Original Article

Eur J Breast Health 2021; 17(1): 1-9
DOI: 10.5152/ejbh.2020.5663

Second Look Ultrasonography-Guided Breast Biopsy with Magnetic Resonance Imaging Confirmation by Intralesional Contrast Injection

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ABSTRACT

Objective: This study aimed to introduce an alternative pre-biopsy confirmation technique that combines sonography-guided intra-lesional contrast injections and single non-enhanced magnetic resonance imaging (MRI) pulse sequence in order to identify sonographic correlates of incidentally detected breast MRI lesions which were occult on primary ultrasonography (USG) and mammography examination.

Materials and Methods: From May 2014 through May 2015, a total of 37 incidental breast lesions of 37 patients, which were detected by breast MRI, were evaluated with targeted second look ultrasound (SLUS). The suspected lesion on USG was marked with a gadolinium-based contrast agent under USG guidance. After a single non-enhanced T1 weighted control MR sequence, positively correlated lesions with initial MRI were sampled by USG guided core biopsy.

Results: Of the 37 lesions evaluated, 32 (86%) lesions showed a correlation between MRI and SLUS findings. On SLUS core biopsy, there were eight (25%) malignant and 11 (34.4%) high-risk lesions among these 32 cases with correlated MRI findings; while the remaining 13 (40.6%) cases had benign histopathology. Eleven (34.4%) of the SLUS-discovered lesions were focus, 11 (34.4%) were non-mass enhancements, and the remaining 10 (31.2%) were mass lesions. Of the five lesions (13.5%) that showed no correlations on MRI and SLUS examinations, four were non-mass enhancements and one was focus.

Conclusion: SLUS represents a method for identifying MRI-detected lesions and provides a bridge to ultrasound-guided biopsy for histopathological diagnosis. There is a need for confirmation of biopsies to avoid false negative results. We describe a cheap, safe, and easy-to-apply USG-guided pre-biopsy lesions marking method in order to ensure definite correlation.

Keywords: Breast cancer, image-guided biopsy, magnetic resonance, ultrasonography

Cite this article as: Kayadibi Y, Kılıç F, Yılmaz R, Velidedeoğlu M, Öztürk T, Tekcan DE, Üre Esmerer E, Aydoğan F, Yılmaz MH. Second Look Ultrasonography-Guided Breast Biopsy with Magnetic Resonance Imaging Confirmation by Intralesional Contrast Injection. Eur J Breast Health 2021; 17(1): 1-9.

Introduction

Mammography and ultrasound represent the conventional imaging modalities. Magnetic resonance imaging (MRI) is an indispensable tool for the detection of breast cancer, given that there is a group of patients in whom cancer can only be detected by breast MRI (1). Although MRI exhibits high sensitivity, false positive findings may be interpreted due to its relatively limited specificity (2-4). Breast MRI is capable of revealing previously undetected lesions on mammography or ultrasound in 6%–34% of cases (5). Suspected abnormalities should be sampled through histopathology if indicated by findings on Breast Imaging-Reporting and Data System (BI-RADS). DeMartini and Lehman (6) reported that MRI-findings prompted that a 3%–16% increase in the number of biopsies was indicated by MRI findings. Lesions which are solely detected on MRI should be sampled primarily using MRI guidance, although the technique is relatively costly, difficult, stressful, and does not allow real-time monitoring of lesions. Furthermore, MRI-guided intervention is not widely accessible (7, 8).

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Received: 09.04.2020
Accepted: 07.06.2020

Physicians and patients favor ultrasound-guided biopsies because this modality is time-effective, cost-effective, and more comfortable for patients. Generally, whenever available, ultrasound-guided biopsies are preferred to MRI-guided biopsies. Incidental MRI-detected lesions require a second-look examination to conduct a "real-time" ultrasound-guided biopsy. The purpose of the second-look ultrasound (SLUS) is to confirm the findings of recent MRI examinations by identifying and characterizing MRI-detected lesions and bridge to ultrasound-guided biopsy for histopathological diagnosis.

However, translating information obtained on MRI to ultrasound is challenging, given the differences in position of the breast (supine vs prone) during examinations as well as the difficulty of distinguishing isoechoic, small, and lesions with indistinct margins from normal breast tissue on ultrasonography (USG) (9). Hence, routinely performed second look sonography guided breast biopsy does not always yield true positive results. Confirming the accuracy of the correlation between MRI lesion and targeted SLUS-guided biopsy should be performed. In this prospective study, we introduced a pre-biopsy confirmation technique that uses sonography-guided intra-lesional contrast injection, followed by a single non-enhanced T1 weighted MR pulse sequence in order to localize the sonographic correlate of incidentally detected breast MRI lesions which were occult on primary USG examination.

