Chapter 11
Targeted Ultrasound After MRI

Chloe Chhor and Adrienne Newburg

Abstract A magnetic resonance imaging (MRI)-directed ultrasound (US), also known as second-look US or targeted US, is performed to assess for a sonographic correlate for a lesion detected by MRI that was not initially seen at mammography or ultrasound. If a correlate is seen at ultrasound, US-guided biopsy is the preferred method as it can be less expensive, faster, easier, and more comfortable for patients than MRI-guided biopsy. Understanding the differences in breast position between MRI (prone) and ultrasound (supine) in addition to knowledge of the location and morphology of the MRI-detected lesion can aid in identifying a sonographic correlate. Performing imaging-histopathologic concordance and imaging follow-up are important in patient management. In the absence of a sonographic correlate, MRI-guided biopsy is still required of any lesion deemed suspicious at MR imaging.

Keywords Magnetic Resonance Imaging • MRI • Ultrasound • US • MRI-directed ultrasound • Directed-ultrasound • Targeted-ultrasound • Second-look ultrasound • Sonographic correlate • Breast cancer • Breast lesions • Incidental breast lesions • Breast biopsy • Ultrasound-guided biopsy • MRI-guided biopsy

11.1 Introduction

Breast MRI has been shown to have a high sensitivity (up to 100 %) for the detection of breast cancer but its specificity and positive predictive value is reported to be lower [2, 9, 11, 15, 18, 20]. Unsuspected suspicious MRI-detected lesions, designated category 4 or 5 according to the American College of Radiology Breast Imaging

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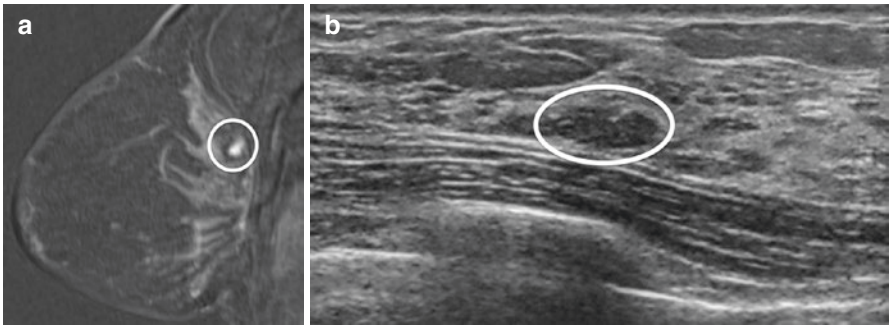

Fig. 11.1 Posteriorly located lesion that is not amenable for MRI-guided biopsy. (**a**) Subtracted sagittal T1W post-contrast image. (**b**) MRI-directed US from right breast. A 27-year-old woman with BRCA2 gene mutation found to have an oval enhancing mass (*circle* in **a**) in the right breast in the far posterior aspect, just anterior to the pectoralis major muscle. MRI-directed US identified a 9-mm oval hypoechoic mass at 10:00, 5-cm from the nipple (*circle* in **b**). US-guided FNA aspiration was performed demonstrating fibroadenoma, which is benign and concordant. This mass remained stable at 12-months follow-up

Reporting and Data System (BI-RADS) [16], therefore warrant biopsy to establish tissue diagnosis. Management options include MRI-directed wire-localization for surgical excision, proceeding directly to MRI-guided biopsy, or performing an MRI-directed ultrasound, also known as second-look or targeted US. An MRI-directed ultrasound is utilized to find a correlate for a lesion detected at MRI that was either not seen on a breast ultrasound performed antecedent to the MRI or because ultrasound had not been previously performed. Identifying a sonographic correlate enables US-guided biopsy. Compared to MRI-guided biopsy or wire-localization, US-guided biopsy is better tolerated, less expensive, more readily available, and faster [1, 5, 6, 13]. In addition, US guided biopsy also allows greater access to lesions in certain locations such as those located posteriorly (see Fig. 11.1), in the axillary tail, or in women with implants that may present a biopsy challenge under MRI guidance.

