Stromal Fibrosis of the Breast

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OBJECTIVE. The purpose of this retrospective study was to describe the imaging features of stromal fibrosis of the breast and to determine the false-negative rate (number of cancers missed) at percutaneous biopsy.

MATERIALS AND METHODS. Between January 1997 and October 1999, 1095 imaging-guided core biopsies were performed. Patients were included in our study if stromal fibrosis was the predominant histologic finding. Cores adjacent to previous excisional biopsies or from calcified lesions were excluded.

RESULTS. Stromal fibrosis was diagnosed in 74 (6.8%) of 1095 imaging-guided core needle biopsies in 73 patients. The 10 mammographic lesions were variable in appearance. Most of the sonographic lesions were indeterminate, with 16 (25%) of 64 showing suspicious features. Discordant imaging resulted in three patients having a second core biopsy and nine patients having an excisional biopsy. The two false-negative findings were the result of an infiltrating lobular carcinoma and an infiltrating ductal carcinoma, the latter diagnosis delayed for 6 months.

CONCLUSION. The low incidence (2.7%) of missed cancers in our series suggests that patients diagnosed at core biopsy as having stromal fibrosis can be treated conservatively with a short-term follow-up protocol. However, it would be prudent to continue to recommend either a second core biopsy or an excisional biopsy for imaging features that cannot be reliably differentiated from malignancy.

Stromal fibrosis in the breast is a pathologic entity characterized by proliferation of stroma with obliteration of the mammary acini and ducts, which results in a localized area of fibrous tissue associated with hypoplastic mammary ducts and lobules [1–5]. Stromal fibrosis has been described by a variety of terms including “focal fibrous disease of the breast,” “fibrosis of the breast,” “fibrous mastopathy,” “fibrous tumor of the breast,” and “focal fibrosis” of the breast [2].

Stromal fibrosis may present as a palpable discrete mass at both mammography and sonography, or as a clinically occult, imaging-detected abnormality [1–6]. The diagnosis has become increasingly common in the era of screening mammography and may represent as much as 2.1–9% of lesions found in patients who undergo imaging-guided core biopsy [1–3, 5].

The imaging features reported include benign-appearing masses as well as lesions that can simulate malignancy [1–6]. Radiologic–pathologic concordance is important to establish, especially for noncalcified lesions, to minimize the risk of a delayed diagnosis of breast cancer. The false-negative rate—the number of cancers “missed” initially because of sampling errors—is difficult to establish from the literature because the follow-up period has been limited.

The purpose of this retrospective study was to describe the sonographic and mammographic features of noncalcified stromal fibrosis lesions diagnosed at breast core biopsies for which sampling error and concordance are the most difficult to confirm. We also determined the incidence of stromal fibrosis in imaging-guided core needle biopsies and report the number of missed breast cancers that were misinterpreted as stromal fibrosis (false-negatives) at our institution.

Materials and Methods

The pathology reports of 1095 percutaneous breast core biopsies performed at our tertiary care institution between January 1997 and October 1999 were reviewed. We identified 110 patients with the diagnosis of stromal fibrosis. Thirty-seven patients were ex-
cluded: four patients because stromal fibrosis was not the primary histologic diagnosis, six because the area sampled was adjacent to a prior excisional biopsy site, and 27 because the lesion was calcified. This latter group was excluded because concordance is easier to establish in cases with calcifications than it is with noncalcified masses or asymmetries.

The study group consisted of 73 patients who underwent 74 core biopsy samples (74/1095, 6.8%) resulting in the diagnosis of marked stromal fibrosis. The women ranged in age from 28 to 87 years (mean, 47 years; median, 47 years).

The pathology was reviewed or reported by one breast pathologist. At the pathologic level, stromal fibrosis was defined as the presence of dense fibrosis occupying more than 90% of the interlobular stroma. No cases showed specific features of diabetic mastopathy, fibromatosis, or other stromal lesions [2]. Histologic subtypes of stromal fibrosis were not specified because no statistical correlation with the imaging findings has been shown [5]. Concordance is determined at weekly radiology–pathology rounds, at which the results of all core biopsies and needle localization biopsies are discussed.