Materials and Methods

Patient selection

This prospective study was performed at the Medical Faculty of İstanbul University, Cerrahpaşa between May 2014 and December 2015. The study was approved by the internal review board and designed in accordance to the Declaration of Helsinki. We included 37 patients (over 18 years of age) with 37 single lesions, on which breast MRI was performed at our Breast Imaging Division of Radiology Department and incidental MRI findings at other clinics. Outpatients were referred to our department due to the need for detailed breast imaging and sequential MRI-guided vacuum-assisted breast biopsies.

Recent USG and mammography data and images were collected. The patients had no primary pathological findings on mammography, USG, or clinical examination that were relevant to the new findings on breast MRI. MRI and current SLUS findings were characterized according to BI-RADS of the American College of Radiology. Mass lesions less than 1 cm and non-mass enhancements of any size and foci, which were described as BIRADS 4 or 5 in the previous MR examination or SLUS, were included in the study. Lesions with a mass appearance larger than 1 cm were excluded from the study. Decisions for biopsy were made by a consensus of two breast radiologists (F.K. and R.Y.).

Lesions classified as BI-RADS 2 or 3 were subjected to a follow-up course instead of intervention. Cases with false positive initial MRI findings, benign MRI lesions, appropriately correlated cases by initial USG, and negative SLUS findings were excluded, since they include patients who declined to undergo the SLUS biopsy procedure. Furthermore, we excluded patients with obvious mass lesions >1 cm in size, which could easily be evaluated by primary USG.

Key Points

- MR-guided biopsy is used for sampling suspicious MRI-detected breast lesions.
- SLUS is used for localization of incidental MRI-detected lesions.
- Inconsistency between SLUS and MRI findings has been reported.
- We introduce an alternative USG-guided pre-biopsy confirmation technique.

Second-look ultrasonography evaluation

There was a maximum interval of 1 month between previous MRI examination and SLUS (7-30 days). Suspicious MRI findings were re-evaluated primarily in three-dimensional (3D) multiplanar views by two radiologists with ten years (F.K.) and nine years (R.Y.) experience on breast radiology using a commercially available computer-aided detection (CAD) system (Dynacad; *In vivo*, Birmingham, MI, USA). Images were evaluated by a routine breast imaging protocol using axial pre-contrast T1-weighted images, axial T2-weighted short tau inversion recovery or fluid attenuation inversion recovery images, axial pre- and post- contrast enhanced T1-weighted 3-D gradient echo sequences, subtracted images, and sagitta-l T1-weighted fat-saturated post-contrast gradient echo images. MRI findings were analyzed conjointly with the mammography and breast ultrasound results. These two latter modalities are typically performed prior to MRI at our institution. Lesion characteristics were determined carefully, particularly for SLUS localization, since the patients were referred for biopsy.

Special attention was paid to the evaluation of lesions detected incidentally on MRI. The localization of lesions on USG was the most important consideration. Hence, all data available on MRI were assessed. We were flexible with respect to define the exact locality of the lesions. Primarily, the clockwise position was decided by the help of coronal imaging plane supported by the CAD system software. Measurements were taken as follows: lesion to nipple, skin, chest wall, horizontal/vertical nipple line, known/prominent adjacent lesions, and intramammary lymph nodes. Anatomic landmarks and reference points were assessed; information on adjacent lesions (cysts and solid lesions), subglandular/subcutaneous fat, parenchyma shape, and distance of landmarks to target lesion was also obtained to facilitate tissue sampling under USG guidance. Data on shape and size of the MRI lesions was done, but no benefits to localization were derived from analysis of the signal or kinetic characteristics of the index lesion.

SLUS and consequent interventions were performed by one of the two radiologists (F.K.) with ten years of breast imaging experience at our breast imaging division. Ultrasound examination was performed while the patients were lying in a supine position, with both hands raised above the head. Particularly for larger breasts, the position of the patient was adjusted by pillow support (if necessary) to ensure that the nipple was positioned to the vertical midline. During the examination, a 4–15 MHz linear transducer (Super-Sonic Imagine, Aix-en-Provence, France) and a 4–11 MHz linear transducer (Antares, Siemens Medical Systems, Malvern, Pa., USA) were used. The localization and biopsy procedure were followed-up if lesion size, shape, and localization on SLUS were in agreement with previous MRI findings.