11.2 Technique in Performing MRI-Directed US

Thorough and careful review of the breast MRI is essential prior to performing an MRI-directed ultrasound. If a technologist performs the ultrasound study, it is also important to review the MRI study with the technologist. When reviewing the breast MRI study, utilization of 3D reconstructions can help make it easier to understand the location of the lesion in all 3 planes (see Fig. 11.2) and its relationship to surrounding structures [24]. The location and morphology of the MRI-detected lesion are important information to know to determine the expected location and appearance of the lesion at ultrasound.

Lesion location information to note includes the quadrant and o'clock position, distance from nipple, skin, and chest wall, anatomic relationship to surrounding tissue, and its relationship to other landmarks. It is important to keep in mind that

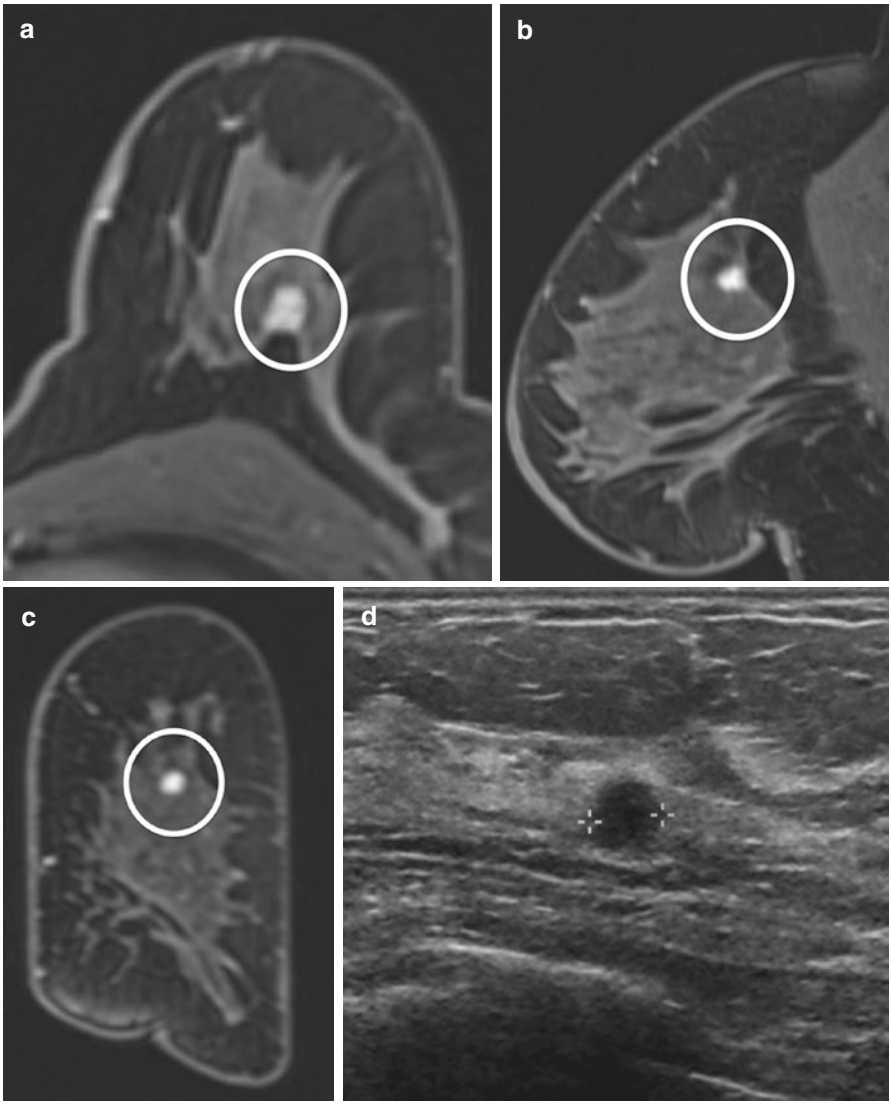

Fig. 11.2 3D reconstructions can help make it easier to understand the location of the lesion in all 3 planes. (**a**) Axial T1W post-contrast image. (**b**) Sagittal T1W post-contrast image. (**c**) Reconstructed coronal post-contrast image. (**d**) MRI-direct US from left breast. 39 year-old found on extent of disease MRI to have an enhancing round mass with irregular margin (*circle*) in the left breast at 12:00, 5-cm from the nipple. The 3 planes aided in ultrasound localization of the mass (calipers). Biopsy demonstrated invasive ductal carcinoma

the positioning of the breast is different between MRI and ultrasound [19, 24]. Breast US is performed with the patient in the supine or supine oblique position with the arm raised while breast MRI is performed with the patient in the prone position. In the supine position with the arm raised, the breast tissue is flattened and widened which makes the breast tissue, including breast lesions, appear more

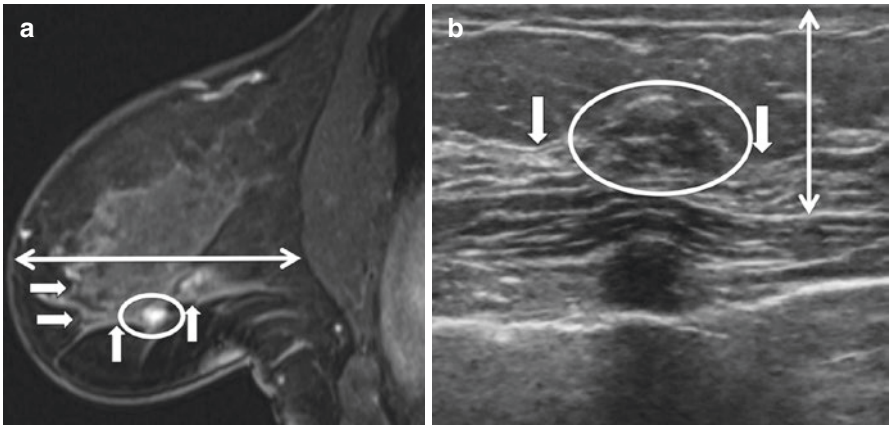

