

Specimen Radiography for MRI-Guided Biopsies

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Abstract

Background: Specimen radiography is important for the biopsy of breast microcalcifications, and MRI is limited in the detection of microcalcifications. It is unknown whether or not the presence of microcalcifications on MRI-guided biopsies is significant. **Purpose:** To determine whether specimen radiography of MRI-guided biopsy samples provides any added benefits in tissue assessment. **Materials and Methods:** This is an IRB-approved, HIPPA-compliant retrospective review of MRI-guided biopsy reports whose tissue underwent specimen radiography from 2010 to 2017. Pathology reports were queried to compare samples with and without calcium and reviewed to determine if calcifications correlated with the lesion of interest. If there was a correlation, the original MRI was reviewed. Final pathology reports were also reviewed if excision was performed. **Results:** A total of 889 patients ages 22 - 85 were included with 140 (15.7%, 140/889) containing calcifications. Of 140 specimens, 119 (85.0%, 119/140) cases separated the calcifications. A total of 41 (34.5%, 41/119) were malignant or high-risk lesions/atypia of which 15 (36.6%, 15/41) showed a higher-grade lesion in the specimen containing calcium. Out of these 15, 4 (26.7%, 4/15) were pathologically associated with calcium; however, pathologic diagnosis was not dependent on the presence of calcifications. All 4 were high-risk lesions and none were malignancies. MRI in these cases showed three enhancing masses and one non-mass enhancement. None were upgraded at excision. **Conclusion:** The presence of microcalcifications on MRI-guided biopsies does not aid in tissue assessment and does not impact pathologic diagnosis. Specimen radiography provides no added benefits in the setting of MRI-guided biopsies.

Keywords

MRI-Guided Breast Biopsy, Specimen Radiography, Microcalcifications, High-Risk Lesion, Breast Cancer, Upgrade

1. Introduction

Specimen radiography is commonly used during imaging-guided breast procedures, primarily during stereotactic-guided biopsies. Stereotactic-guided breast biopsies are often performed to obtain tissue containing suspicious microcalcifications best seen on mammography. The collected biopsy cores undergo intra-procedural radiography to determine the adequacy of sampling. At many institutions, the tissue is subsequently separated based on visualization of radiographically visualized calcium. Specimen radiography has been an important part of image-guided biopsy for many years. In 1975, Gallagher discussed this in the *American Journal of Clinical Pathology*, noting its importance when performing biopsies solely for the acquisition of X-ray detected abnormalities [1].

Numerous authors have reported the importance of specimen radiography including Margolin *et al.* in *Radiology* in 2004, who retrospectively evaluated core biopsy samples with and without calcium, finding that those with calcium had a higher likelihood of malignancy [2]. In 2013, Gumus *et al.* discussed breast microcalcifications obtained from stereotactic-guided biopsies in *The Breast Journal*, evaluating cores with and without calcium. Cores with calcium contained the lesion of interest in 99% of cases. Cores without calcifications contained the lesion of interest in only 87% of cases [3]. Samples containing tissue only (no calcium) changed diagnosis 1% of the time.

Calcium is one of the known mammographic manifestations of breast malignancy, often as an indicator of comedonecrosis within ducts, representing non-invasive malignancy [4]. Calcium can also be seen with invasive breast cancer, accompanying focal asymmetries or malignant masses [5]. While malignant calcium is the concern prompting biopsy, non-malignant calcium is the most common finding on the pathology of biopsied calcifications, often signifying fibrocystic changes, calcifying fibroadenomas, or sclerosing adenosis [6].

Calcifications can also be visible on ultrasound, though less conspicuous than on mammography. According to the Breast Imaging Reporting and Data System (BI-RADS) Atlas, calcifications are described on ultrasound as being intraductal, within a mass, or outside of a mass. Sonography provides a more comfortable and less time-consuming method of tissue acquisition for microcalcifications. Specimen radiography is crucial in these cases to ensure appropriate targeting and adequate tissue sampling [7].

