

Sclectrosing adenosis of the breast: radiologic appearance and efficiency of core needle biopsy

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PURPOSE

To examine the mammography and ultrasonography findings of patients who have a final histopathological diagnosis of sclerosing adenosis after breast biopsy, and to evaluate the follow-up results of patients who underwent core needle biopsies.

MATERIALS AND METHODS

Seventy-six of the 723 patients who underwent breast biopsy in our institution were diagnosed with sclerosing adenosis on histopathological examination. Mammography and ultrasonography findings from these 76 lesions were analyzed retrospectively. Thirty-seven of these lesions were sampled by image-guided core needle biopsy; the remaining lesions were excised surgically. Mammograms and ultrasound images of the lesions were re-evaluated, and the post-biopsy medical records of these patients were evaluated.

RESULTS

Sclectrosing adenosis was the main diagnosis in 41 patients and the complementary diagnosis in 35 patients. Among the first 41 lesions in which sclerosing adenosis was the main diagnosis, there were 18 (44%) mass lesions, 16 (39%) microcalcification clusters, two (5%) lesions with asymmetrical opacity, three (7%) lesions with architectural distortion, and two (5%) lesions with focal acoustical shadowing that was only detected by ultrasonography. No alterations suggesting malignancy were noted during the follow-up examinations of 35 patients who underwent core needle biopsy.

CONCLUSION

Sclectrosing adenosis is a benign proliferative disease of the breast that can be confused with malignancy on clinical, radiological, and even histopathological examination. There is no typical radiological criterion for diagnosis. Core needle biopsy or excisional biopsy can be used, depending on the lesion's characteristics. Core needle biopsy can be the first step in the diagnosis of sclerosing adenosis.

Key words: • breast • mammography • breast ultrasound • sclerosing adenosis

Sclectrosing adenosis is a benign proliferative disease of the breast that may present a broad spectrum of imaging findings, from minimal lobular changes to macroscopic mass lesions. The main histopathological alterations of the terminal ductal lobular unit present as a widening and distortion of lobules, an increased number of acini and stromal fibrosis. The lesion is called an “adenosis tumor” or “nodular sclerosing adenosis” if it presents as a tumoral mass. Sclectrosing adenosis is present in 12% of benign and 5%–7% of malignant specimens on histopathological examination (1). The disease has an increased incidence among reproductive-age and perimenopausal women, especially between 35 and 50 years of age. The clinical, radiological, and histopathological properties of sclerosing adenosis may resemble the masses that are usually associated with malignancy, which is the factor responsible for the clinical significance of the disease (1–7). Mammography and ultrasonography findings in sclerosing adenosis have only rarely been described in the literature (8–10). In asymptomatic patients, various findings such as mass lesions, microcalcifications, focal asymmetrical opacities and architectural distortions can be detected at mammography. If there is a palpable mass, a tumoral mass lesion can also be detected by both mammography and ultrasonography. The aim of this study is to review the mammography and ultrasonography findings of sclerosing adenosis patients, to correlate these findings with histopathological examinations and to evaluate the follow-up period of patients who underwent core needle biopsy.

Materials and methods

Our study is a retrospective review of data obtained from the clinical, radiology, and pathology archives of our institution. An application was not submitted to the ethical committee.

The medical records of 723 patients who underwent breast biopsy at our institution (14G core needle biopsy or excisional biopsy) between 2000 and 2009 were analyzed retrospectively. The clinical, radiological, and histopathological findings of 76 patients with a final diagnosis of sclerosing adenosis were re-evaluated. The mammograms and ultrasound images of these patients were re-examined by two radiologists who were experienced in breast imaging. Cranio-caudal and mediolateral oblique mammograms of both breasts were obtained using Mammoray 4000 equipment (Philips Medical Systems, Eindhoven, The Netherlands). Ultrasonography examinations were conducted with a 7.5-MHz linear array transducer mounted on an EUB 420 ultrasound unit (Hitachi Medical Systems, Tokyo, Japan) and with a 6- to 12-MHz broadband transducer mounted on an Aplio 80 (Toshiba Medical Systems, Otawara, Japan) ultrasonography unit. Thirty-seven of the 76 lesions were sampled by ultrasound-guided 14G core needle biopsy