Fig. 11.3 Effects of the breast in the prone position at MRI and supine position at US and the relationship of lesion to surrounding tissue. (**a**) Subtracted sagittal T1W post-contrast image with patient in prone position. (**b**) MRI-directed US image from left breast. Breast tissue in the prone position appears more stretched in the anterior to posterior dimension (double arrowhead in **a**) while in the supine position along with compression by the ultrasound probe, the breast tissue becomes flattened and widened. In the supine position, the breast tissue, including breast lesions, appear more compact (*double arrowhead* in **b**). 41-year-old woman with a strong family history of breast cancer was found to have an oval irregular enhancing mass (*circle* in **a**) in the left breast middle depth which at ultrasound, the mass (*circle* in **b**) appears more posteriorly located due to flattening of the breast tissue. However, the lesion's relationship to surrounding tissue is maintained between the two modalities (glandular tissue indicted by *arrows*). Biopsy demonstrated fibroadenoma

compact. The distance between the chest wall and the glandular tissue is decreased on US relative to MRI (see Fig. 11.3). With MRI, the breast in the prone position is pendant with little to no compression; this results in the tissue appearing more stretched in the anterior to posterior dimension (see Fig. 11.3). The distance between the chest wall and the glandular tissue is increased and lesions can appear more anterior on MRI than on US images [19, 24]. Carbonaro et al. showed lesion displacement of about 3–6 cm along the three orthogonal directions on prone versus supine MRI [4]. The o'clock position of the lesion in ultrasound can also vary by one or two hours compared to the MRI [17]. Since lesion displacement can vary between ultrasound and MRI, the anatomic relationship of the lesion to surround tissue (subcutaneous fat, glandular tissue, or retroglandular fat) (see Fig. 11.3) can be used to help in identifying a correlate with more confidence [19]. The relationship of the lesion to surrounding tissue is maintained between the two modalities.