The mammograms of the 10 patients who underwent stereotactically guided core needle biopsy were retrospectively reviewed. A dedicated stereotactic table was used (Stereoguide and DSM [Digital Spot Mammo- graphy]; Lorad Medical Systems, Danbury, CT). Sixty-four biopsies were performed using sonographic guidance with a 7.5-MHz linear array transducer (Acoustic Imaging Technologies, Phoenix, AZ). The sonographic studies were reviewed retrospectively from digital display or from hard copies. All biopsies were performed with a spring-loaded biopsy gun (Pro- Mag 2.2L; Manon Medical Products, Northbrook, IL), most with a 14-gauge Tru-Cut needle (Medical Device Technologies, Gainesville, FL). A mean of four samples was obtained under sonographic guidance and a mean of five cores under stereotactic guidance. In our department we prefer to perform a sonographically guided biopsy when possible. No vacuum-assisted biopsy device was used in our series.

We applied the BI-RADS (Breast Imaging Reporting and Data System) [7] lexicon to the mammographic lesions. For the sonographic abnormalities, we used the criteria established by Stavros et al. [8] and, when possible, the BI-RADS lexicon. The sonographic criteria included lesion shape, echogenicity, margin assessment, and sound transmission.

Follow-up included imaging studies, telephone calls to the referring physicians, and selected chart reviews.

**Results**

Stromal fibrosis was diagnosed in 74 (6.8%) of 1095 imaging-guided core needle biopsy samples in 73 patients. (One patient had two samples sampled by core biopsy.) Six women had a strong family history (first-degree relative) of breast carcinoma. Ten women had a previous history of breast cancer: in six patients stromal fibrosis was diagnosed in the ipsilateral breast but distant from the previous lumpectomy scar; in four, stromal fibrosis was diagnosed in the contralateral breast.

Lesions ranged in size from 0.5 to 6.2 cm (mean, 1.9 cm). The biopsies were almost equally distributed between the left (36 biopsies) and right (38 biopsies) breasts.

Twenty-six lesions were palpable: 25 lesions were biopsied with sonographic guidance and one was biopsied using stereotactic guidance (because it was not seen on sonography). Forty-eight lesions were impalpable: 39 were biopsied under sonographic guidance either because the lesion was mammographically occult or because it was seen on both modalities and sonographic guidance was used preferentially, and nine were biopsied with stereotactic guidance.

Fifty-five patients underwent mammography. For 33 patients the lesion was mammographically occult, and for 12 of 55 patients the mammogram was concordant with the sono- graphic findings. Mammograms showed the lesion to be a well-circumscribed mass for eight of 12 patients, a partly circumscribed mass for one patient, and an ill-defined mass for one patient. Two patients showed an area of focal asymmetry with architectural distortion. No mammograms existed for 10 of 18 patients because of their young age. Neither reports nor mammograms were available for eight of 18 patients.

Sonography was performed on 68 patients (63 of whom had sonographically guided biopsies and five of whom underwent stereotactic core biopsies). Sonographic reports only were used for 11 patients. For 57 patients, hard-copy or digital display of the sonographic abnormalities was available. For five of 10 patients having stereotactic core biopsy, sonography was performed but no lesion could be seen.

The mammographic features of the 10 lesions biopsied with stereotactic guidance had variable appearances (Table 1). Most (6/10) were oval in shape and most (8/10) had circumscribed or partly circumscribed margins.

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>Results of Stereotactic Core Biopsies in 10 Patients</th>
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</thead>
<tbody>
<tr>
<td><strong>Mass Features</strong></td>
<td><strong>No. of Lesions</strong></td>
</tr>
<tr>
<td><strong>Shape</strong></td>
<td></td>
</tr>
<tr>
<td>Oval</td>
<td>6</td>
</tr>
<tr>
<td>Lobular</td>
<td>1</td>
</tr>
<tr>
<td>Irregular</td>
<td>3</td>
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<tr>
<td><strong>Margins</strong></td>
<td></td>
</tr>
<tr>
<td>Circumscribed</td>
<td>8</td>
</tr>
<tr>
<td>Indistinct</td>
<td>6</td>
</tr>
<tr>
<td>Obscured</td>
<td>2</td>
</tr>
</tbody>
</table>

*Note.*—For some lesions, margins had more than one feature.

