# Chapter 13 Breast MRI and the Benign Breast Biopsy

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**Abstract** This chapter, appearing in the section on MRI Findings, Interpretation, and Management, reviews the issues relevant to benign MRI-guided biopsy results. The discussion includes challenges in assessing radiologic-pathologic concordance specific to MRI, approaches for discordant biopsy results, and a review of the literature on appropriate imaging follow-up recommendations for benign concordant MRI-guided biopsy results. High risk lesions from MRI-guided biopsy are addressed in a separate chapter.

**Keywords** Benign • MRI-guided biopsy • Radiologic-pathologic concordance • Discordance • Management • Recommendations • Follow-up imaging

## Abbreviations

ACR	American College of Radiology
BI-RADS®	Breast Imaging-Reporting and Data System
ER+	Estrogen receptor-positive
HER2	Human epidermal growth factor receptor 2
MRI	Magnetic resonance imaging
PACS	Picture archiving and communication systems
PPV	Positive predictive value
PR+	Progesterone receptor-positive

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#### 13.1 Introduction

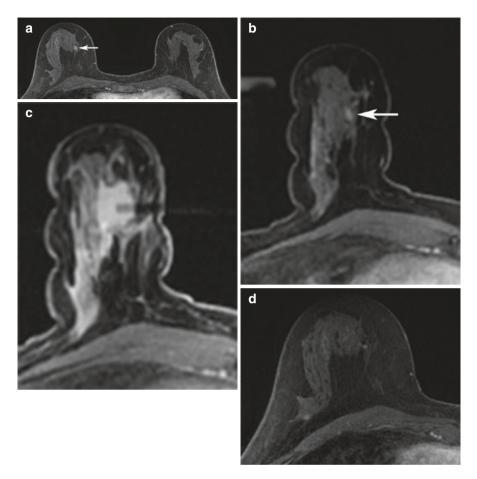
Breast MRI utilization is increasing in clinical practice in the United States. Nearly 11.5 breast MRI examinations per 1000 women undergoing breast imaging were reported to have occurred in 2009 [1]. Clinical indications for contrast-enhanced breast MRI include supplemental screening for women with greater than 20 % life-time risk of breast cancer, preoperative planning for women with newly diagnosed breast cancer, evaluation of response to neoadjuvant chemotherapy, and occult primary tumor localization in women presenting with biopsy-proven metastatic axillary lymphadenopathy [2].

Breast MRI is the most sensitive modality for breast cancer detection [3]. When used as a supplement to mammography for high risk screening, the cancer detection rate increases from approximately 8.2 to 26.1 per 1000 women [4]. However, breast MRI is not a perfect test and its specificity is lower than its sensitivity due to overlapping imaging features of benign and malignant lesions [3]. For example, the current American College of Radiology (ACR) Breast Imaging-Reporting and Data System (BI-RADS<sup>®</sup>) practice benchmark for positive predictive value of biopsies performed (PPV<sub>3</sub>) is 20–50 % for breast MRI screening programs [5]. Thus, many biopsies will yield benign results. It is imperative that radiologists have a solid understanding of the management of benign results, including the assessment of adequate tissue sampling, the process for determining whether the histopathologic result appropriately explains the imaging finding, and recommendations for followup imaging. This chapter focuses on these important issues surrounding benign MRI-guided breast biopsy results. The management of high risk lesions identified at MRI-guided biopsy is not addressed in this chapter.

## 13.2 Radiologic-Pathologic Concordance for MRI-Guided Breast Biopsies

Percutaneous biopsy is preferred over needle localization and surgical excision for findings visualized only on MRI [6, 7]. If percutaneous biopsy results are benign and concordant, unnecessary surgical excisional biopsy and its associated greater cost, time, morbidity, and cosmetic changes can be avoided. For patients with malignant results, surgical planning can be optimized reducing the total number of surgeries required for complete breast cancer treatment. MRI-guided breast biopsy has been shown to be a safe alternative to MRI-guided wire localization and excisional biopsy with comparable diagnostic accuracy [8–11].

