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BEST PRACTICE APPROACHES BREAST RADIOLOGY-PATHOLOGY CORRELATION AND MANAGEMENT (J SCHEEL AND MR KILGORE, SECTION EDITORS)

Best Practice Approaches to Breast Radiology–Pathology Correlation and Management

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Abstract

Purpose of Review Image-guided percutaneous breast biopsy has become the gold standard for diagnosis of breast lesions. The radiologist's role in managing patients who undergo a breast biopsy extends beyond just the diagnostic imaging and performing the procedure. The radiologist must be cognizant of radiology-pathology correlation to determine concordance of the biopsy result and make the appropriate management recommendations.

Recent Findings We will review the significance of accurately determining radiology-pathology concordance between imaging findings and biopsy results as they relate to calcifications, masses, asymmetries, and architectural distortions.

Summary Radiologic-pathologic correlation after breast biopsy is crucial for the radiologist to be involved to best assist and manage our patients.

Keywords Breast cancer · Calcifications · Breast mass · Architectural distortion · Radiologic-pathologic correlation

Introduction

As breast imaging techniques have evolved and improved, so has our ability to detect early stage and potentially curable forms of breast cancer. Historically, diagnostic surgical excision biopsies were the mainstay of pathologic diagnosis. Concurrent with the evolution of our imaging techniques, our ability to perform image-guided percutaneous biopsies has become the new gold standard. Whether the guidance be ultrasound, stereotactic, tomographic, or magnetic resonance imaging, the number of percutaneous breast biopsies has steadily risen over time. The use of image guidance in breast biopsies has steadily rose since the 2000s with now a majority of all breast biopsies performed utilizing image guidance [1]. With the prevalence of minimally invasive breast biopsies and increased participation by radiologists, one needs to be familiar with the: (1) classification of breast imaging reporting and data system (BI-RADS) 4 and 5 lesions including suspicious microcalcifications, masses, asymmetries, and architectural distortion across multiple imaging modalities; (2) use of the appropriate imaging modality for percutaneous biopsy; (3) correlation and concordance of imaging findings with the expected histology result; and (4) appropriate follow-up and management of patients based on radiologic-pathologic concordance (Fig. 1a,b).

The advantages of minimally invasive image-guided breast biopsy over surgical biopsy, which include shorter recovery time, lower patient cost, minimal scarring, and relative safety, are without question. Additionally, the sensitivity and specificity of image-guided biopsy approaches that of open-surgical biopsy secondary to our improvement in imaging technique and biopsy equipment [2].

In the following accompanying sections, we will discuss by modality how radiologic-pathologic correlation should be performed and management recommendations.

This article is part of the Topical Collection on *Best Practice Approaches Breast Radiology-Pathology Correlation and Management*.

