pat-

Table 4. Surgical excision results of high-risk lesions

	Surgical excision		
MRI-guided VABB (n=14)	No upgrade	Upgrade to DCIS	Upgrade to invasive cancer
ADH (n=5)	3	2	0
Papillary lesion (n=6)	5	1	0
LCIS (n=2)	2	0	0
Flat epithelial atypia (n=1)	1	0	0
Total	11	3	0

VABB, vacuum-assisted breast biopsy; DCIS, ductal carcinoma in situ; ADH, atypical ductal ectasia; LCIS, lobular carcinoma in situ.

 Table 5. Morphologic characteristics and histopathologic results of false-negative lesions

			Surgical excision	
False-negative lesions (n=5)	Lesion type	Size (mm)	DCIS	Invasive cancer
ADH (n=2)	NME: linear clustered (n=1)	21	1	0
	NME: clustered ring (n=1)	25	1	0
Papillary lesion with atypia (n=1)	NME: linear clustered	18	1	0
Fibrosisª (n=1)	NME: focal heterogeneous	14	0	1
Fibrocystic changes ^b (n=1)	Focus	4	0	1

DCIS, ductal carcinoma in situ; ADH, atypical ductal ectasia; NME, non-mass-like enhancement. ^aLesion was surgically excised due to radio-pathologic discordance.

^bLesion was surgically excised due to shape alteration during follow-up.



Figure 1. a, b. A 47-year-old high-risk woman with clustered linear non-mass-like enhancement on her left breast. Axial MRI images show the lesion (**a**) and the postbiopsy changes (**b**). MRI-guided biopsy result was atypical ductal hyperplasia, but the diagnosis upgraded to ductal carcinoma in situ after surgical excision.

tern or size of the lesions and malignancy. The relationship between MRI characteristics of mass lesions and histopathologic results could not be evaluated statistically because of the small number of lesions.

Discussion

In this study, 65% of the lesions had a benign diagnosis with MRI-guided biopsy.

Approximately 75% of the MRI-guided biopsies result with a benign diagnosis in the literature (4–9). The main difference of this study was distribution of lesion types. The rate of mass lesions was lower compared with the literature (4, 8, 9, 11). In our daily practice, all cases directed to breast MRI are evaluated with mammography and US in detail and second-look US is successfully

used to detect masses. Low number of mass lesions in our study can be explained within this context.

In this study, foci constituted 24% of all lesions. Cancer detection rate of foci are variable (0.6%-30.7%) in the literature (12-16). In this study, 21% of the foci were malignant. The variability in the reported rates may be due to lesion characteristics and/or differences between focus determination criteria. Interval change and hypointensity on T2-weighted sequence are reported as the most important predictors of malignancy in the evaluation of foci, and these parameters are used as the selection criteria for biopsy (12, 14, 16). Management of foci still remains as a challenge, because of absence of clearly established guidelines (16). Current opinion suggests that follow-up is a reliable option for incidentally detected T2-weighted bright lesions, if simultaneous cancer and high-risk family history is absent (14, 16).

NME is a widely encountered lesion in breast MRI done for any indication, and possesses a challenge for the interpreting radiologist. Most of these lesions cannot be seen on mammograms or US in daily practice. Mass lesions have the highest cancer detection rates with MRI-guided VABB in the literature. In our study, 68% of the VABB lesions were NME and the highest cancer detection rate was recorded in this group (40%). Rauch et al. (17) also reported that 34% of their NME lesions were malignant. They concluded that the discrepancy between the studies was probably related with the different success rates of second-look US for mass detection. Segmentally and regionally distributed, clustered enhanced, or clustered ring enhanced lesions were found to have significantly higher cancer detection rates among NME lesions. Another recent study about NME reported highest cancer detection rates in clustered ring enhanced, branching ductal pattern, and clustered NME lesions (18). Considering these patterns is recommended for biopsy decision making and evaluating radio-pathologic concordance. Radiologic follow-up and assessing the radio-pathologic concordance is particularly important for those NME lesions with larger dimensions and in case of lesion continuity out of the biopsy site (19). In daily clinical practice, we carefully evaluate the histopathologic concordance of the lesions with larger dimensions than the biopsy site. This situation is similar to the residual microcalcifications present after mammography-guided biopsy. Such



Figure 2. a, **b**. A 56-year-old woman with a diagnosis of breast cancer on her right breast. Another suspicious lesion detected on her left breast during preoperative staging. Sagittal contrast-enhanced MRI (**a**) obtained before biopsy shows focal non-mass-like enhancement. The lesion disappeared on axial MRI (**b**) after biopsy. Histopathologic diagnosis was fibrosis. Surgical excision was performed due to radio-pathologic discordance and the final diagnosis was invasive ductal carcinoma.

lesions with a high-risk benign or discordant benign diagnosis create difficulty for the radiologist to decide the next step. According to our experience, a multidisciplinary approach concerning the clinical risks of these cases should be provided.

In this study, high-risk benign lesions were 19% of all lesions, concordant with the relevant literature (4%-21.5%) (19-25). Underestimation rate for high-risk benign lesions in this study was 21.4% (3/14), which was also similar with recent studies (19-25). Heller et al. (21) reported that upgrade rates of high-risk lesions were significantly higher in cases with a history of malignant lesion in the same breast, recently diagnosed cancer, or history of high-risk lesion. No statistically significant relationship between lesion type or size and the underestimation rates was found in the literature (11, 19–25). Surgical excision is mandatory for high-risk lesions found at MRI-guided VABB, similar to other imaging-guided biopsy procedures.

Complications from MRI-guided VABB may include bleeding or pain during the procedure, postbiopsy pain, bleeding, and hematomas (4, 5). In this study, immediate postbiopsy hematoma (1–4 cm) was observed in 7 out of 112 patients and was managed conservatively. Technical success of the MRI-guided biopsy cannot always be assessed during the procedure, because of inherent limitations of the technique. Several tissue changes such as edema or

hemorrhage at biopsy site may impair visibility of the lesions during or after biopsy. To cope with these shortcomings, markers should be placed after procedures and benign lesions should be followed up with MRI (4–9, 19, 26). With short-term follow-up, success of procedure can be verified and lesion alterations can be assessed.

MRI-guided VABB is a reliable diagnostic tool with a 11% false-negative rate. False-negative rate of the technique varies between 0%-17% in the literature (4-9, 25). Cases with specific benign diagnosis, radio-pathologic concordance, and no clinical suspicion of malignancy can easily be followed up (18, 25-27). Cancer detection rate within short-term follow-up after MRI-guided VABB is extremely low in the literature and several authors recommend annual follow-up instead of short-term follow-up (27). In this study, only one case of invasive ductal cancer was detected with surgical excision because of morphologic alteration on follow-up MRI. According to our experience, follow-up should be recommended for cases with a specific benign diagnosis even if there is no radio-pathologic discordance or clinical suspicion.

The main limitation of this study is that our findings come from a single center. Therefore, the present results need to be confirmed with further multicenter studies.

In conclusion, MRI-guided VABB is a safe and successful procedure for the evaluation of MRI-only breast lesions. Radio-pathologic concordance is critically important, because of technical limitations and relatively higher underestimation rates. According to our experience, annual follow-up may be recommended for cases with a specific benign diagnosis if there is no radio-pathologic discordance or clinical suspicion.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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