Three lesions had the more suspicious features of irregular shape and indistinct margins.

The sonographic features of 64 lesions (38 impalpable, 26 palpable) biopsied under sonographic guidance were variable (Table 2). Most of the lesions (58/64) were hypoechoic (Fig. 1): 30 homogenous; 20 heterogeneous; for eight, the internal echogenicity was not specified. One lesion was echogenic, two were isoechoic, and for three lesions, echogenicity was not specified in the report. Posterior acoustic shadowing was seen in 25 (39%) of 64 lesions, three of which were well-defined masses. Enhancement was present in 11 lesions and was not specified in 28 lesions.

Margins were well-defined in 35 (55%) of 64 lesions (three with posterior shadowing and 10 with posterior enhancement). Twenty-six lesions (26/64, 40.6%) were ill-defined masses, 22 (22/64, 34.3%) with shadowing and four with no posterior acoustic artifact. Two masses showed microlobulations. The margins were not specified for one lesion. Six of the ill-defined masses were taller than they were wide, and in four posterior shadowing was also seen. Three lesions were uniplanar areas of shadowing with no visible mass. The area of shadowing was broader in one scanning plane than in the orthogonal view (Fig. 2).

Overall, according to the criteria of Stavros et al. [8], 16 (25%) of 64, or a quarter of the le-
sions, had a combination of sonographic features (hypoechoic, irregular in shape, and shadowing) that were suspicious for malignancy. Twelve patients had further intervention (nine excisional biopsies, three repeated core biopsies). For the remaining four patients, two have had stable sonographic findings (range, 12–30 months), one patient with a prior contralateral mastectomy opted for a mastectomy and bilateral reconstructions, and one patient has been lost to follow-up.

Three patients had a second core biopsy that confirmed stromal fibrosis in two patients. One biopsy was repeated because of technical difficulties in the first stereotactic core biopsy. (There was concern that the lesion had not been sampled.) The second patient had a second core biopsy because of the large size (6 cm) of the well-defined hypoechoic sonographic mass. The third biopsy was repeated after 6 months of follow-up because the palpable mass had increased in size and changed appearance on sonography. The mass proved to be infiltrating ductal carcinoma (Fig. 3).

Nine patients had an excisional biopsy (Table 3). The diagnosis of stromal fibrosis was confirmed in eight patients. Infiltrating lobular carcinoma was diagnosed in the ninth patient, who had a history of a contralateral mastectomy for breast cancer (Fig. 4).

The mean period of the follow-up was 23.1 months (range, 6–42 months). Fifty patients have had stable imaging findings. In addition, two young patients (<30 years old) had stable clinical follow-up for 24 months, and one elderly patient died of unrelated disease. Twelve patients have not had imaging follow-up at this time.

Discussion

Before the era of screening mammography, focal breast fibrosis was diagnosed infrequently [1–6]. It was described as a distinct clinicopathologic entity presenting as a palpable mass that showed “proliferation of the mammary stroma with obliteration of lobular ductal parenchyma”[4]. The cause of stromal fibrosis is not known, “although several causes including an estrogen-related fibroblastic proliferation and a variant of mammary involution have been suggested” [5]. Stromal fibrosis is accepted as a specific diagnosis for circumscribed nodules [9, 10].