SLUS localization and MRI examination

A localization procedure was followed such that SLUS- and MRI-detected lesions were in agreement prior to tissue sampling. The suspected lesion on USG was marked with a gadolinium-based

contrast agent under ultrasonographic guidance by one of the two radiologists (FK). The agent was diluted to 0.5% by mixing 0.1 cc gadopentetate dimeglumine (Magnevist®, Bayer Schering Pharma, Germany) with 20 cc saline. Approximately 0.1 cc diluted contrast agent was applied percutaneous into the target lesion using a 21-G needle. The location of the target lesion was also marked over the skin using a surgical marker pen to alleviate the recurring search for lesion to biopsy after MRI examination.

In a maximum of 30 minutes after applying the contrast medium into the lesion, the patient underwent an additional MRI examination to verify the concordance between the initial lesions detected on previous MRI and suspected lesions on SLUS. Initial known MRI lesion localization and injected contrast enhancement area should be the same before it is considered as concordance. The MRI examination included a T1-weighted fast low-angle shot (FLASH) pulse sequence with 3D fat-selective inversion (TR/TE=11/5.16 ms; thickness=1.5 mm; gap=0, field of view=330, matrix=320×320, flip angle=00; frequency direction: R > L). The axial sequence was performed using one of the two 1.5 Tesla scanners (Avanto, Siemens Healthcare, Malvern, PA, USA and Achieva, Philips Healthcare, Best, Netherlands) with dedicated breast array coil with seven channels. Fat saturation was preferred such that the injected contrast agent was more visible. The examination lasted for 2 to 5 minutes. Two different pre- and post- localization MRI images (Figure 1) were compared in dual screens. In the case of positive correlation (22/25 cases), SLUS-guided biopsy was performed using a 14-G biopsy needle (Max-Core®, BardBiopsy Systems, Tempe, AZ, USA) immediately. A minimum of four samples (range=4–8 samples) were obtained. A routine histopathological evaluation was performed. After the pathological evaluation, the lesions were evaluated in terms of pathological - radiological correlation. Patients with malignant pathology were referred to the surgical procedure, while those with benign pathology were followed by radiological follow-up of a total of 3 years at 6-month intervals. During this period, no malignancy occurred in the benign group.

Statistical analysis

Descriptive statistics was performed. The frequency of correlation status was determined and correlations between MRI and SLUS characteristics were compared.

Results

The patients' ages, MRI indications, lesion characteristics on MRI and SLUS, correlation status, and histopathological results are summarized in Table 1. Mean age of the patients was 44.94 years (range=18–65 years). MRI indications were as follows: inconclusive USG/mammography findings 12 (32%); breast cancer staging/surgical planning was 13 (35%); screening for high-risk cases was six (16%); bloody nipple discharge with negative sonographic findings was 1 (2%); and information not available was 5 (13%).

A total of 32 (86%) out of the 37 lesions (among the 37 patients) exhibited a correlation between MRI and SLUS findings. On SLUS core biopsy, there were eight (25%) malignant (Figure 2) and 11 (34.4%) high-risk lesions among the 32 cases with correlated MRI findings, while the remaining 13 (40.6%) cases had benign histopathology (Figure 3). Eleven (34.3%) of the SLUS-discovered lesions were foci, 11 (34.3%) were non-mass enhancements, and the remaining 10 (31.2%) were mass lesions.

As expected, the mean lesion size differed between MRI and SLUS [8.13 mm (range=3–30 mm) vs 7.5 mm (range=3–20 mm), respectively]. This difference in lesion size according to imaging modality was mainly due to differences in size of the non-mass enhanced lesions. Of the 5 lesions (13%) that showed no correlation for sizes on MRI and SLUS examinations, four were non-mass enhancements and one was focus (size on MRI=5, 8, 8, 15, and 30 mm) (Figure 4). No mass lesions were discovered on SLUS evaluation. Therefore, MRI contrast agents were applied to the suggested pathologic area due to MRI measurements and morphological findings, as well as architectural distortions and inhomogeneous parenchyma. The distance error between the contrast marker and lesions was 1 cm in multiplanar reconstructions. In one