Breast Magnetic Resonance Imaging (MRI) with gadolinium-containing contrast has the highest sensitivity of all imaging modalities for detecting breast cancer [8]. Although mammographically visualized calcifications are typically not

visualized on MRI, the detection of high-grade Ductal Carcinoma in Situ (DCIS) on MRI has been shown to be excellent with a sensitivity of almost 100%. However, small (often low-grade) DCIS lesions, while detectable as microcalcifications on mammography, may not display brisk enhancement and subsequently be occult on MRI [8] [9] [10].

On MRI, malignancy involves various degrees of contrast enhancement and can present in the form of a mass, non-mass enhancement, or focus of enhancement [11]. For lesions seen only on MRI, the biopsy is performed under MRI guidance, typically using a 9-gauge vacuum-assisted core needle biopsy system. Because contrast enhancement, not microcalcifications, is used to identify and characterize lesions, specimen radiography is not routinely performed during MRI-guided biopsies. It is unknown whether or not calcifications are associated with the MRI biopsy lesions of interest. Furthermore, it is unknown whether or not separating specimens with calcifications from MRI-guided biopsies provides any added benefits in the detection of malignancy.

2. Materials and Methods

This study was a HIPAA compliant, IRB-approved retrospective review of MRI-guided breast biopsies. The reports were queried from patients who had an MRI-guided biopsy and whose tissue sample underwent specimen radiography from January 1, 2010 to November 30, 2017. Patients included in the study were female patients ages 18 - 99 who underwent MRI-guided biopsy for any indication. Male patients, those under 18 years of age, and pregnant patients were excluded.

2.1. Specimen Radiography

When performing specimen radiographs of biopsy samples, the standard practice included transporting the specimen in saline to the mammography department where a Faxitron (Hologic, Marlborough, MA, US) machine was used to perform the specimen radiograph. Tissue was transported and managed by the mammography technologists trained to perform specimen radiography. Separation of tissue was performed per protocols for stereotactic biopsy. The technologist separated the core biopsy tissue samples into groups “with calcium” and “without calcium”, which was noted in the requisition to pathology.

2.2. Data Collection

At this institution, the pathology report is directly copied and pasted into an addendum to the biopsy report. MRI-guided biopsy reports containing pathology addendums were searched using terms to query for calcifications. Specimen radiographs of cases reporting calcifications were individually assessed to confirm samples were imaged with specimen radiography (*i.e.*, ensure report accuracy) if available (some purged from PACS archive) and the samples separated if containing calcifications. Chart review of pathology was performed of each calcium specimen. Data was recorded in a Microsoft Excel spreadsheet, listing the pathology of each biopsy (labeled “calcification” and “tissue”). Reports were queried to search

for the malignant and high-risk pathologies. High-risk was defined in this paper to include atypia, Complex Sclerosing Lesions (CSL), radial scars, papillomas, Lobular Carcinoma in Situ (LCIS), Atypical Lobular Hyperplasia (ALH), and Atypical Ductal Hyperplasia (ADH). Core biopsy specimens demonstrating malignancy or atypia were assessed to determine if the lesion was present in the specimen with or without calcifications. Of those cases with a higher-grade (“grade” in this manuscript refers to malignant potential. From high to low, malignancy > high-risk lesion > benign) lesion in the sample containing calcifications, the pathology report was further assessed for specific association between calcification and lesion. Furthermore, if calcifications were associated with the higher-grade lesion, the MRI was reviewed to assess for the specific characteristics of the suspicious biopsy target. Final pathology was also reviewed if excision was performed. **Figure 1** provides a flowchart delineating the steps in data gathering.