A critical component that is essential for robust diagnostic accuracy of MRIguided breast biopsy procedures is determination of radiologic-pathologic concordance. A biopsy result is defined as concordant when the histopathology sufficiently explains the imaging findings that prompted the recommendation for biopsy (see Fig. 13.1) [12]. A discordant result is one in which the histopathology



**Fig. 13.1** Fifty-five-year-old asymptomatic woman undergoing screening breast MRI for elevated lifetime risk of breast cancer due to family history. (a) Axial T1-weighted post-contrast images demonstrated a 5 mm oval mass (*white arrow*) with circumscribed margins and heterogeneous internal enhancement in the right breast at 5 o'clock middle depth with initial rapid and delayed washout kinetics (BI-RADS<sup>®</sup> 4A). Targeted ultrasound showed no correlate. (b) MRI-guided biopsy was performed of the right breast mass (*white arrow*) using a medial approach with ten specimens obtained from a 9 gauge vacuum-assisted device. (c) Axial contrast-enhanced postbiopsy sequences demonstrated hematoma at the expected site of biopsy. Histopathology results were benign (breast tissue with cysts, fibrosis, apocrine metaplasia, and usual ductal hyperplasia) and concordant. (d) Six-month follow-up MRI was recommended which demonstrated susceptibility artifact from the biopsy clip and no residual enhancing mass (BI-RADS<sup>®</sup> 2)

does not explain the imaging findings and most often occurs when a benign pathology is reported for a highly suspicious imaging finding.

The purpose of determining concordance is to minimize the potential for falsenegative biopsies resulting from inadequate sampling or inaccurate targeting and to avoid a delayed diagnosis of cancer. The frequency of inadequate tissue sampling of MRI lesions has been reported as 6-14 % [13–15]. Use of vacuum-assisted devices, typically with 9 gauge needles, are encouraged which yield generous amounts of tissue for thorough histopathologic examination [7]. As for other breast imaging modalities, when a malignancy is detected within one year at the site of a benign MRI-guided biopsy it is considered a false-negative [5]. False-negative rates for MRI-guided breast biopsies range from 0.9 to 11.7 % [10, 13–17]. Accurate determination of a program's false-negative biopsy rate is inherently challenging due to the potential lack of patient follow-up at the same institution. Audit data linkage with state or regional cancer registries can be helpful to improve the accuracy of false-negative biopsy rate.

Information used in determination of radiologic-pathologic concordance starts at the time of the diagnostic examination. A BI-RADS<sup>®</sup> assessment of 5 (highly suggestive of malignancy) indicates that a benign biopsy result should, in most instances, be deemed discordant. Furthermore, subcategorization of BI-RADS<sup>®</sup> 4 assessments into 4A, 4B, and 4C (low, moderate, and high suspicion for malignancy, respectively) is also informative. In contrast to mammography and ultrasound, subcategories for BI-RADS<sup>®</sup> 4 assessments are not included for MRI in the most current edition of the BI-RADS<sup>®</sup> Atlas [5]. However, subcategorization of BI-RADS<sup>®</sup> 4 assessments can be particularly useful for breast MRI radiologic-pathologic correlation because the level of concern for malignancy is more stratified. For example, a lesion with a 4C assessment that yields benign biopsy results should be reviewed with particular scrutiny. Particular benign pathologies that are well-known to present as suspicious imaging findings, such as fat necrosis, could be considered concordant in these instances.

Assessing the adequacy of tissue sampling at the time of biopsy also contributes to concordance determination. Immediate post-biopsy images are obtained and reviewed during the procedure to allow for adjustment and additional sampling if needed. Some practices perform a second injection of contrast to revisualize the lesion [11]. However, the presence of blood and air in the biopsy cavity frequently limits the utility of this approach.