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with an automated biopsy gun (Bard Magnum, Covington, Georgia, USA), and the remaining lesions were excised surgically. Nineteen patients with microcalcifications on mammography, 11 patients who had a spiculated mass lesion or architectural distortion and one patient with an asymmetric opacity underwent needle-wire localization procedures with mammography or ultrasonography, and these lesions were excised. Complete excision was verified with specimen mammography or ultrasonography. Eight palpable mass lesions were excised without localization. The remaining 37 lesions were sampled with ultrasound-guided core needle biopsy. Two of the 37 lesions that were diagnosed by core needle biopsy had undergone excisional biopsy. There was radiological-histopathological discordance in one case, and the other was a case of atypical ductal hyperplasia. The diagnosis was confirmed in both cases. Lesions were classified according to morphological properties and Breast Imaging Reporting and Data System (BI-RADS) criteria (11). All surgical or biopsy specimens were re-evaluated by a pathologist who was experienced in breast pathology. Imaging findings were compared to histopathological results.

Results

The average age of the 76 patients in this study group was 48±5 years old (range, 32–64 years). The average lesion diameter was 13±7 mm (range, 4–41 mm). Sixteen lesions (21%) were palpable on physical examination. There was a family history of breast cancer in 15 (20%) patients. The primary complaint of 14 (18.5%) patients was breast pain (uni- or bilateral, focal or diffuse).

Sixty-nine of the 76 lesions were detected by mammography. The distribution of the lesions was as follows: 25 (36%) mass lesions, 21 (30%) microcalcifications, 15 (22%) asymmetrical opacities and eight (12%) architectural distortions. The remaining seven lesions were detected by sonography: four were mass lesions and three were cases of acoustical shadowing. Twenty-three of the 25 mass lesions detected with mammography and three mass lesions detected only with ultrasonography were solid lesions. The remaining masses were complex cystic lesions (two with a solid component, one with

irregular wall thickening). Only seven out of 15 asymmetrical opacities were visible with ultrasonography as focal acoustical shadowing and/or focal heterogeneity. Seven of the eight architectural distortion findings did not show any evidence of abnormality on ultrasonography. The remaining patient had a simple 4 mm-diameter cyst in a distorted area of the ultrasound. In total, 41 lesions were sonographically visible.

Sclerosing adenosis was the main diagnosis in 41 patients. The distribution of these lesions was as follows: 18 (44%) mass lesions, 16 (39%) microcalcifications, two (5%) focal asymmetrical opacities, three (7%) architectural distortions and two (5%) cases of focal acoustical shadowing at ultrasonography (Figs. 1–3). These results are summarized in the Table. Of these 41 lesions, 17 were diagnosed by core needle biopsy. In the remaining 35 patients, sclerosing adenosis was present in several benign (31 patients) and malignant (four patients) lesions. Benign lesions included fibrocystic alterations (ductal hyperplasia, cystic changes, and apocrine metaplasia) in 15 (43%) patients, fibroadenomas in eight (23%) patients, intraductal papilloma in five (14%) patients, and atypical ductal hyperplasia in three (9%) patients. Of the malignant cases, there were two (6%) cases of ductal carcinoma in situ (DCIS) and two (6%) cases of invasive ductal carcinoma with sclerosing adenosis as the

minor component. Two spiculated lesions visualized on mammography and sonography were diagnosed as invasive ductal carcinoma as the major component. One irregularly contoured mass lesion and one clustered pleomorphic microcalcification were diagnosed as DCIS as the major component. Results are summarized in Fig. 4.