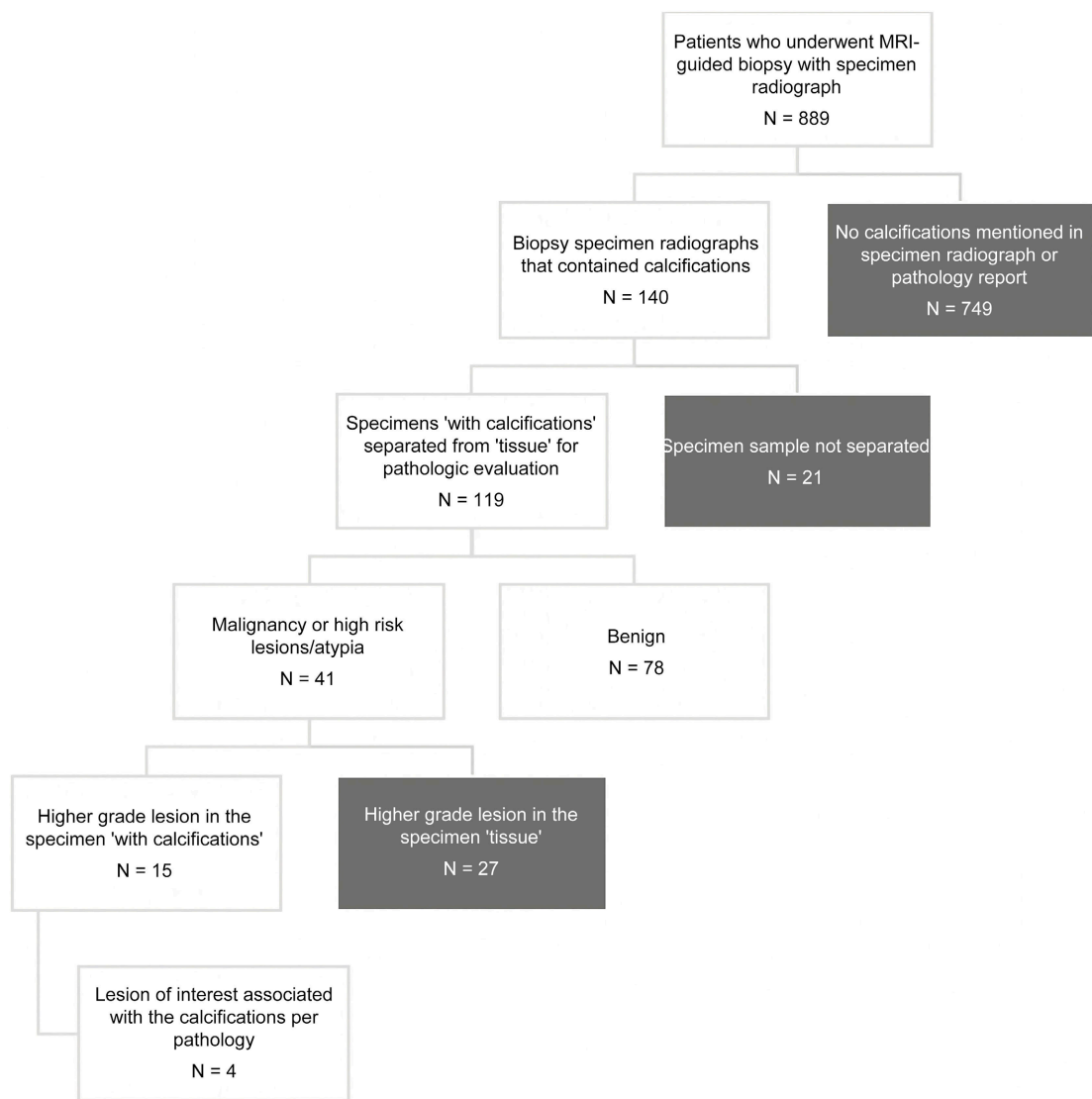


Figure 1. Flow diagram of report query and number of patients after each selection criteria.