Adequate communication with the interpreting pathologist is another key factor in optimizing radiologic-pathologic concordance. Inclusion of key clinical information, indication for biopsy, imaging features of the biopsied lesion, potential differential diagnoses based on imaging, and the BI-RADS<sup>®</sup> assessment on the pathology requisition form provides a quick and focused method for conveying this important information. For complicated cases or those with unusual or unexpected histopathologic results, the pathologist may contact the radiologist who performed the procedure with specific questions before issuing their final report. Being available and engaged in these conversations further improves radiologic-pathologic concordance and strengthens the multi-disciplinary approach to patient care.

Once biopsy results are issued by pathology, the methods used for assessing radiologic-pathologic concordance vary by institution and practice type. One approach involves a dedicated multidisciplinary clinical conference. The radiologist presents the clinical history and imaging studies performed before, during, and after

the biopsy to demonstrate initial findings and level of suspicion for malignancy, adequate targeting and sampling, and appropriate marker clip placement. This is followed by presentation of the histopathologic results by the pathologist. Group consensus is reached regarding concordance, and management recommendations are determined. This method can foster interdepartmental professional relationships and can be achieved in this modern electronic era through remote Picture archiving and communication systems (PACS) and scanned histology slides through programs available on the internet and/or video-conferencing. An approach such as this may be more amenable to implementation at teaching institutions. For settings in which it might not be practical for a physical radiology-pathology correlation conference such as high-volume clinical services, the radiologist may perform dedicated review of imaging findings independently or together with other radiologists in the group using the written pathology report.

Determining radiologic-pathologic concordance relies upon knowledge of the acceptable histopathology for particular imaging findings. For breast MRI, most of the research has focused on the imaging features that are predictive of malignancy. For example, foci have been shown to have lower probabilities of malignancy compared to masses or non-mass enhancement [18]. For masses on MRI, margins have been found to be an important imaging predictor [19, 20]. However, there are relatively few data regarding the MRI features that are associated with particular benign histopathology outcomes. Biopsies of breast MRI findings have been shown to result in a spectrum of benign, concordant histopathology results. These include nonspecific findings such as fibrocystic change, sclerosing adenosis, fibrosis, pseudoangiomatous stromal hyperplasia, and normal breast parenchyma [20, 21]. More specific benign and concordant results include fibroadenoma, papilloma, and lymph node. In general, nonspecific results have been more frequently associated with non-mass enhancement [20, 21], but further studies are warranted to clarify acceptable MRI lesion and histopathology outcomes.

Once radiologic-pathologic correlation has been performed and concordance has been determined, management recommendations are made and communicated to the referring physician and the patient. Patients with malignant results are referred to a breast surgeon and/or medical oncologist for treatment. Management of patients with benign results that are discordant and those with benign results that are concordant are discussed in the subsequent sections of this chapter. Importantly, an addendum is made to the original biopsy report with the histopathologic results, radiologic-pathologic concordance, and management recommendations.

Practice guidelines regarding MRI-guided breast biopsy procedures have been published by the American College of Radiology (ACR) and as a report from a European interdisciplinary consensus meeting [6, 7]. The ACR states that the physician who performed the procedure "is responsible for obtaining results of the histopathologic sampling to determine if the lesion has been adequately biopsied and is concordant or discordant with the imaging findings" [7]. The European interdisciplinary consensus report recommends "all available clinical and imaging information and VAB results be compared and discussed in an interdisciplinary conference to achieve a consensus recommendation in each case" [6]. These reports reinforce the importance of assessing concordance.

For several reasons, radiologic-pathologic concordance is more challenging for MRI-guided biopsies compared to stereotactic- and ultrasound-guided biopsies. First, there is no specimen radiograph to confirm adequate sampling due to the lack of tissue enhancement *ex vivo*. Second, there is no "real-time" visualization of the needle at the time of tissue sampling since the biopsy is performed when the patient is outside of the magnet. Determining whether the targeted finding has been appropriately sampled on post-biopsy MRI sequences has limitations as lesions with washout contrast kinetics become less conspicuous over time while enhancement of normal breast parenchyma increases. Also, lesions can be obscured by hematoma and air on post-biopsy sequences. These factors together with the higher pre-test probability of malignancy in women undergoing breast MRI support adopting a careful approach to radiologic-pathologic concordance to avoid a delayed cancer diagnosis.