No alterations suggesting malignancy were noted during the follow-up examinations of 35 core needle biopsy patients and no repeat biopsies were performed. During follow-up, only one of the patients who had an excisional biopsy developed a new suspicious lesion. This lesion was seen as a nodular density on mammograms and as a hypoechoic focus on ultrasound examination of the previous biopsy site. The previous diagnoses of this case were sclerosing adenosis and fibrocystic change. Repeat biopsy resulted in a diagnosis of focal fibrosis.

Discussion

Sclerosing adenosis is a benign proliferative breast disease that presents with acinar, myoepithelial, and connective tissue changes in the terminal ductal lobular unit and is frequently seen in the perimenopausal period. On histopathological examination, sclerosing adenosis may be confused with invasive carcinoma because of stromal fibrosis and elastosis, either micro- or macroscopically. Smooth muscle actin dye is used to demonstrate the patency

Table. Radiological findings of cases with histopathologically diagnosed sclerosing adenosis as the major component

Lesion	Number of lesions	Mammography	Ultrasonography
Mass (n=18)			
Well-defined	10	9	10
Ill-defined	6	5	6
Spiculated	2	2	2
Microcalcification (n=16)			
Clustered amorphous	7	7	1
Clustered punctate	5	5	0
Clustered pleomorphic	2	2	0
Diffusely pleomorphic	1	1	0
Diffusely punctate	1	1	0
Focal architectural distortion	3	3	1 ^a
Focal asymmetric opacity	2	2	1 ^a
Focal acoustic shadowing on US	2 ^a	0	2
Total	41	37	23

^aFocal acoustic shadowing and/or focal heterogeneity without a mass lesion with ultrasonographic examination.

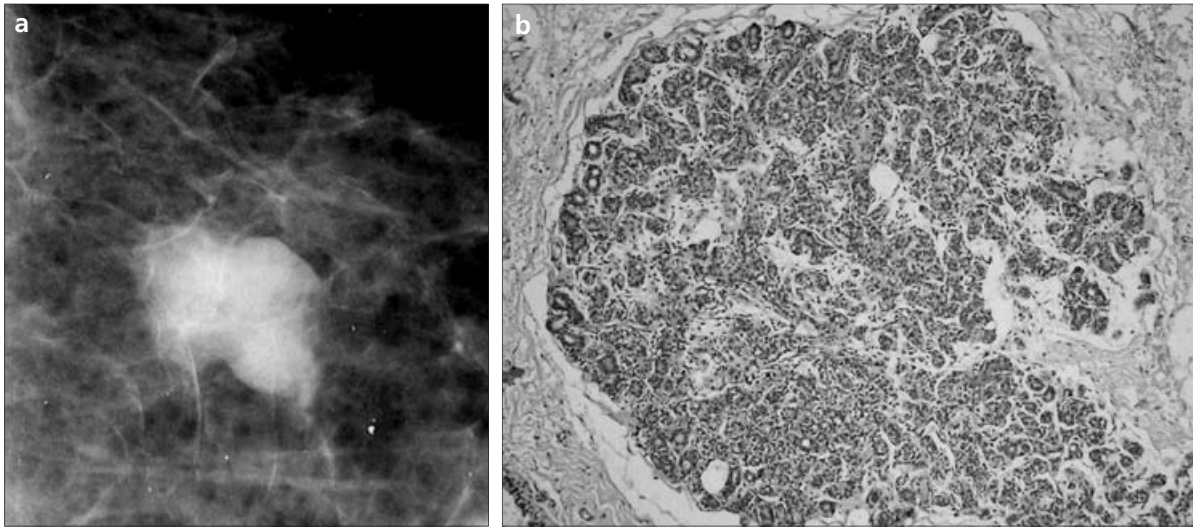


Figure 1. a, b. Mass lesion in a 46-year-old woman who presented with thickening in the left upper outer quadrant. The spot craniocaudal mammogram (a) shows a lobular mass lesion with a partially irregular margin. The photomicrograph (b) shows increased numbers of glands, some cystic enlarged glands at the periphery and centrally located fibrosis ($\times 100$, hematoxylin-eosin).