More reliable location information to note is the distance to the skin and nipple (see Fig. 11.4) as suggested by Carbonaro et al. [4]. The median lesion-to-skin and lesion-to-nipple displacements were less than 1 cm and that the lesion-to-nipple distance may be the most reliable measure to be used for MRI-directed US [4]. In addition to using the skin and nipple as fixed markers, the relationship of the lesion to co-existing lesions such as cysts, scars, implants, clips, known cancer (see Fig. 11.5), or known fibroadenomas may be helpful. Knowledge of co-existing lesions is

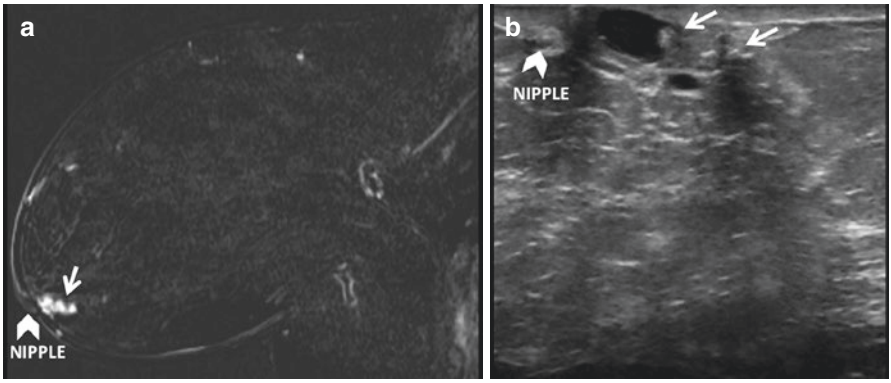

Fig. 11.4 Nipple as a fixed landmark. (**a**) Subtracted T1W post-contrast image. (**b**) MRI-directed US from left breast. Sixty-eight year-old with history of breast cancer found on surveillance MRI to have an oval mass with irregular margins (*arrow*) in the left retroareolar breast subjacent to the nipple (*arrowhead*). Using the nipple (*arrowhead*) as a fixed landmark, an irregular hypoechoic mass was identified within a focally dilated duct at US. Biopsy yielded papillary lesion

also important to prevent erroneous correlation, particularly in patients with multiple lesions within a similar region of the breast [19].

MRI lesion morphology with respect to shape, size and contours can also be useful in finding a lesion on MRI-directed ultrasound (see Fig. 11.6). Perfect morphologic agreement of lesions between the two modalities must not necessarily be expected [10]. Lesions at US tend to look smaller than at MRI as they are compressed in a vertical direction by the ultrasound probe. In addition, round lesions at MRI often appear oval or elliptical at ultrasound [19].

If no sonographic correlate is identified or confident correlation is difficult, MRI-guided biopsy must be performed on all lesions classified as BI-RADS category 4 or 5 at MRI [5, 10, 13, 19, 25].

11.3 Evidence-Based Findings

11.3.1 Frequency of Sonographic Correlate for MRI-Detected Lesions

Several studies have investigated the frequency at which MRI-directed ultrasound identifies a sonographic correlate for a lesion initially detected on MRI. These studies vary widely in rates of correlate, most likely because of heterogeneous methodologies and study populations, and also the inherently user-dependent nature of ultrasound [12, 22]. Limitations of the studies generally included retrospective design and lack of defined protocol establishing which lesions underwent MRI-directed ultrasound versus MRI-guided biopsy directly [5, 12, 13, 22]. In 2014 Spick and Baltzer published a meta-analysis of 17 studies that found a pooled detection rate for sonographic