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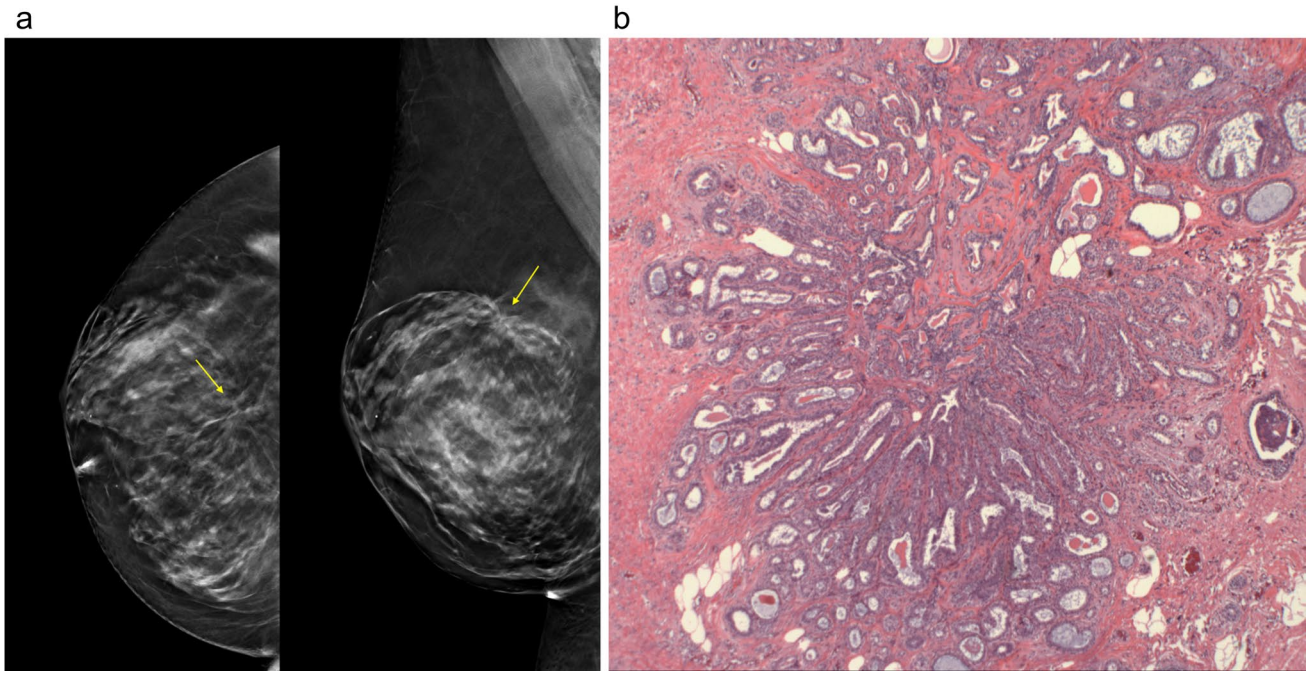

Fig. 1 **a** Architectural distortion detected in the right breast at the 12:00 position on screening digital breast tomosynthesis. Histologic sampling revealed radial scar. **b** Radial scar on histologic slide with a central sclerotic core and slender bands of stroma extending into the adjacent fat

Stereotactic or Tomosynthesis-Guided Biopsy

Stereotactic or tomosynthesis-guided biopsy should be performed for imaging findings that are best seen or only seen on mammography. Traditionally, this would include microcalcifications, asymmetries, focal asymmetries, masses, or architectural distortions.

Microcalcifications

When performing stereotactic-guided biopsies for calcifications, one should also be prepared to determine radiologic-pathologic concordance. Microcalcifications visualized on mammography make up approximately 55% of non-palpable detected breast malignancies [3]. Additionally, they account for 85–95% of all screening detected cases of ductal carcinoma in situ (DCIS) [4]. The BI-RADS lexicon for calcifications has allowed radiologists to not only describe calcifications based on their morphology and distribution but also to risk stratify and predict the malignant potential of microcalcifications based on their BI-RADS descriptors (see Table 1).

When performing stereotactic or tomosynthesis-guided biopsies for microcalcifications, two components should be included: (1) radiographic examination of the specimen and (2) placement of a biopsy marker with post-procedure imaging. Radiographic examination of the specimen is key when managing microcalcifications. This is the first step to ensure that the correct calcifications in question were sampled adequately. This can be accomplished by imaging the

Table 1 Calcification risk stratification based on BI-RADS calcification lexicon for morphology and distribution [5, 8]

		Morphology					**Total**
		Fine linear	Fine pleomorphic	Coarse heterogeneous	Amorphous	Round	
Distribution	Linear	75–86%	67%	–	0%	0%	**67–68%**
	Segmental	100%	67%	–	0–20%	–	**38–74%**
	Grouped	36–75%	22%	7%	13–24%	0–11%	16–36%
	Regional	0%	0%	–	67%	0%	0–46%
	Diffuse	0%	–	–	–	–	0%
	Total	**53–81%**	29%	7%	13–26%	0–9%	

biopsy specimen to confirm that the morphology of the sampled calcifications is similar in appearance to your diagnostic imaging. Secondly, a biopsy marker should be placed after sampling to facilitate confirmation that the correct calcifications were sampled. In addition, the marker indicates the biopsy site should there be a need to excise the residual calcifications or surrounding tissue after histologic analysis. After completion of the procedure, a two-view mammogram (typically CC and ML views) should be obtained to confirm that the correct calcifications were sampled, and the biopsy marker is appropriately positioned.