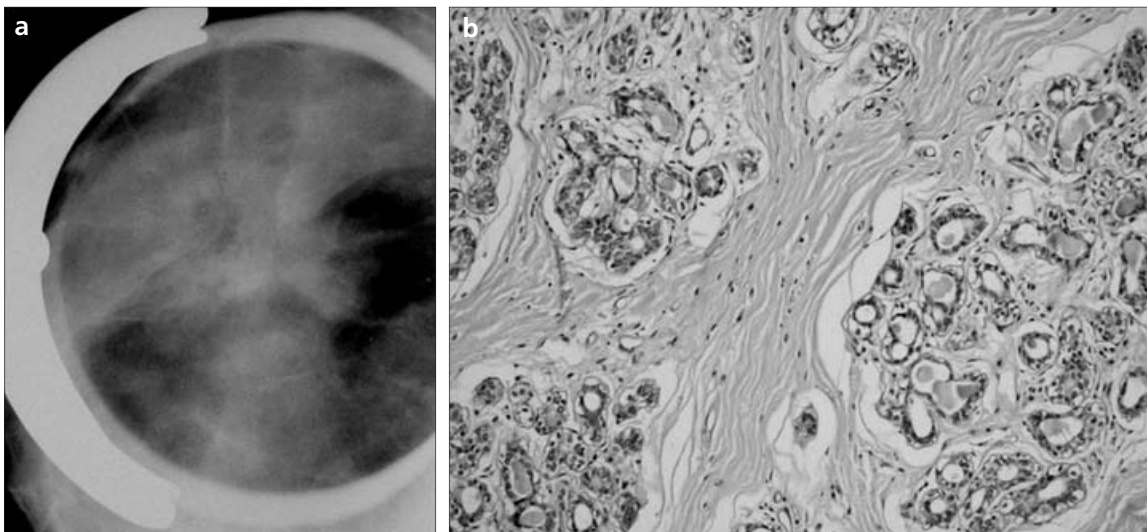


Figure 2. a, b. Architectural distortion in a 41-year-old asymptomatic woman with no palpable abnormality on physical examination. The spot craniocaudal mammogram (a) shows an architectural distortion with a dense center. The photomicrograph (b) shows mild cystic enlargement in mammary glands, intraluminal eosinophilic secretions, and fibrosis ($\times 100$, hematoxylin-eosin).

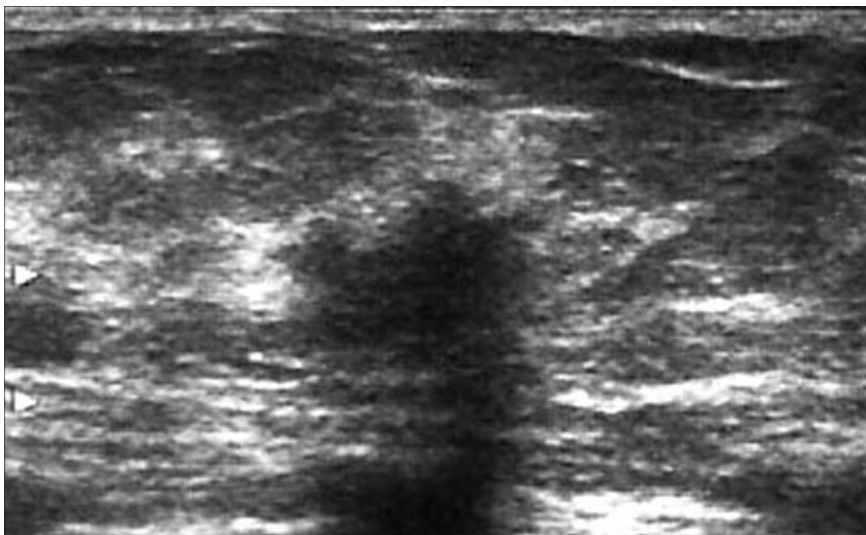


Figure 3. Ultrasonography of a mass lesion with acoustic shadowing in a 48-year-old asymptomatic woman with no palpable abnormality on physical examination. Mammography was negative because of extremely dense breast tissue (not shown here). The transverse ultrasonography shows an irregularly contoured mass lesion with acoustic shadowing. The final diagnosis was sclerosing adenosis.