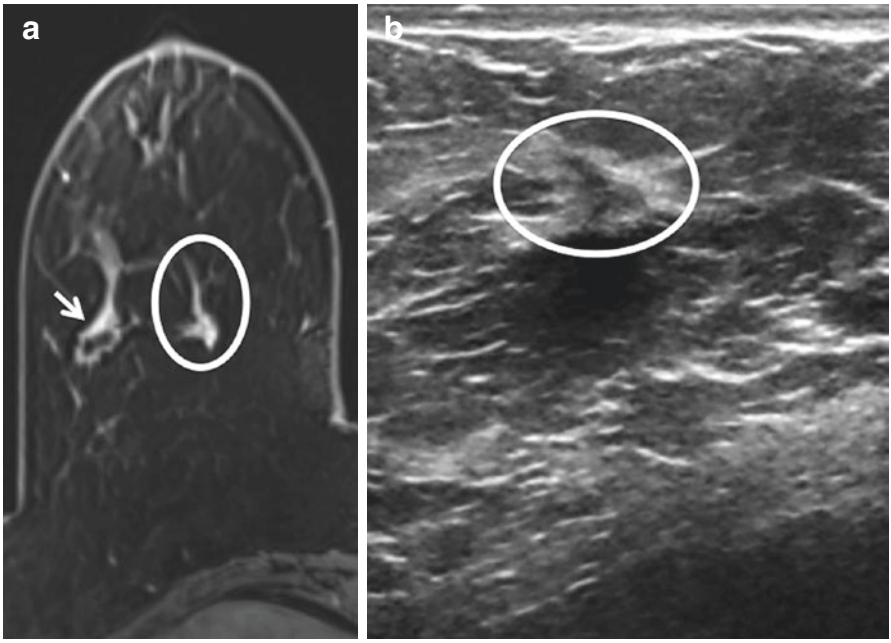

Fig. 11.5 Known cancer as a landmark. (**a**) Axial T1W post-contrast image. (**b**) MRI-directed US from right breast. Sixty-four-year-old woman with known right breast invasive ductal carcinoma (*arrow*) found on extent of disease MRI to have an irregular enhancing mass (*circle* **a**) medial to the known malignancy. Using the known malignancy as a landmark, a subtle sonographic correlate (*circle* **b**) was identified. Biopsy demonstrated a second area of invasive ductal carcinoma.

correlate of 58 %, with a wide reported range of 22–82 % [22]. Analyses of lesion characteristics have helped to understand which given MRI lesions are the most likely to have ultrasound correlates, with most studies showing masses and malignant lesions to be the most likely MRI-detected findings to also be seen on ultrasound.

11.3.2 Lesion Type

The three primary enhancing lesion types as defined by the BI-RADS lexicon [16], mass, focus and non-mass enhancement, show varying rates of sonographic correlate. Masses have been shown by many studies to be the lesion type most likely to have a correlate. In their meta-analysis, Spick and Baltzer found that mass lesions were more likely than non-mass enhancement to have a correlate ($p < .0001$) [22]. Many single studies have also demonstrated statistical significance for MRI-detected masses having a higher rate of sonographic correlate than non-mass enhancement. Meissnitzer et al. found a sonographic correlate for 62 % of masses and 31 % of