If possible, separate your specimen samples that contain the calcifications and send the specimen radiograph with the samples to the pathologist. This will make it easier to identify the calcifications within the specimen, and your pathologist will thank you. When determining radiologic-pathologic correlation on a microcalcification specimen, the pathologist will first acknowledge that calcifications were seen within the specimen. The next step is then to determine if the histologic diagnosis matches your expectation based on the morphology of the calcifications. For example, if you biopsy round or amorphous calcifications and the pathology results return as "calcifications associated with fibrocystic change and benign ducts," this would be concordant as this is an expected finding. However, if you biopsy fine-linear branching calcifications and the same above results returns, this would be a discordant finding as the expectation would be for at least ductal carcinoma in situ (DCIS).

The overall positive predictive value (PPV) for biopsy for all microcalcifications for malignancy is approximately 21.7% [5]. When reviewing pathology results for concordance, one must ensure that microcalcifications are identified within the histologic specimen. The specific pathologic diagnosis should be consistent with the morphology of the microcalcifications on diagnostic imaging and one's pre-test probability. Correlation of the mammographic findings with the pathologic diagnosis allows determination of appropriate follow-up.

In the setting of a benign result for calcifications, the radiologist must first reassess if the specimen obtained was a satisfactory sample of the finding. The next question would be to assess if the pathology explains the imaging findings. Does the patient require surgical excision? After stereotactic-guided biopsy for calcifications, if the pathology is deemed benign and concordant, some institutions have the patient return in 6 months for a short-term follow-up mammogram with magnification views to ensure stability of the biopsy site [6]. At follow-up, if there has been no significant or worrisome change in the morphology or extent of calcifications, the patient can return to the routine annual screening mammography. If the biopsy result is a specific benign result and concordant with imaging, then a return to normal screening intervals can also be considered.

Architectural Distortions

With the rapid adoption of digital breast tomosynthesis (DBT), the detection and management of architectural distortions have come to the forefront. Architectural distortion is often subtle and can be masked by overlying breast tissue on conventional 2D digital mammography. The advent of DBT has shown an increased detection of architectural distortions nearly twice as many as conventional 2D digital mammography [7–9]. Architectural distortions are disruptions of the normal breast parenchymal architecture with "thin straight lines or spiculations radiating from a point with focal retraction, distortion, or straightening at the anterior or posterior edge of the parenchyma."

Like the above discussion about microcalcifications, biopsy marker should be placed after sampling. Post-biopsy digital breast tomosynthesis exam should be performed to ensure that the marker lies within in the architectural distortion. Imaging of the specimen radiograph can be optionally performed. In this scenario, you want to ensure that fibroglandular tissue is seen within the specimen and not just fatty tissue.

The positive predictive value (PPV) for malignancy of architectural distortion seen on DBT is as high as 50.7% [10]. These malignancies were most commonly attributed to invasive ductal carcinomas followed by invasive lobular carcinomas. The most common benign entity associated with architectural distortions are radial scars (see image 1); however, other less common benign diagnoses to be considered include stromal fibrosis, sclerosis adenosis, fat necrosis, or post-surgical scarring [11]. The patient's past surgical history, previous biopsies, and prior mammograms may assist in troubleshooting.