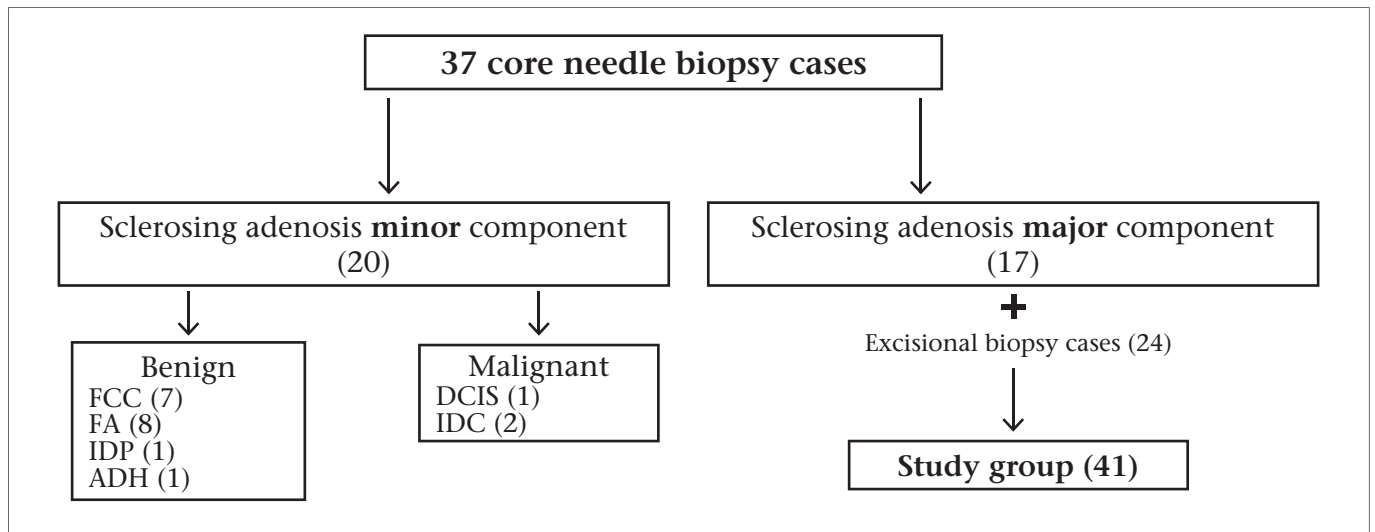


Figure 4. Diagram of core needle biopsy cases and study population. FCC, fibrocystic changes; FA, fibroadenoma; IDP, intraductal papilloma; ADH, atypical ductal hyperplasia; DCIS, ductal carcinoma in situ; IDC, invasive ductal carcinoma.

of the myoepithelium for differential diagnosis. In addition, the demonstration of preserved lobule architecture by high-magnification microscopy is a useful adjunct in differentiating benign proliferative breast disease from invasive carcinoma (1–7). Sclerosing adenosis can also be clinically or radiologically confused with invasive carcinoma. Physical examination may reveal a firm mass. Various findings suggesting malignancy may be observed upon radiological evaluation (9, 10, 12, 13).

Sclerosing adenosis is not considered a pre-malignant lesion. On the other hand, in a study of 349 patients, Jensen et al. (4) found a 1.7- to 3.7-fold increase in breast carcinoma risk in patients with sclerosing adenosis. In the same study, sclerosing adenosis was found to be correlated with premenopause, a positive family history of breast carcinoma and atypical ductal hyperplasia. Lobular carcinoma in situ (LCIS) is another relatively frequent condition found with sclerosing adenosis, and in this case, differentiating the lesion from invasive carcinoma is much more problematic (3–7). None of the patients in our study group had atypical lobular hyperplasia or LCIS on histopathological examination. Sclerosing adenosis was the accompanying diagnosis in two cases of invasive ductal carcinoma and two DCIS cases. All of these patients were premenopausal and did not have a family history of breast carcinoma. In our study, 5.3% of sclerosing adenosis cases were asso-

ciated with malignancy. This finding is interesting, and further investigation is needed to determine whether it is incidental or relevant.