#### 13.3 Discordant MRI-Guided Breast Biopsy Results

A discordant biopsy result is one in which the histopathology does not sufficiently explain the imaging findings [12]. The discordance rates for MRI-guided breast biopsies using vacuum-assisted devices range from 0 to 9 % [9, 10, 22–26]. The rates of discordant biopsies are higher for MRI-guided biopsies compared with stereotactic- or ultrasound-guided biopsies (approximately 3 %) [12, 24]. Interestingly, discordance has not been shown to occur more often with BI-RADS<sup>®</sup> category 5 compared with category 4 lesions or to occur more often for radiologists with less experience with MRI-guided biopsies, factors that are known to affect discordance rates for stereotactic- and ultrasound-guided biopsies [24].

Further tissue sampling is warranted in cases of discordant MRI-guided biopsy results (see Fig. 13.2) [6, 7]. Options include repeat MRI-guided biopsy or surgical excision. The method used for preoperative wire localization prior to surgical excision includes mammographic-guidance if the marker clip placement is deemed appropriate. If there is significant clip displacement and mammographic landmarks are lacking, MRI-guided wire localization can be performed. The malignancy rate for discordant lesions that subsequently undergo surgical excision is 30–50 % [22, 24]. Thus, appropriate recognition and management of discordant lesions is clinically significant.

For discordant lesions undergoing repeat MRI-guided biopsy, radiologicpathologic concordance should again be determined. Similarly, review of final histopathologic results for cases recommended for surgical excision are informative and recommended [6]. Important factors to note include the presence or absence of prior biopsy site changes in the excised specimen and whether any residual lesion exists in the specimen as well as final histopathologic size since small lesions may be completely removed during the biopsy procedure.

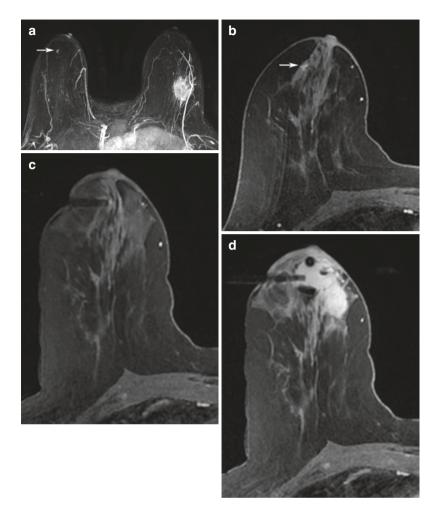


Fig. 13.2 Forty-nine-year-old woman with newly diagnosed left breast cancer undergoing preoperative breast MRI for extent of disease evaluation. (a) Maximum intensity projection images demonstrate the biopsy-proven malignant mass in the left breast and a 6 mm irregular mass (white arrow) with irregular margins and homogeneous internal enhancement in the right breast at 9 o'clock anterior depth with initial rapid and delayed plateau kinetics (BI-RADS® 4B). Axial T1-weighted post-contrast images of the right breast mass (*white arrow*) are shown in (b). (c) MRI-guided biopsy was performed of the right breast mass using a lateral approach with 8 specimens obtained from a 9 gauge vacuum-assisted device. Preferential sampling was performed in the superior and lateral directions to account for patient motion noted after targeting. (d) Post-biopsy hematoma was located in the expected site of biopsy. Histopathology results were benign breast tissue. The anterior location of the lesion and relative lack of sufficient compression to prevent motion were inherent technical challenges encountered since the patient was undergoing bilateral MRI-guided breast biopsies for an additional lesion in the left breast located at middle to posterior depth. (e) Review of post-biopsy images demonstrated a persistent enhancing mass (white arrow) indicating insufficient tissue sampling. The benign biopsy result was deemed discordant and repeat MRI-guided biopsy of the right breast was performed with more anterior compression. Histopathology results were ductal carcinoma in situ, low grade, ER+PR+