3. Results

There were 889 specimen radiographs performed on unique patients undergoing MRI-guided biopsy samples from January 1, 2010 to November 30, 2017. Of these, 140 (15.7%, 140/889) biopsy specimens showed calcifications on radiography per the biopsy report. The remaining 749 (84.3%, 749/889) cases did not report calcium identified on specimen radiography. Out of the 140 specimens containing calcifications on radiography, 21 (15.0%, 21/140) did not undergo separation of the specimen containing calcifications, and were; therefore, excluded. For those 21 cases, presumably the pathologic evaluation was not altered in any way compared to those cases in which specimen radiography was not performed. In 119 (85.0%, 119/140) cases, the sample was separated into specimens with and without radiographically identified calcifications.

A total of 41 (34.5%, 41/119) specimens were determined to be malignant or high risk. Of those 41 cases, 15 (36.6%, 15/41) showed a higher-grade lesion in the specimen containing calcium compared to the corresponding specimen without calcium. Further assessment of the pathologic report was then performed to assess for the association between the higher-grade lesion of interest and microcalcifications. Out of the 15 cases, only 4 (26.7%, 4/15) of the lesions were found to be associated with radiographically visualized calcium per the pathology report (no additional levels taken). The pathology reports for the 11 (73.3%, 11/15) other cases described the calcifications as associated with concomitant benign lesions in the specimen. The pathology of all 15 cases of MRI-guided biopsies with mammographically visible calcium on specimen radiography is presented in **Table 1**.

Table 1. Cases with higher-grade lesion in the specimen with calcifications than without calcifications (n = 15).

Age	Pathology with calcifications	Pathology without calcifications	Calcifications associated with higher grade lesion
41	RS	Benign	NO
44	ADH	Benign	YES
45	LCIS	Benign	NO
47	Papilloma	Benign	NO
51	IDC Tubular	CSL, FEA	NO (calcifications with FEA)
53	Papilloma	Benign	NO
57	Papilloma	Benign	YES
58	IDC	DCIS	NO (calcifications with DCIS)
58	ALH	Benign	NO
62	CSL/RS	Benign	YES
65	DCIS	Benign	NO
65	ALH, Papilloma	ALH	NO
67	Papillomatosis	Benign	YES
71	ILC	Benign	NO
72	DCIS	Benign	NO

Four Specific Cases

Specific case review was performed for the four cases (case 1 including **Figure 2** and **Figure 3**, case 2 including **Figure 4** and **Figure 5**, case 3 including **Figure 6**, and case 4 including **Figure 7**) where calcifications on specimen radiography were associated with the higher-grade lesion of interest. MRI examination showed one case with clumped non-mass enhancement (**Figure 2**) and three cases involving masses (**Figure 4**, **Figure 6**, and **Figure 7**). Specimen radiography was purged from the Picture Archiving and Communications System (PACS) archive for two cases (cases 3 and 4). Sizes of the MRI findings of interest ranged from 6 to 20 mm. The pathology of all four cases was identified without the need for obtaining deeper levels. All four cases went to surgery and none were upgraded at excision.

Case 1 (**Figure 2**, **Figure 3**) was a 67-year-old female with right breast Invasive Ductal Carcinoma (IDC) presenting for evaluation of extent of disease. MRI



Figure 2. Case 1: A. T1 Contrast-Enhanced (CE) Fat-Saturated (FS) subtraction sagittal image demonstrated clumped segmental non-mass enhancement in the upper inner quadrant right breast middle depth (oval); B. Axial T1 FS CE MRI showing clumped NME in the upper inner right breast (oval); C. Entire specimen radiograph from MRI-guided biopsy before tissue separation. One specimen contained calcification (circle); D. Digitally magnified image of the specimen containing punctate microcalcifications (circle).