As with all other image-guided biopsies, pathology concordance must be considered carefully after histologic sampling of architectural distortions. Given the high PPV for malignancy, questions should again be asked specifically if there is a benign histologic diagnosis. Discordant radiologic-pathologic findings have been shown to have upgrade rates of up to 25% after surgical management. [10]

Ultrasound-Guided Biopsy

Using the BI-RADS lexicon makes characterization and risk stratification of malignant breast masses with ultrasound (US) more straightforward. According to the BI-RADS lexicon, a mass is defined as a "space-occupying lesion seen in two different projections" [12]. Most masses that are detected on mammography should be further evaluated with spot compression views and ultrasound so the characteristics of the mass can be further evaluated, i.e., shape, margins, and density. The use of appropriate BI-RADS lexicon

descriptors of breast masses can help dictate the BI-RADS assessment and recommendation. US mass descriptive features likewise include shape, margins, echo pattern, but also a description of mass orientation, boundaries, and posterior acoustic features.

The BI-RADS lexicon should be utilized appropriately as these terms are not only descriptive of the masses, but they also provide the radiologist with a level of suspicion. Certain descriptors favor benign or malignant diagnoses. The BI-RADS mass characteristics with the highest PPV for malignancy are those with an irregular shape and spiculated margins, 73% and 81%, respectively [13–15], The BI-RADS mass descriptors aid in risk assessment and determination of the appropriate BI-RADS category for all lesions from benign (B2) to highly suspicious (B5).

Determining radiologic-pathologic concordance after US-guided biopsy follows similar steps and procedures. First, according to ACR practice guideline, you want to ensure capturing pre-biopsy images of the mass and biopsy images demonstrating the biopsy device traversing the mass in question. As with other image-guided breast biopsies, a marker should be placed within the mass after sampling and correlated with post-biopsy imaging.

Certain questions should be asked when determining radiology-pathology concordance. Does the histologic diagnosis correlate with imaging findings? If a discrete mass was biopsied, do the histologic results provide a specific diagnosis? Did the biopsy of the well-circumscribed, oval mass reveal a discrete lesion like a fibroadenoma or a less specific diagnosis like benign breast tissue. If the results are discordant or unexpected, one should recommend either surgical excision or possibly re-biopsy depending on the pathology results and risk. If the histology correlates with the imaging findings as expected, then the patient can return to annual screening mammography if they are over the age of 40. Optional 6-month follow-up post-biopsy can be performed. If follow-up is pursued, the mass should be assessed by mammography and/or ultrasound to ensure stability. If the mass has grown in size or changed in morphology (becoming more suspicious in nature), appropriate action should be taken, typically surgical removal [6].

Management

For all lesions, the radiologist must assess the adequacy of the sample and evaluate for concordance. The pathologist should address if calcifications are seen and accounted for histologically, if that was the indication for biopsy. In the setting of a BI-RADS 4 lesion, a benign result is typically acceptable. However, specific diagnoses may not explain the imaging finding. If a discrete mass undergoes biopsy, then the resulting histology should be recognized to be a reasonable explanation. For results deemed *benign concordant*, a 6-month follow-up can be performed. If the lesion is stable at follow-up, then the patient can return to screening. If there is a change, for example, the calcifications increase in number or extent or the mass changes (enlarges or becomes more suspicious in its features), surgical excision is typically recommended. For results felt to be *benign discordant*, surgical excision is recommended. One could also consider repeat core-biopsy if there was a sampling issue at time of biopsy. For example, the lesion sampled under ultrasound is ultimately not felt to correlate with the initial mammographic finding and may undergo stereotactic core biopsy. Table 2, while not exhaustive, does present expected concordant benign and malignant results for specific imaging findings. For results that are *high-risk* or *malignant*, referral to a breast surgeon is recommended, and treatment is planned after appropriate staging as needed.