In their study of 43 patients with sclerosing adenosis (all diagnosed by excisional biopsy), Günhan-Bilgen et al. (9) reported the following radiological findings and frequencies: microcalcification (56%), mass (12%), focal asymmetrical opacity (7%) and focal architectural distortion (7%). Gill et al. (10) evaluated 33 patients with sclerosing adenosis. A total of 18 (54.5%) patients presented with a mass lesion and the remaining 15 (45.5%) presented with microcalcifications. In our study, sclerosing adenosis was the primary diagnosis in 41 patients, and the most frequent lesions were masses (44%). There is a wide spectrum of radiological findings for sclerosing adenosis in the literature. The contour properties of mass lesions may vary from well-defined to irregular and spiculated forms. According to a recent study of the mammographic and ultrasonographic findings of nodular sclerosing adenosis (8), 70% of lesions had well-defined contours, whereas the remaining lesions were irregular. On the other hand, 80% of the mass lesions had irregular contours and only 20% of them had well-defined contours in a study by Günhan-Bilgen et al. (9). There were 17 mass lesions among the sclerosing adenosis series reported by Gill et al. (10), and 59% of them had well-defined contours, 29% had irregular contours and 12% had partially irregular con-

tours. Of the 18 masses in our study with a diagnosis of sclerosing adenosis as the major component, 10 (55.5%) were well-defined and eight (44.5%) had irregular contours. Five of the 13 irregularly contoured masses had internal coarse calcifications. Several recent studies (8, 10) have also described these coarse calcifications in mass lesions on mammograms. Contour irregularity is related with local invasion, periductal fibrosis and desmoplastic reactions in malignant lesions and is associated with fibrosis and stromal sclerosis in benign masses. Radiologically detected contour irregularity of sclerosing adenosis masses reflects stromal sclerosis, and this property cannot be used to differentiate benign masses from malignant masses.

In the available literature, the most frequent microcalcification patterns associated with sclerosing adenosis are amorphous or pleomorphic punctate clusters and scattered amorphous punctate calcifications (4, 9, 10, 12–14). Clustered amorphous, pleomorphic and punctate calcifications were the most frequent types found by Jensen et al. (4). In our study, 80% of the microcalcifications were in clusters, and the remainder were scattered diffusely. The microcalcification patterns in our study also show properties attributable to the “probably benign” or “high probability of malignancy” categories, which is compatible with findings in the literature (11, 15). No microcalcification patterns suggesting a “high probability of malignancy”, such as segmental-linear,

linear, or irregularly branching patterns, were observed.

Focal architectural distortion and radial sclerosing lesions on mammography are mostly associated with malignancy. Sclerosing adenosis, fat necrosis, radial scars and surgical scars are the benign entities in which these spiculated lesions may be seen. Franquet et al. (16) found that central portions of these lesions were radiodense in cases of malignancy and less radiodense or radiolucent in benign lesions. However, several other (17, 18) studies have reported that this finding is unreliable for differential diagnosis. Biopsy is the only method that can be used for the differential diagnosis of an architectural distortion because of the gross overlap between benign and malignant entities. In our study, there were eight lesions that presented as architectural distortions, three of which were cases of pure sclerosing adenosis.

The role of ultrasonography in the diagnosis and description of lesions in extremely dense breasts (as diagnosis of a mass lesion is almost impossible by mammography) is well recognized. Focal acoustic shadowing is described as a focal shadowing area without a mass lesion on ultrasound. The lesion should be visible in at least two ultrasound planes, and lesion configuration should be the same when the patient is in different positions. Focal acoustic shadowing is a rare but useful finding for the radiologist and has also been described by Günhan-Bilgen et al. (9). In our experience, focal acoustic shadowing is not a specific criterion for sclerosing adenosis because this finding can be observed in various benign and malignant diseases of the breast.