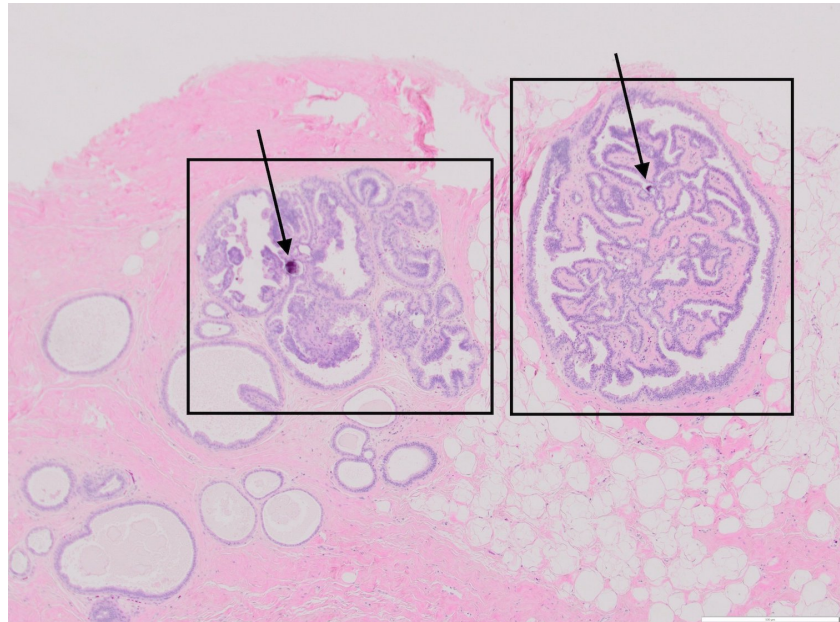


Figure 3. Case 1: Intraductal papillomas (squares) with associated microcalcifications (arrows). Hematoxylin & eosin, original magnification X40.

was performed (**Figure 2(A)**, **Figure 2(B)**) and clumped segmental non-mass enhancement (ovals) in the ipsilateral breast was biopsied under MRI guidance. Core samples underwent specimen radiography demonstrating microcalcifications (**Figure 2(C)**, **Figure 2(D)**). The specimen with calcification was separated and histology (**Figure 3**) showed papillomatosis (rectangles) with associated microcalcifications (arrows). Specimen without calcifications (not shown) yielded fibrocystic change, Usual Ductal Hyperplasia (UDH), and benign breast tissue. Mastectomy was performed and pathology (not shown) noted papillomatosis with other benign tissue. No malignancy was identified.

Case 2 (**Figure 4**, **Figure 5**) was a 62-year-old female diagnosed with invasive tubular carcinoma in the left breast. She presented for evaluation of extent of disease, and in the right breast on MRI (**Figure 4(A)**, **Figure 4(B)**) a mass (circles) was suspicious and recommended for biopsy. Specimen radiography (**Figure 4(C)**, **Figure 4(D)**) yielded one specimen with a single punctate calcification (circles). Pathology (**Figure 5**) in the specimen with calcifications showed complex sclerosing lesion and radial scar associated with microcalcifications (arrows). Specimen without calcifications (not shown) demonstrated sclerosing adenosis. Pathology from excision (not shown) demonstrated fibrocystic changes with UDH, apocrine metaplasia, and sclerosing adenosis. No malignancy or atypia was found.

Case 3 (**Figure 6**) was a 44-year-old female with left breast IDC presenting for MRI to evaluate extent of disease. An ipsilateral oval mass was identified and recommended for biopsy (circles). Pathology of the specimen with calcifications showed ADH arising in a background of FEA and associated calcifications. Pathology of specimen without calcifications showed benign breast tissue. Specimen