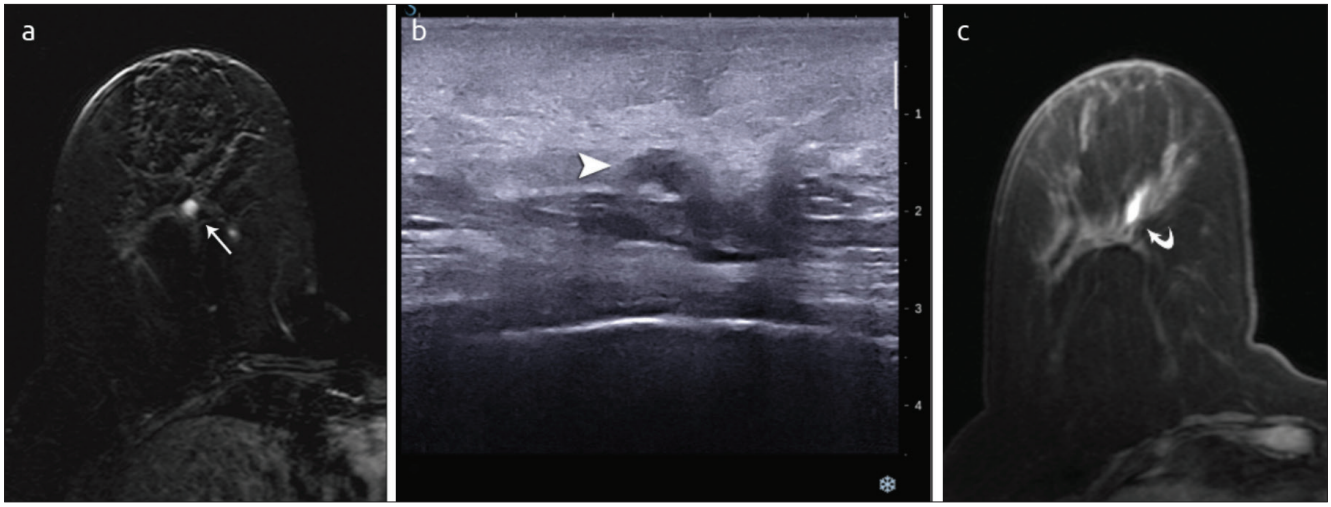

Figure 1. a-c. A 54-year-old woman who underwent breast MRI for inconclusive findings of USG and mammography. **(a)** Axial contrast enhanced and subtracted T1 weighted MRI shows an unexpected round shaped micro lobulated lesion (white arrow) with washout contrast enhancement kinetics (Type III, not shown). **(b)** Targeted second look ultrasonography shows micro lobulated margins and hypoechoic echotexture of the lesion (arrowhead). No posterior acoustic shadowing was observed. Final assessment of the lesion was BI-RADS category 4. **(c)** T1 weighted fat saturated MRI after contrast marking of the lesion confirms the localization (curved arrow). Subsequently, ultrasound-guided core needle biopsy was performed and pathology result was complex sclerosing lesion

MRI: Magnetic resonance imaging; USG: Ultrasonography, BI-RADS: Breast Imaging Reporting and Database System

Table 1. MRI indications, patients' ages, lesion characteristics on MRI and SLUS, correlation status, and histopathological results of patients

	MRI characteristics					SLUS characteristics			
					Enhancement			Correlation	
No	**MRI indication**	**Age**	**Morphology**	**Size (mm)**	**Curve type**	**Morphology**	**Size (mm)**	**Status**	**Pathology**
1	Contralateral malignancy	42	Well-defined margins, mass	8	3	Well defined margins, hypoechoic	7	Positive	Fibroadenoma
2	NA	40	Focus with distortion	4	3	Spiculated margins, hypoechoic	4	Positive	Complex sclerosing lesion
3	Inconclusive findings	45	Non-mass enhancement	6	1	Lobulated margins, hypoechoic	5	Positive	Intraductal papilloma
4	NA	43	Non-mass enhancement	15	2	Heterogeneous hypoechoic	20	Negative	Excision; Low grade proliferation with atypia
5	NA	51	Non-mass enhancement	14	2	Dilated duct with nodularity	10	Positive	Low grade proliferation without atypia
6	Bloody nipple discharge	45	Focus	4	3	Well defined margins, hyperechoic	5	Positive	Fibrosis - adenosis
7	Contralateral malignancy	49	Focus	4	2	Lobulated margins, hypoechoic	5	Positive	Sclerosing lesion
8	Inconclusive findings	49	Mass with spiculated margins	5	2	Spiculated margins, hypoechoic	5	Positive	Fat necrosis and lipogranuloma formation
9	Contralateral malignancy	51	Non-mass enhancement	8	2	Indistinct margins, hyperechoic	6	Positive	Fibrosis-adenosis
10	High risk	33	Non-mass segmental enhancement	30	2	Indistinct margins, heterogeneous	20	Positive	Sclerosing adenosis
11	Contralateral malignancy	32	Lobulated margins, mass	7	2	Lobulated margins, Heterogeneous	7	Positive	Fibroadenoma and atypical lobular hyperplasia
12	Contralateral malignancy	41	Lobulated margins, mass	7	2	Lobulated margins, isoechoic	7	Positive	Atypical intraductal papilloma and apocrine metaplasia
13	High risk	47	Non-mass enhancement	6	2	Hypoechoic nodule with distortion	6	Positive	Fat necrosis and lipogranuloma formation
14	Inconclusive findings	47	Non-mass enhancement	15	2	Heterogeneous hypoechoic	10	Negative	NA
15	Inconclusive findings	62	Focus	4	3	Indistinct margins, hypoechoic	4	Positive	Invasive ductal carcinoma
16	Ipsilateral malignancy	40	Lobulated margins, mass	10	2	Lobulated margins, hypoechoic	8	Positive	Intraductal papilloma