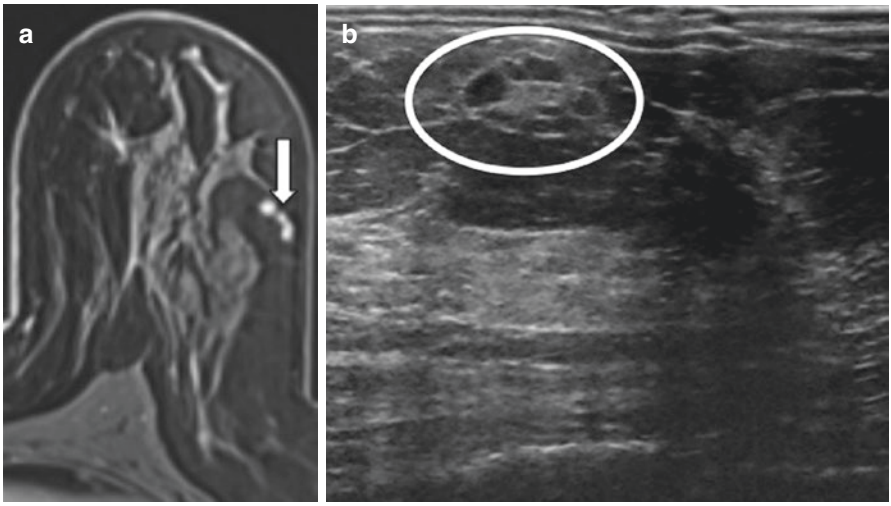

Fig. 11.6 Shape, size and contours can be useful in finding a lesion on MRI-directed ultrasound. (**a**) Axial T1W post-contrast image. (**b**) MRI-directed US from left breast. Forty-seven year-old woman with known malignancy was found on extent of disease MRI to have several enhancing contiguous masses (*arrow*) in the left breast at 2:00, 5 cm from the nipple. At ultrasound, several oval, circumscribed adjacent hypoechoic masses (*circle*) were identified similar in shape, size, and contour to the MRI lesion. At biopsy, the masses represented the lobulated cortex of a benign lymph node

non-mass enhancement ($p < 0.001$) [13]. Abe et al. found a correlate for 67 % of MRI-detected masses and 12 % of non-mass enhancement ($p < 0.005$) [1]; these authors also reported a 46 % correlate rate for foci, an intermediate rate between that of the other two lesion types [1]. Similarly, Hollowell reported a correlate rate of 49 % for masses, 42 % for foci, and 15 % for non-mass enhancement ($p = .0006$) [7]. DeMartini et al. found MRI-directed ultrasound yield to be higher for masses (58 %) than for foci (37 %) or non-mass enhancement (30 %) [5].

11.3.3 Size

Some studies have shown lesion size to affect chance of identifying an ultrasound correlate, with larger lesions more likely to have a correlate. Meissnitzer et al. found that for both masses and non-mass enhancement, increasing lesion size resulted in increasing ultrasound conspicuity that was statistically significant [13]. Wiratkapun et al. found a positive association between increasing size of MRI mass lesions and detection of ultrasound correlate (odds ratio 1.23, $p = .01$) [25]. Several other authors did not find lesion size to significantly affect frequency of detection [3, 5, 8, 10].

Spick and Baltzer also did not find size to be a significant predictor of sonographic correlate detection rate on meta-regression analysis, but recommended caution when interpreting this result because of the small number of studies that specifically reported on lesion size and lack of stratification by lesion type [22].

11.3.4 Level of Suspicion and Kinetics

Meissnitzer et al. found that BI-RADS category 5 versus 4 lesions were significantly more likely to have a correlate, both for masses (81 % versus 59 %, $p = 0.005$) and for non-mass enhancement (75 % versus 26 %, $p = 0.009$) [13]. However, level of suspicion was not reported upon or not found to be statistically significant in many other studies. Similarly, there is limited reported data regarding MRI lesion enhancement kinetics and rate of correlate. Meissnitzer et al. found no significant effect of enhancement kinetics on correlate detection rate [13].

11.3.5 Histology

Many studies have shown malignant lesions to be statistically more likely than benign lesions to have a sonographic correlate [1, 7, 10, 13, 21], including on meta-analysis ($p < .0001$) [22]. However, investigators have shown that malignancy is not excluded if a sonographic correlate is not found, with rate of sonographically occult malignancy reported at 12 % in pooled estimate on meta-analysis [22] and with a wide range on single studies, up to 53 % [1, 5, 6, 10, 13, 25]. Thus, there is consensus among numerous authors who endorse that absence of a correlate does not obviate biopsy, such that suspicious MRI-detected lesions without sonographic correlate should go on to MRI-guided biopsy [5–7, 10, 12, 13, 21, 22, 25].