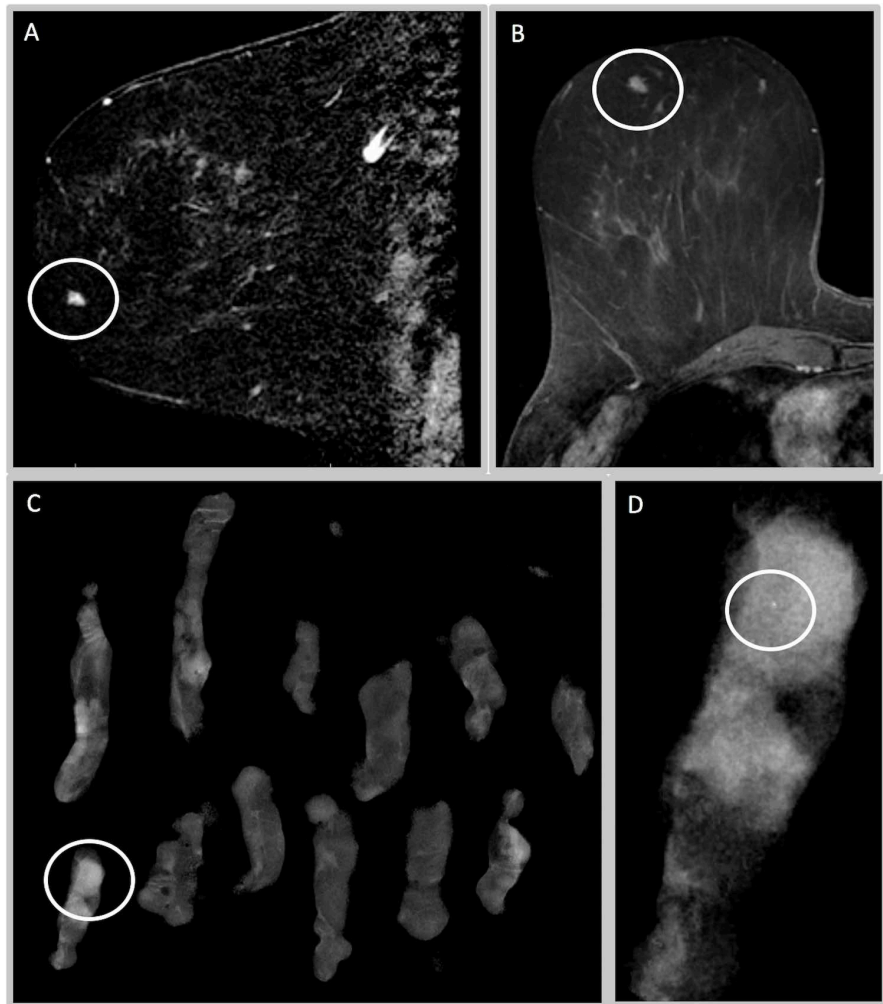


Figure 4. Case 2: A. Sagittal T1 CE FS subtraction MRI of the right breast showing an irregular mass in the lower outer quadrant anterior depth (circle); B. Axial T1 FS CE MRI demonstrating the mass (circle) in the right breast; C. Entire specimen radiograph from MRI-guided biopsy before tissue separation with one core containing calcifications (circle); D. Digitally magnified image of the specimen containing a punctate microcalcification (circle).

radiography was purged from PACS archive and unavailable. The patient ultimately underwent bilateral mastectomy which demonstrated focal atypical hyperplasia at this site.

Case 4 (**Figure 7**) was a 57-year-old female with a remote history of right breast cancer presenting for MRI after having persistent pain in the right breast. An irregular mass in the left breast (A) was suspicious and underwent MRI-guided biopsy (B). Pathology of the specimen with calcifications showed intraductal papilloma with associated microcalcifications. Pathology of specimen without calcifications showed UDH. Specimen radiography was purged from the PACS archive and was unavailable. Excision was performed showing intraductal papillomatosis, fibrocystic change, and microcalcifications with benign ducts. No malignancy was identified.