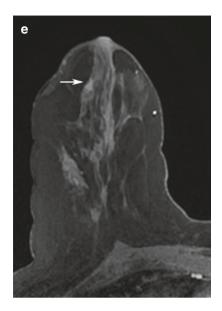
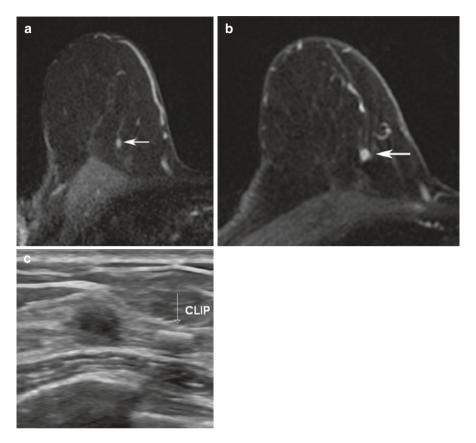


Fig. 13.2 (continued)

# 13.4 Management Recommendations for Patients with Benign Concordant Biopsy Results

Due to the challenges involved in confirming adequate sampling at the time of the MRI-guided biopsy procedure, a follow-up MRI examination is recommended for patients with benign concordant biopsy results to identify any delayed false-negative cases. The overall cancer yield at follow up-MRI has been reported as 0.9–2.3 % [13, 16, 17, 20]. The recommendation for follow-up MRI also includes when biopsies of suspicious MRI findings are performed using ultrasound guidance of presumed correlates identified on MRI-targeted ultrasound. The rationale for this recommendation is based on the results of Meissnitzer et al. which demonstrated that the presumed correlate on ultrasound did not correspond to the MRI finding of concern in 12.5 % of cases (10/80) with 5 cancers diagnosed in 9 lesions that underwent subsequent MRI-guided biopsy [27].

Ideally, the follow-up examination should be performed at the same institution using the same imaging acquisition protocol to best evaluate for potential interval change. Two studies have described an increase in the largest lesion dimension by 10 % as evidence of an interval size change, but there is no standardized definition for what constitutes clinically significant change [13, 16]. Lesions demonstrating concerning enlargement or development of more suspicious imaging features should undergo repeat biopsy or surgical excision (see Fig. 13.3) [16]. If the biopsied lesion decreases in size or resolves completely on the follow-up MRI, adequate sampling



**Fig. 13.3** Seventy-four-year-old woman with a personal history of prior treated right breast cancer and BRCA1 gene mutation undergoing asymptomatic screening breast MRI. (a) Axial T1-weighted post-contrast images demonstrated a new 3 mm focus of enhancement (*white arrow*) in the right breast at 1 o'clock posterior depth with initial rapid and delayed plateau kinetics (BI-RADS<sup>®</sup> 4A). MRI-guided biopsy was performed and ten specimens were obtained using a 9 gauge vacuum-assisted device. Histopathology results were benign and concordant. Six-month follow-up MRI was recommended. (b) Axial T1-weighted post-contrast images demonstrated a 6 mm round mass with a circumscribed margin and homogeneous enhancement (*white arrow*) in the right breast at 1 o'clock posterior depth with initial rapid and delayed plateau kinetics (BI-RADS<sup>®</sup> 4B). Susceptibility artifact from the previous placed MRI-guided biopsy clip was present along the posterior aspect of the mass. (c) Targeted ultrasound demonstrated an irregular hypoechoic mass with indistinct margins which correlated with the mass seen on MRI. A biopsy clip was noted adjacent to the mass. Histopathology results from ultrasound-guided biopsy were invasive ductal carcinoma, grade 2, ER-PR-HER2-