High-Risk Lesions

High-risk breast lesions are not malignant but do confer greater lifetime risk of the development of breast cancer. These included diagnoses of atypical ductal hyperplasia (ADH), lobular neoplasms (including lobular carcinoma in situ [LCIS] and atypical lobular hyperplasia [ALH]), papillary lesions, and radial sclerosing lesions (or radial scars). Historically, when these lesions were seen in pathology results, surgical excision was routinely recommended because of a potential upgrade rate to malignancy at time of excision. There is controversy now regarding the surgical and oncologic management for these lesions, such that

Table 2 Concordant benign and malignant pathology results

Finding	Concordant benign pathology results	Concordant malignant pathology results
Oval/round mass	Fibroadenoma, papilloma, adenosis, pseudoangiomatous stromal hyperplasia, focal fibrosis	Invasive ductal carcinoma (subtypes including papillary carcinoma, mucinous carcinoma, and medullary carcinoma) and phyllodes tumor
Architectural distortion	Radial scar, focal fibrosis	Invasive ductal carcinoma, invasive lobular carcinoma
Amorphous calcifications	Fibrocystic change, sclerosing adenosis, papilloma	Ductal carcinoma in situ (typically lower grade)
Heterogeneous calcifications	Fibrocystic change, fibroadenoma	Ductal carcinoma in-situ (typically higher grade)

excision is not always the answer. The best way to approach these lesions on radiologic-pathologic correlation is on a case-by-case basis. A multi-disciplinary conference and discussion between specialties including radiology, pathology, oncology, and oncologic surgery is recommended to discuss options and treatment plans. In some cases, surgical excision is pursued and in others close radiologic observation can also be pursued [16–19].

ADH can be associated with increased lifetime risk for development of breast cancer and has been shown to have variable malignancy upgrade rates (> 20%) at surgical excision [20–23]. On core biopsy specimens, it can sometimes be difficult for a pathologist to differentiate ADH from low-grade DCIS. Management algorithms have been proposed, and this is where discussion with your pathologist and surgical oncologist is critical. Some institutions have guidelines that ADH can be managed conservatively based on pathologic size and extent [24]. Given the variable upgrade rates cited in the literature, most cases of ADH should be surgically excised.

Lobular neoplasms have been treated similarly to ADH, given their association with increased lifetime risk of developing breast cancer and increased malignancy upgrade rates at surgical excision. Similar to ADH as well, the upgrade rates are highly variable in the literature [25–27]; therefore, lobular neoplasms were historically always excised. Newer literature, however, now suggests that upgrade rates can be low (< 5%) with small volume lobular neoplasia [26, 28, 29]. Additionally, if lobular neoplasia is the only diagnosis made on core biopsy with no other associated high-risk lesions (i.e., ADH, papillary lesions, complex sclerosing lesions), then excision may not be necessary.

Management of papillary lesions has also evolved over time. Historically upgrade rates at excision for papillary lesions were as high as 20% [30–32]; however, recent literature and larger scale studies are showing the rate may be as low as 10% [33–35]. Management is controversial and varied. Papillary lesions that show any associated atypia should be excised. The decision to excise a papillary lesion without atypia should be discussed in consensus with the management team and the patient. Factors such as size of the lesion, patient symptomatology, and breast cancer risk factors should be considered in the decision-making process. If excision is not pursued, then close imaging follow-up is reasonable.

Complex sclerosing lesions or radial scars were previously shown to have upgrade rates of up to 25% at excision, but newer studies report now rates closer to 10% [36, 37]. In general, given the often spiculated mass appearance on breast imaging, surgical excision should be pursued. Close imaging follow-up could be considered for small lesions or lesions that were completely removed at core biopsy with concordant radiologic-pathologic findings.

Conclusions

Image-guided, minimally invasive breast procedures are the mainstay of breast lesion diagnosis. The radiologist's role in establishing radiology-pathology concordance is paramount in this process. Understanding the differential diagnoses for common mammographic findings will help the reader recognize discordant biopsy results [38].

Declarations

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