Table 1. Continued

	MRI characteristics					SLUS characteristics			
					Enhancement			Correlation	
No	**MRI indication**	**Age**	**Morphology**	**Size (mm)**	**Curve type**	**Morphology**	**Size (mm)**	**Status**	**Pathology**
17	Inconclusive findings	44	Non-mass enhancement	10	2	Dilated duct with nodularity	10	Positive	Hyperplasia with atypia
18	High risk	46	Indistinct margins, mass	6	3	Lobulated margins, hypoechoic	5	Positive	In-situ lobular carcinoma
19	Inconclusive findings	46	Indistinct margins, mass	8	2	Lobulated margins, isoechoic	8	Positive	invasive ductal and medullar carcinoma
20	Contralateral malignancy	50	Focus	4	3	Spiculated margins, hypoechoic	4	Positive	Complex sclerosing lesion
21	Inconclusive findings	54	Indistinct margins, mass	6	2	Lobulated margins, hypoechoic	5	Positive	Complex sclerosing lesion
22	Contralateral malignancy	32	Lobulated margins, mass	6	1	Lobulated margins, hypoechoic	5	Positive	Fibroadenoma
23	High risk	32	Non-mass enhancement	8	2	Micro lobulated margins, Hypoechoic	7	Negative	Excision planning
24	Inconclusive findings	65	Focus	4	2	Spiculated margins, hypoechoic	4	Positive	Invasive ductal carcinoma
25	Inconclusive Findings	42	Non-mass Enhancement	10	2	Indistinct margins, Hypoechoic	8	Positive	Invasive ductal carcinoma
26	Ipsilateral malignancy	44	Focus	3	2	Indistinct margins, hypoechoic	3	Positive	Invasive ductal carcinoma
27	High risk	52	Non-mass enhancement	17	1	Lobulated margins, Hypoechoic	16	Positive	Fibroadenoma
28	Contralateral malignancy	44	Focus	4	3	Indistinct margins, Hypoechoic	5	Positive	Invasive lobular carcinoma
29	Contralateral malignancy	49	Focus	6	1	Micro lobulated margins, hypoechoic	6	Positive	Hyperplasia with atypia
30	Ipsilateral malignancy	43	Non-mass enhancement	8	3	Indistinct margins, Hypoechoic	7	Positive	Fibrocystic change
31	Inconclusive findings	62	Lobulated margins, mass	6	2	Indistinct margins, Hypoechoic	7	Positive	Fibroadenoma
32	Contralateral malignancy	48	Non-mass enhancement	8	2	Micro lobulated margins, hypoechoic	9	Negative	Excision planning

Table 1. Continued

	MRI characteristics						SLUS characteristics		
					Enhancement			Correlation	
No	**MRI indication**	**Age**	**Morphology**	**Size (mm)**	**Curve type**	**Morphology**	**Size (mm)**	**Status**	**Pathology**
33	Inconclusive findings	42	Non-mass enhancement	13	2	Indistinct margins, Hypoechoic	12	Positive	Stromal fibrosis
34	High risk	47	Focus	4	2	Indistinct margins, Hypoechoic	5	Positive	In-situ ductal carcinoma
35	NA	49	Non-mass enhancement	12	1	Indistinct margins, Hypoechoic	14	Positive	Radial scar
36	NA	39	Focus	4	3	Micro lobulated margins, hypoechoic	5	Positive	Invasive ductal carcinoma
37	Inconclusive findings	18	Focus	4	2	Micro lobulated margins, hypoechoic	5	Negative	Follow-up