The mammographic and sonographic features of stromal fibrosis are nonspecific and variable [1–6]. A minority of patients may present with well-circumscribed benign-appearing masses and are suitable for a follow-up protocol [9, 10]. However, stromal fibrosis may mimic malignancy at clinical examination and on imaging. Almost one quarter of the lesions on sonography in our series showed features suggestive of malignancy: irregular in shape, hypoechoic with shadowing (Table 2, Fig. 1). Early in the study, breast sonography was not done by breast imagers experienced in sonography. Articles on stro-
Discordance between the imaging features and the benign diagnosis of stromal fibrosis prompted three repeated core biopsies and nine excisional biopsies (Table 3). At least two false-negatives (2.7%) were discovered in our series: one infiltrating ductal carcinoma (Fig. 3) and one infiltrating lobular carcinoma (Fig. 4). Possibly, additional false-negative findings may appear as our data mature. As shown in Figure 3, the initial core biopsy was directed to the sonographic lesion, which was a vague hypoechoic area. The diagnosis of stromal fibrosis was accepted as concordant. The histology showed only stromal fibrosis. Six months later, the mass had increased in size on clinical examination. The area had a different sonographic appearance, being quite ill-defined, irregular, and hypoechoic with posterior shadowing (Fig. 3B). We made the conservative assumption that carcinoma was present at the time of the earlier core biopsy but was not diagnosed because of sampling error. For the second missed cancer, discordance was reported within a day of the core biopsy results, and definitive surgery was performed within a month of the biopsy. Sampling error is again the likely explanation for the false-negative finding in this case.

Our study is limited by the lack of 2-year follow-up for all patients. Our inability to obtain sonographic images for 11 patients is another limitation of this retrospective study. No false-negative findings were reported in the study of focal fibrosis by Rosen et al. [1], in which the mean follow-up period was 27 months. A percentage (not stated) of their biopsies were performed as vacuum-assisted biopsies, which may have contributed to their results. No missed cancers were reported by Harvey et al. [2], who also used a vacuum-assisted biopsy technique.

Table 3

<table>
<thead>
<tr>
<th>Patient</th>
<th>Shape</th>
<th>Margins</th>
<th>Hypoechoic</th>
<th>Shadowing</th>
<th>Palpable</th>
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<tr>
<td></td>
<td>Oval</td>
<td>Irregular</td>
<td>Planar</td>
<td>Circum.</td>
<td>Ill-Defined</td>
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Note: Circum. = circumscribed.
\textsuperscript{a}False-negative for stromal fibrosis; excisional biopsy found infiltrating lobular carcinoma (Fig. 4).
Stromal Fibrosis of the Breast

Fig. 4.—72-year-old woman with infiltrating lobular carcinoma.
A, Cropped right mediolateral oblique mammogram shows architectural distortion.
B, Corresponding sonogram reveals irregular hypoechoic area (arrows) considered discordant with core diagnosis of stromal fibrosis. Excisional biopsy proved infiltrating lobular carcinoma.

Their follow-up period was limited to 1 year. Generally, for all lesions undergoing stereotactic core biopsy, the reported frequency of missed carcinoma after correlation with surgery ranges from 1.2% to 10.9% [10, 12, 13]. As stated by Lee et al. [10], we also recommend a short-term (6 months) follow-up protocol for patients having a concordant diagnosis of stromal fibrosis on core biopsy.

Three (4.7%) of 64 lesions were shown as uniplanar hypoechoic shadowing areas. Patients with these lesions may be suitable for a short-term follow-up protocol (BI-RADS category 3) rather than excisional biopsy. One patient in our series had the palpable uniplanar area excised, which confirmed stromal fibrosis (Fig. 2), and two other patients have shown stability at follow-up sonography.

In conclusion, our experience indicates that stromal fibrosis can reveal a spectrum of appearances, as stated in the literature [1–6]. Although the duration of substantial clinical follow-up is limited, the low incidence of missed cancers in our series (two [2.7%] of 73 patients) suggests that patients with palpable or impalpable stromal fibrosis diagnosed at core biopsy can be managed conservatively with a short-term follow-up imaging protocol. However, as recommended in the literature [3], it would be prudent to continue to recommend either a second core biopsy or an excisional biopsy for findings that cannot be reliably differentiated from malignancy.

References

1. Rosen EL, Soo MS, Bentley RC. Focal fibrosis: a common breast lesion diagnosed at imaging-guided core biopsy. AJR 1999;173:1657–1662