11.4 Potential Limitations of MRI-Directed US

With increasing availability of breast MRI, some facilities proceed directly to MRI-guided biopsy, as there are some potential disadvantages for performing MRI-directed US rather than proceeding directly to MRI-guided biopsy. MRI-directed ultrasound may prolonged work-up time resulting in delay of diagnosis, added expense of performing the ultrasound prior to MRI-guided biopsy, and patients may experience a false sense of reassurance in the setting of a negative ultrasound [5, 10, 12, 13, 21]. In addition, confident correlation on MRI-directed US can be challenging and can result in inaccurate correlations. In one study it

was reported that the follow-up imaging in 80 benign, concordant ultrasound-guided biopsies, 10 of the sonographic lesion did not correspond to the MRI finding [13]. Five cancers were diagnosed in 9/10 lesions that underwent MRI-guided biopsy.

11.5 Imaging-Histopathologic Correlation

Determining concordance between imaging findings and histologic results is important and is the responsibility of the radiologist who performed the biopsy. Whether the histolopathologic diagnosis correlates with the imaging findings will determine patient management with respect to recommendation for surgical excision or short-term follow-up. In the case of MRI-directed ultrasound, imaging-histopathologic correlation should be made based on the level of suspicion with both the presumed ultrasound correlate and the lesion initially detected on MRI.

Following ultrasound-guided biopsy, a clip should be routinely placed at the site of biopsy with a post-procedure mammogram performed to help facilitate assessment of concordance and for subsequent imaging follow-up (see Fig. 11.7). Breast-MRI imaging in more than one plane or reformatting MR images into more than one plane can help assess correlation of lesion location marked by the biopsy clip on the post-ultrasound guided biopsy mammogram and the location of the lesion on MRI [12, 17, 19, 24]. Immediate action for the MRI-detected lesion is often prompted by histopathologic discordance but will not typically occur if the result is benign concordant. For benign concordant results, some practices will wait for MRI follow-up, typically 6 months after ultrasound biopsy which may delay management of the MRI detected lesion if the presumed ultrasound correlate is not the same as the MRI lesion [17, 23, 24]. To minimize delay in patient care, a more definitive confirmation of MRI-sonographic correlation can be obtained on the same day as the US-guided core biopsy by getting a fast single T1 weighted gradient echo (GE) sequence without fat saturation [14, 17, 24]. The T1 weighted GE sequence (3D rapid EG, TR/TE, 8/4.6; matrix, 276 × 464; flip angle 16° voxel size, 0.8 × 0.8 × 0.8 mm) [17, 24] is sensitive to artifacts with magnetic susceptibility and will help verify MRI-sonographic correlate. The acquisition time is between 2 and 4 min. A biopsy under MRI should be recommended if there is disagreement between the biopsy performed with ultrasound and the MRI lesion. Depending on the practice workflow and availability of the MRI scanner, MRI-guided biopsy can be done on the same day if the US-guided biopsy site is found not to correlate with location of MRI lesion. It is important to keep in mind that evaluation of the biopsy site and targeted lesion may be limited because of hematoma and other post-biopsy changes. For any benign concordant result after ultrasound-guided biopsy of a sonographic correlate to a lesion initially detected on MRI a 6-month follow-up MRI is recommended [23].