MRI: Magnetic resonance imaging; SLUS: Second-look ultrasound; NA: Not available

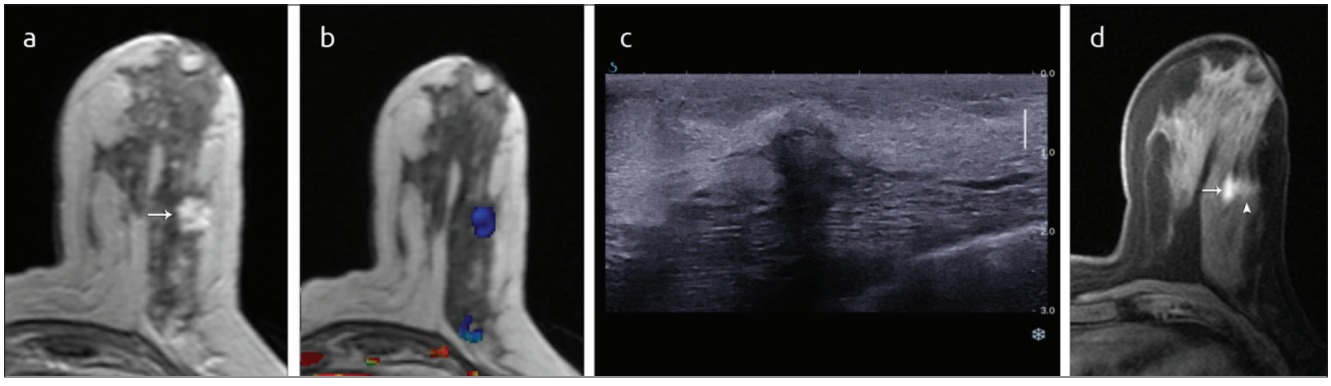

Figure 2. a-d. A 46-year-old woman with previous history of breast cancer underwent breast MRI for inconclusive findings of USG and mammography. **(a, b)** Axial contrast enhanced T1 weighted MRI shows a mass lesion with ill-defined contours (white arrow) and persistent contrast enhancement kinetics (Type I). **(c)** SLUS was performed due to suspicious margins of the lesion. Mass with slightly ill-defined contours and posterior shadowing (arrow) was seen on ultrasound in left breast. **(d)** T1 weighted fat saturated MRI after contrast marking of the lesion confirms the localization. Arrowhead indicates the needle tract with contrast and contrast accumulation is seen just posterior of the lesion (arrow). Histopathology results revealed mixt type, invasive ductal, and medullary carcinoma

MRI: Magnetic resonance imaging; USG: Ultrasonography; SLUS: Second-look ultrasound

case, we achieved signal void instead of contrast enhancement due to high concentration of contrast medium (Figure 5).

Discussion and Conclusion

This study, which presented an alternative marking/localization method to target incidental MRI lesions, was inspired by an initial study on radio-guided occult lesion localization (ROLL) under MRI guidance (10). The MRI ROLL technique also uses transdermal contrast injections for pre-operative localization and has been applied successfully at our clinic for 5 years. In our series, SLUS-guided contrast injections were successful in majority of the cases, as 32 of 37 (86%) lesions were biopsied correctly. In addition, negative correlations are also the success of the technique, considering the avoidance false negative biopsies.

SLUS aims to detect and confirm incidental MRI lesions. Several studies have investigated the utility and performance of SLUS, but they all used a retrospective design and revealed informal key points (11, 12). There are no strict guidelines for the management of SLUS-guided

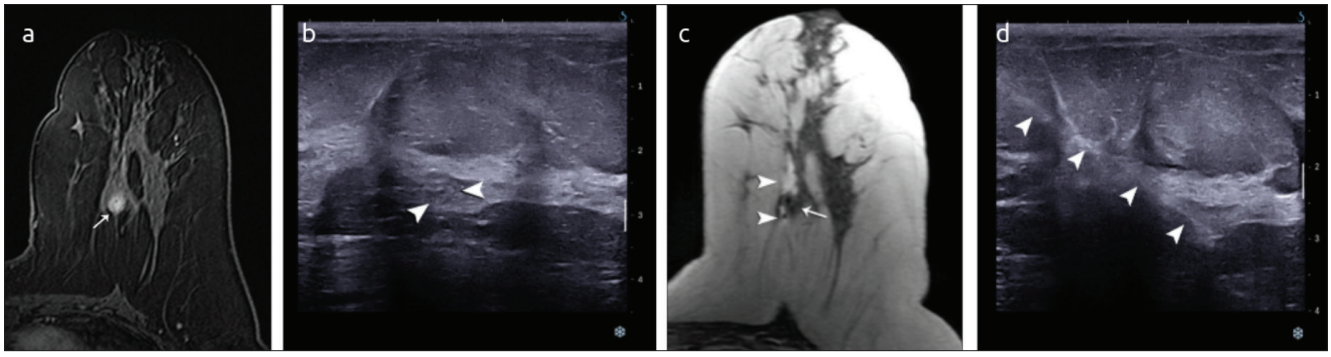

Figure 3. a-d. A 51-year-old woman underwent breast MRI for staging due to contralateral breast carcinoma. **(a)** Axial contrast enhanced and subtracted T1 weighted MRI shows a non-mass contrast enhancement with indistinct margins (arrow) and plateau enhancement kinetics (Type II, not shown). **(b)** SLUS was performed and a 6-mm hypo-isoechoic area was barely seen. **(c)** Subsequent contrast marking of the lesion was confirmed by axial T1 weighted MRI. The lesion (arrow) was covered by the contrast (arrowheads) anteriorly and posteriorly. **(d)** Biopsy needle (arrowheads) was shown to represent the correct sampling. The pathology result reported the benign nature of the lesion as fibrosis and adenosis