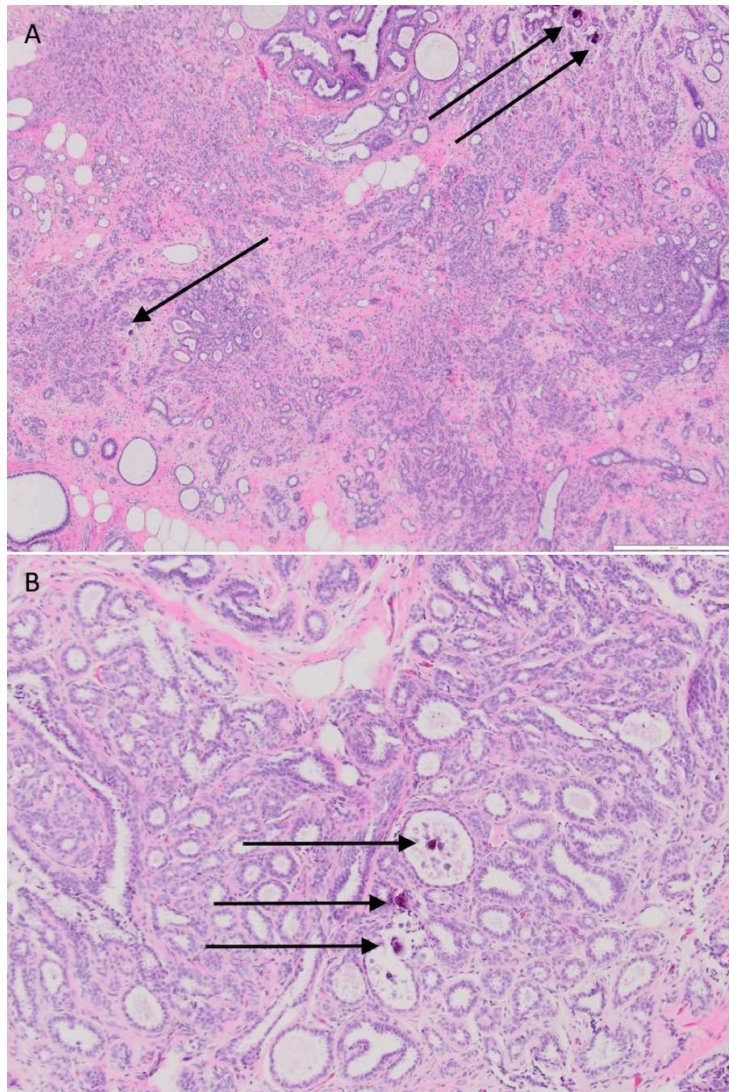


Figure 5. Case 2: A complex sclerosing lesion with associated microcalcifications (arrows). Hematoxylin & eosin, original magnification X40 (A) and X100 (B), respectively.

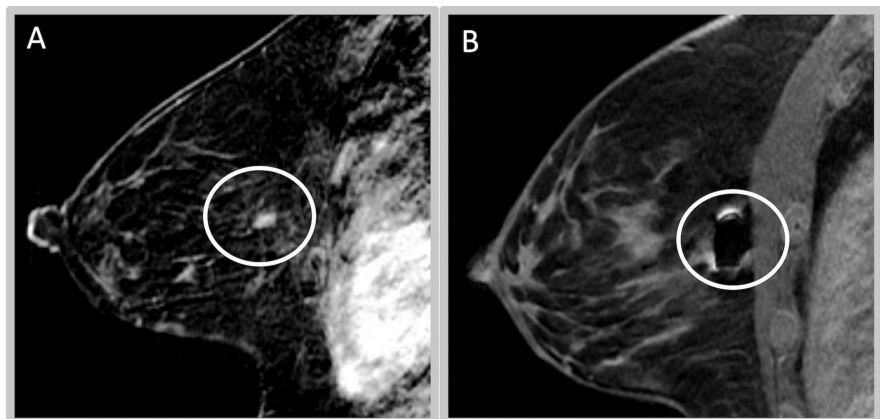


Figure 6. Case 3: A. Sagittal T1 FS subtraction CE MRI with an irregular mass in the left central breast posterior depth (circle) and biopsy image (B) showing the site appropriately sampled with air at the expected location (circle).