is confirmed and no further surveillance is required [15, 16]. This approach is supported by data of Dratwa et al. that showed no interval change at a 12 month followup MRI for 117 benign concordant lesions that had decreased or resolved at the initial 6 month examination [20]. There is currently no consensus on the optimal interval for the initial follow-up MRI nor the duration of follow-up imaging. In general, initial follow-up MRI is performed at 6–12 months after the index MRI [7, 28]. Several studies have been reported that recommend 6 month follow-up for all benign concordant lesions [9, 14, 15, 23, 25, 26, 28, 29]. Others base the follow-up interval on the specificity of the histopathologic result. For example, follow-up MRI is recommended at 6 months and 12 months after a nonspecific benign concordant biopsy result and at 12 months for a specific result such as a fibroadenoma, fat necrosis, or benign lymph node [11]. One study proposes that specific benign concordant diagnoses may not require further follow-up MRI [10]. Further evidence is necessary to support guidelines for optimal follow-up MRI interval.

For lesions that are stable on the initial follow-up MRI (see Fig. 13.4), recommendations for subsequent imaging are mixed. Some recommend returning to routine screening [9]. Given the potential uncertainty of adequate sampling during the biopsy procedure, others recommend continued follow-up MRI in 6–12 months [15, 16].

Studies investigating the short-term and long-term outcomes of benign concordant biopsy results are increasing in number [13–17]. Li et al. reported results from a retrospective review of 177 lesions with benign concordant MRI-guided biopsy results. Although the follow-up recommendations varied at the discretion of the procedure radiologist, all cases had follow-up MRI within 12 months [13]. Most of the lesions (155/177) had decreased in size or resolved at the initial follow-up MRI with no subsequent cancer diagnosis. Seventeen lesions were felt to warrant a second biopsy and four were found to be cancers, for an overall cancer yield of 2.3 % (4/177). All cancers detected were  $\leq 1.0$  cm in pathologic size, lymph node negative, and occurred in women with a personal history of breast cancer. Two cancers presented as enlarging non-mass enhancement at 6 and 12 months after the initial benign concordant biopsies. Given the potential for detection of false negatives, a 6 month follow-up interval was deemed most appropriate by this research group [30, 31].

A recent retrospective study by Dratwa et al. reported that 1.7 % (2/119) of benign concordant lesions displayed interval increase in size at the 6 month followup MRI [20]. Both lesions underwent surgical excision and yielded malignancy. These results also support an initial 6 month follow-up MRI recommendation.

While a 6 month follow-up MRI is a conservative method for minimizing delayed false-negative biopsies, some disadvantages exist to this approach. New lesions requiring further workup can occur on the follow-up MRI. While new cancers can be discovered (3/12, 25 %) as in Li et al. [13], additional false-positive findings may also occur. Furthermore, patient compliance is integral for the effectiveness of short-interval follow-up imaging. Rates of compliance for 6 month follow-up MRI are 43–63 % [16, 17, 29, 32]. Women with the indication of high-risk screening for the initial MRI are more likely to return for follow-up imaging compared to women having MRI for problem-solving or for extent of disease [17]. Women referred from outside institutions are less likely to be compliant with recommended follow-up



**Fig. 13.4** Thirty-two-year-old woman undergoing asymptomatic screening breast MRI for a personal history of treated left breast cancer. (a) Maximum intensity projection images from the initial MRI examination performed for extent of disease evaluation demonstrate the biopsy-proven malignant mass in the left breast. The patient underwent left breast lumpectomy with oncoplastic reduction, radiation therapy, and right breast reduction surgery. Final surgical margins were negative for carcinoma. (b) The patient's first screening MRI was performed 10 months following surgery and demonstrated an 8 mm area of focal non-mass enhancement (*white arrow*) in the left breast at 4 o'clock posterior depth with initial rapid and delayed plateau kinetics (BI-RADS<sup>®</sup> 4B). Diagnostic mammogram and targeted ultrasound showed no correlate. Histopathology results from MRI-guided biopsy were benign (breast tissue with radiation changes and focal changes from prior surgery) and concordant. (c) Six-month follow-up MRI was recommended which demonstrated no significant interval change (*white arrow*). An additional short-interval follow-up MRI was recommended in 6 months (BI-RADS<sup>®</sup> 3)

compared to those within the same institution [32]. Potential deterrents to compliance include the relatively high cost and variable insurance coverage for shortinterval follow-up breast MRI.