MRI: Magnetic resonance imaging; USG: Ultrasonography; SLUS: Second-look ultrasound

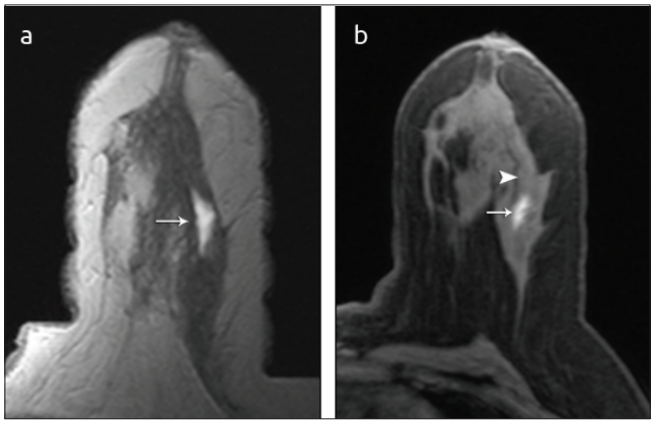

Figure 4. a, b. A 43-year-old woman underwent breast MRI (inaccessible indication). **(a)** Axial contrast enhanced T1 weighted MRI shows non-mass enhancement (arrow) with plateau curve (not shown). **(b)** The contrast marking (arrow) was not correlated to the suspected lesion localization (arrowhead). Excisional biopsy after MR guided radionuclide occult lesion localization revealed low-grade epithelial proliferation with atypia

MRI: Magnetic resonance imaging

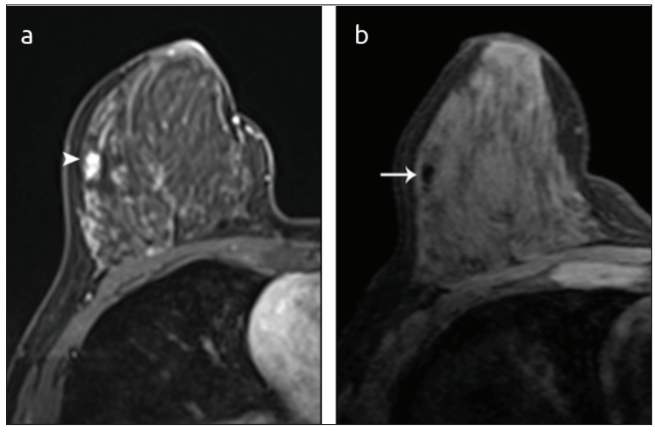

Figure 5. a, b. A 41-year-old woman who underwent breast MRI for staging due to contralateral breast carcinoma. **(a)** Axial contrast enhanced and subtracted T1 weighted MRI shows a 7 mm nodule with lobulated margins and plateau type (Type II) contrast enhancement (arrowhead). **(b)** Control axial T1 weighted MRI after marking reveals signal void just in the relevant lesion localization (arrow) due to high concentration of the contrast medium. Final histopathology result of the lesion was atypical intraductal papilloma with apocrine metaplasia

MRI: Magnetic resonance imaging

biopsy and follow-up. The reported detection rate of incidental MRI lesion on SLUS ranges from 22% to 100% due to the relatively low specificity of breast MRI (13-21). Inconsistency between SLUS and MRI findings has been reported in up to 12.5% of followed-up lesions with benign pathology (14). Similarly, in our study, there was a distance error of approximately 1 cm in 3 of the 37 total cases (8.1%). The other two had distance errors of 1.5 cm and 1.7 cm. Of these three cases, one was high-risk and the remaining two were unconfirmed. All three were non-mass enhancement areas with no visible prominent sonographic equivalent. It has been reported that non-mass lesions of 6–10 mm are 13% less likely to be discovered by sonography compared with mass lesions, while lesions >15 mm are 42% less likely to be detected (13, 22). In our study, there was a 100% positive correlation between SLUS and MRI for mass lesions <10 mm (mean=5.7 mm).