According to Stavros (19), various ultrasonography findings can accompany sclerosing adenosis. Ultrasonographically detectable lesions are seen when the diameter of the terminal ductal lobular unit exceeds 5 mm. Lesions can be detected as microlobulated, angulated or spiculated mass lesions. Tumoral adenosis may be undefined because of peripheral fibrous tissue or it can be apparent if surrounded by isoechoic fat tissue. Stavros recommends the use of vocal fremitus to differentiate similar echogenicities that are indistinct from one another in an isoechoic area, a finding that can be associated with several benign or ma-

lignant conditions. This type of evaluation was not done in our study.

Among the 35 patients in this study with sclerosing adenosis as the complementary diagnosis, the most frequent benign conditions were fibrocystic changes, fibroadenoma and intraductal papilloma. Fibroadenoma and intraductal papilloma were also the most frequent benign diagnoses in the series reported by Gill et al. (10). Fibroadenomas are termed "complex fibroadenomas" if they contain a sclerosing adenosis focus. Dupont et al. (20) reported a 3.1-fold increase in malignancy risk in patients who have a complex fibroadenoma. Post-biopsy clinical and radiological follow-up should not be impeded in these patients.

In summary, sclerosing adenosis is a benign condition that does not have any typical signs to aid in radiological diagnosis. Sclerosing adenosis can occasionally mimic in situ or invasive carcinoma. The selection of biopsy methods and post-procedural management is very important because of histopathological tissue variations, increased atypical cellularity and the risk of malignancy. As far as we know, breast lesion biopsies are frequently performed in BI-RADS 4 lesions, and 60%–80% of these lesions are actually benign lesions (21). Therefore, the aim of the biopsy should be to obtain the best sampling of the lesion with the least invasive technique. Core needle biopsies should be adequate to avoid overlooking possible malignant alterations. The biopsy type, the volume of the sample and the experience of the operator can all affect the accuracy of a core needle biopsy (21–24). Core needle biopsies can be sufficient for the diagnosis of small spiculated lesions such as focal architectural distortions or radial sclerosing lesions (25, 26). In this study, all microcalcification clusters and most of the focal architectural distortion areas and spiculated lesions were surgically excised after needle wire localization to guarantee sample adequacy and to prevent possible problems related to poor localization. All masses, most asymmetrical opacities and lesions with focal acoustical shadowing at ultrasonography were sampled by core needle biopsy. During follow-up, none of these lesions demonstrated any alterations compatible with malignancy, and no repeat biopsies were necessary.

Imaging-guided core needle biopsy of the breast is a widely used procedure for the diagnosis of masses or lesions detected on radiological evaluation. The procedure provides reliable histopathological results and is also cost-effective and minimally invasive. In this study, we observed 100% diagnostic accuracy of the 14 G core needle biopsy. The false negative rate of the core needle biopsy varies from 0.3% to 3.2% (mean, 2.8%) in the literature. Wire localization procedures have a similar false negative rate (0%–8%; mean, 2%) (27–30).

Further evaluation in these cases was determined according to a collective decision made during multi-disciplinary meetings between the surgery, pathology, and radiology departments in our institution. As a result of our increased experience with this technique, we currently use core needle biopsy for microcalcification clusters and architectural distortions more often than in the past. Our study precludes the generalization of the accuracy of core needle biopsies for the diagnosis of sclerosing adenosis because not all patients were sampled by this method. However, we can state that core needle biopsies minimize the need for surgical excision of sclerosing adenosis lesions in selected patients. Core needle biopsies can be the first step toward the diagnosis of sclerosing adenosis. As in other diagnostic situations, if malignancy cannot be excluded, if there is discordance between radiological and histopathological findings or if atypical cells are present, excisional biopsy should be the next step to complete the evaluation.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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