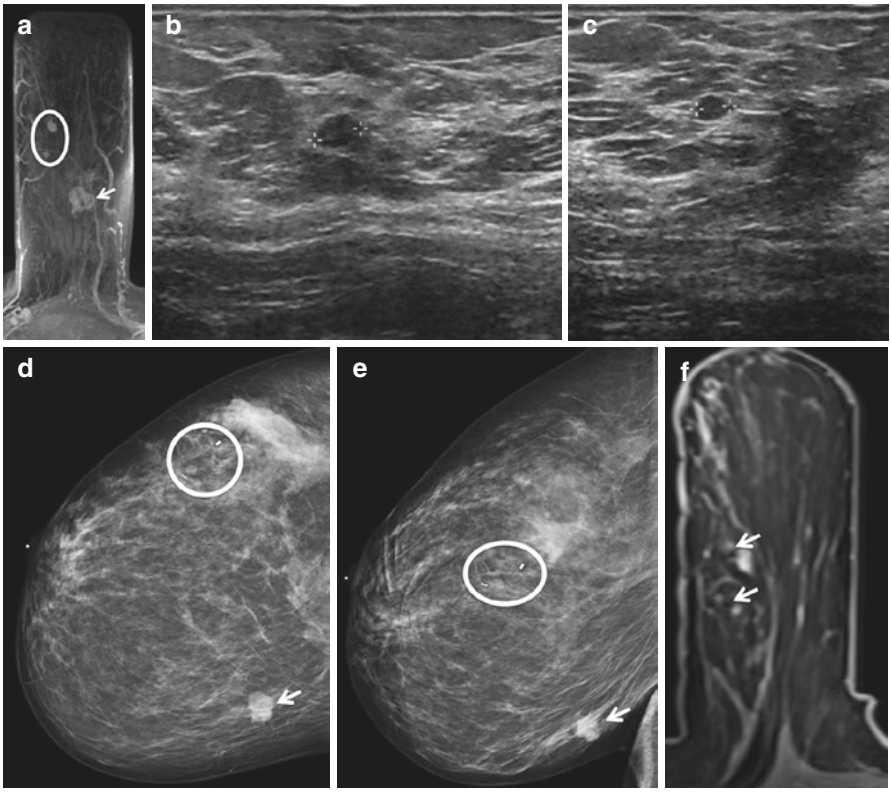

Fig. 11.7 Imaging correlation after biopsy of MRI-detected lesion with sonographic guidance. (**a**) Axial T1W post-contrast MIP image. (**b**) MRI-US from right breast at 9:30, 6-cm from the nipple. (**c**) Targeted US of right breast at 10:00, 7-cm from the nipple. (**d**) Right CC view after US-guided biopsy. (**e**) Right LM view after US-guided biopsy. (**f**) Axial T1W post contrast image. Forty-two-year-old female with recent diagnosis of invasive ductal carcinoma (*arrow*) in the lower inner quadrant posterior depth. At extent of disease MRI, 2 additional lesions (*circle*) were seen. Possible correlates (calipers) were identified at ultrasound with biopsy and clip placement yielding fibroadenoma for the 9:30 6-cm from the nipple 0.6-cm mass and papillary lesion for the 10:00, 7-cm from the nipple 0.5-cm mass. Post-US guided biopsy mammogram (CC and LM views) shows the biopsy clips (*circle*) to be within expected location of the MRI lesions. This was confirmed on MRI showing susceptibility artifacts (*arrows* in **f**) associated with lesions of interest

11.6 Conclusion

MRI-directed ultrasound is an important adjunctive tool in the evaluation of lesions detected at MR imaging. Identification of a sonographic correlate enables US-guided biopsy of the MRI-detected lesions which is the preferred method as it can be less expensive, faster, easier, and more comfortable for patients than MRI-guided biopsy. To help facilitate identifying an MRI-sonographic correlate, it is important to thoroughly review the breast MRI prior to performing the targeted ultrasound and

understand the differences in breast position between the two modalities. Lesion location, depth, and characteristics, as well as the appearance of the surrounding tissue and relationship to other focal lesions that may be present, must be considered. The likelihood of finding a correlate to an MRI lesion varies depending on lesion size and morphology with larger lesions and masses being easier to identify at US. Following biopsy, it is important to confirm accuracy of MRI-ultrasound correlation and perform imaging-histopathologic correlation. MRI-guided biopsy needs to be performed for any MRI-US discordant cases. Also for benign concordant MRI-US cases, a follow-up breast MRI must be carried out 6 months after the biopsy.

Not all MRI-detected lesions will be seen at ultrasound. Absence of a sonographic correlate for a MRI-detected lesion with suspicious imaging features does not preclude the need for biopsy under MRI-guidance.

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