Magnetic navigation system was developed to determine the corresponding localization of the target lesion, similar to image co-registration method of SLUS with MRI. In the study by Nakano et al. (23), 90% of all lesions were detected using real-time virtual sonography and, in comparison, conventional B-mode imaging had a markedly lower detection rate of only 30%. There are also studies in literature that indicate higher detection rates of real-time virtual sonography (83.8%–100%) (21, 23). Notwithstanding, the methods used in these studies require sophisticated technical devices and experience. Although the relatively low number of patients and small size of the lesions should be mentioned, B-mode sonography had a high detection rate (88%) in our study. We suggest that the easy-to-apply SLUS marking method could decrease the requirement for navigation-based techniques.

Agreement between SLUS and MRI findings increases in accordance with the level of expertise of the operator and amount of time allowed for the interpretation of initial MRI and sonographic results (11). However, even for professional radiologists, potential

false-negative biopsies should not be followed-up due to high rates of underestimation (17). Consensus among experts, with respect to interpretation of breast radiology results, is not always reached. In addition, the correlation between radiological and pathological results for MRI-detected lesions is lower when compared with stereotaxis due to the lack of opportunity for specimen radiography. Therefore, confirmation of sampling process is highly important.

It is possible and reasonable to insert a clip into the biopsy site and then perform a T1-weighted sequence without fat saturation in order to assess the relationship between the position of the clip and the lesion on initial MRI (24). However, even if the radiologist plans this procedure prospectively, its success would be apparent only during the post-biopsy period. As an alternative, the use of pre-biopsy contrast-marking eliminates unnecessary core biopsies as well as the use of MR-compatible clips, which can increase stress in the patient, workload of the radiologist and pathologist, and overall cost of the procedure.

The cost of MR-guided vacuum biopsy far exceeds that of USG-guided non-vacuum core biopsy. Furthermore, MR-guided non-vacuum core biopsy is not safe for small lesions that cannot be detected reliably on SLUS evaluations. Unfortunately, MR-guided vacuum systems are considerably more expensive in terms of parts and operation; however, SLUS-guided breast biopsy with MRI confirmation could significantly lower the costs by increasing pre-biopsy confidence and circumventing the requirement for post-biopsy marking or MRI follow-up.

SLUS, which displays occult lesions that are not detected by primary sonography, is a time-consuming method. In our study, several evaluations took a similar amount of time with that of regular breast USG procedures because a significant amount of attention was paid to "tough" lesions. There were seven focus lesions, in which 10 of the 25 total lesions were non-mass. The median duration of SLUS was 7 min (range: 3–15 min). We found no previous studies or reviews that addressed the time expended on SLUS. The time taken for marking was approximately 12 min (range: 9–15 min), which was shorter when compared with that reported previously for the similar radio-guided occult lesion localization method (25). The MRI gantry time of the 242 axial T1-weighted scan was 2 to 5 minutes.

Other important parameters include the position and morphological changes in the breast on both primary and contrast injected control MRIs. No standardized protocol was followed pertaining to either amount of compression or nipple position, although both examinations were performed with patients in a prone position. The position of the lesion relative to the parenchyma, adjacent structures, and fat lobules was considered in comparison of the contrast marker and lesion enhancement. The location of lesions was agreed upon by at least two radiologists for all procedures.

This study had several limitations. First, we could not obtain pathology results for two non-correlated lesions due to difficulties with operation planning and loss of contact with the patient. Second, SLUS and marking methods were performed by a single experienced radiologist. Thus, the number of uncorrelated lesions might have been lower if there had been more than one assessor. Third, the number of included patients was low due to the initial results of study. In addition, we did not use a clip marker after the biopsies.

In conclusion, SLUS represents a useful method for identifying MRI-detected lesions on USG and provides a bridge to ultrasound-guided biopsy for histopathological diagnosis. In this study, we introduced an alternative pre-biopsy confirmation technique, which uses a combination of sonography-guided intra-lesional contrast injections and single non-enhanced MR pulse sequence to identify sonographic correlations with incidentally detected MRI lesions. Future studies involving larger numbers of patients are may be required to confirm the utility of this approach.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of İstanbul University-Cerrahpaşa (no: 41281, date: 10.02.2015).

Informed Consent: Written informed consent was obtained from the patients who participated in this study.

Peer-review: Externally peer-reviewed.

Authorship Contributions:

Concept: F.K.; Design: M.H.Y.; Supervision: F.A.; Resources: R.Y.; Materials: Y.K.; Data Collection and/or Processing: D.E.T.; Analysis and/or Interpretation: T.Ö.; Literature Search: E.Ü.E.; Writing Manuscript: Y.K., F.K.; Critical Review: M.V.

Conflict of Interest: We certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Financial Disclosure: The authors declared that this study received no financial support..

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