Two studies have been subsequently published suggesting that 6 month follow-up MRI may not be necessary and that initial MRI follow-up at 12 months is acceptable [16, 17]. Shaylor et al. reported results from a retrospective review of 113 benign concordant lesions with follow-up MRI [17]. One malignancy (ductal carcinoma in

situ) was detected 2 years after the initial benign biopsy for an overall cancer yield of 0.9 % (1/113). Since no cancers were detected at the 6 month follow-up MRI examination, the authors propose that annual screening MRI is a reasonable approach.

Similarly, results from Lee et al. suggest that the initial follow-up MRI examination can be deferred to 12 months without reducing cancer detection rates [16]. This study was a retrospective review of 85 eligible cases of benign concordant MRIguided biopsies with a minimal follow-up of 2 years. Most of the lesions (57/70) had decreased in size or resolved at the initial 6 month follow-up MRI and all of these were confirmed as benign with  $\geq$ 2 years of imaging and clinical follow-up. No cancers were detected at the 6-month or 12-month follow-up MRI. One malignancy (invasive ductal carcinoma with a micrometastatic sentinel lymph node) was detected after the biopsied mass enlarged at 24 months post biopsy despite being stable on the MRI performed at 10 months. The overall cancer yield was 1.2 % (1/85). The authors concluded that deferring the initial follow-up MRI to 12 months after biopsy is acceptable and that follow-MRI examinations should be continued for a minimum of 2 years to confirm benignity.

Some studies have reported no malignancies during their follow-up imaging period, also supporting that short-interval follow-up MRI may not be necessary. Perlet et al. reported results from a multicenter European study of 316 of 362 benign MRI-guided biopsies followed for a median of 32 months [11]. Subsequent repeat biopsy occurred in 3 patients; however, no malignancies were detected. Similarly, no cancers were found at follow-up MRI in 12 of 20 benign lesions followed for a mean of 7.5 months (range 3-14 months) reported by Hauth et al. or during the follow-up period of Bahrs et al. (mean 13 months; range 5–22 months) [14, 15]. It is important to note that these latter two studies performed immediate follow-up MRI 24-48 h after biopsy and resampled any lesions that appeared unchanged and that the study reported by Perlet et al. performed a second contrast injection at the time of biopsy and resampled any lesions remaining visible with minimal to no change. These important technical differences limit the generalizability of the follow-up results. Recently, Rauch et al. reported no malignancies during follow-up of 133 of 218 benign concordant lesions for a mean of 39 months (range 6–69 months) [29]. The biopsy protocol performed by this group more closely reflects the majority of practices in the United States which typically do not perform a second contrast injection or immediate follow-up MRI 24-48 h after biopsy.

Overall, a follow-up MRI in 6–12 months is typically warranted after benign concordant MRI-guided biopsies, particularly for histopathology results that are nonspecific [7]. In the future, imaging follow-up in this scenario may evolve to be less intensive, as has occurred for other image-guided percutaneous biopsies [33–36]. It is important, however, to recognize that patients undergoing MRI-guided biopsies have a higher risk of malignancy than those undergoing stereotactic- or ultrasound-guided biopsies. Accordingly, management recommendations should be based on the scientific evidence available and should be specific to the patient populations undergoing MRI-guided biopsies.

## 13.5 Summary

Clinical issues relevant to the care of patients undergoing MRI-guided biopsy have been reviewed. Assessment of radiologic-pathologic concordance is critical in cases of benign results to avoid a delayed diagnosis of cancer and can be more challenging for MRI-guided biopsies compared to other image-guided techniques. Discordant biopsy results are typically managed with repeat biopsy or MRI-guided wire localization and surgical excision. Evidence-based recommendations for optimal follow-up of benign concordant MRI-guided breast biopsy results continue to evolve.

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