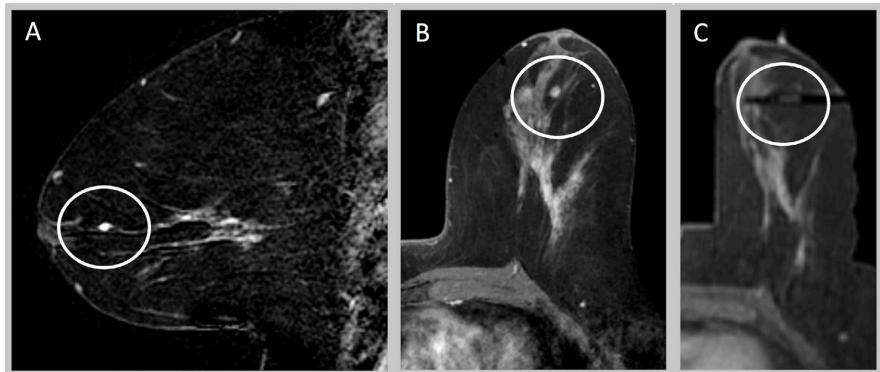


Figure 7. Case 4: A. Sagittal T1 CE FS subtraction MRI demonstrated an oval mass in the left breast subareolar anterior depth (circle) also circled on non-subtraction FS T1 CE axial MRI (B). MRI-guided biopsy axial T1 CE image (C) demonstrates the biopsy needle in appropriate location (circle).

4. Discussions

The presence of microcalcifications in specimens obtained during MRI-guided biopsies did not lead to an upgrade in any patients. Although microcalcifications are known to be indicative of malignancy or atypia on mammography, their presence in specimens from MRI-guided biopsies did not identify any additional disease. In four cases, specimen radiography demonstrated calcium that was associated with a higher-risk lesion than tissue not containing calcium. None of these cases involved malignant diagnoses but yielded high-risk lesions only. Furthermore, none of the high-risk lesions associated with calcifications found during MRI-guided biopsies were upgraded at the time of excision.

It is possible that indicating “calcification” on a requisition and separating the sample may aid a pathologist in finding a lesion that otherwise may have been overlooked. It is uncertain if the four lesions in this study would have been detected without the aid of specimen radiography. However, given that no additional levels were performed in these four cases and the pathologic lesion of interest was far more conspicuous than the mammographically visible or histologically visible calcifications, the lesion of interest would presumably have been discovered regardless of specimen separation.

There are several limitations to this study. This was a single institution, retrospective study at a tertiary care academic medical center. The patient population is inherently more enriched with high-risk patients and those with known malignancy; however, this is a common population of patients undergoing MRI-guided biopsies. Also, not all specimen radiography was still available for image review (some purged from PACS archive). Thus, the study is dependent on the accuracy of the radiologists’ reports. The study was also dependent on pathology requisition from the radiologist and pathology reports as all 889 cases were not individually reviewed. Specimen reports also occasionally listed “density” (indicating that an area of more dense tissue was seen in a portion of one of the cores) in the request. This was not investigated. Specimens with higher-risk le-

sions in the sample containing “tissue” rather than the sample containing calcium were not investigated. Finally, the specimen radiograph tissue separation is not evaluated by the radiologist as the separation of tissue is performed by technologists in a separate location from the MRI biopsy.

This investigation sought to assess whether or not performing specimen radiography on MRI biopsy samples was warranted. Arguments against specimen radiography of MRI biopsy tissue include the significant technologist time to separate samples and appropriately label containers, use of a mammography room or Faxitron machine to X-ray, and cost of performing the specimen X-ray. Furthermore, the pathology request for evaluating calcium in a biopsy performed for contrast enhancement is questionably misleading to the pathologist. Future investigations could further use data to assess mammograms performed prior to biopsy to evaluate if microcalcifications associated with high risk or malignant lesions could have been seen retrospectively.

In conclusion, obtaining specimen radiography for certain breast biopsies is helpful to a pathologist during histologic evaluation; however, for MRI-guided biopsies, specimen radiography adds more time and labor to the procedure without adding significant value. The potential benefit of identifying high-risk lesions associated with calcium hinges on altering patient management. Unless the pathologist was influenced by the labelling of the specimen, it is likely these lesions would have been found without specimen radiology. The time, cost, and work hours spent performing specimen radiology are sizable in comparison to its demonstrated value. Based on results from this study, specimen radiography is not a recommended routine step during MRI-guided biopsies.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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