The Ochsner Journal 7:121–124, 2007

Effect of Breast Core Needle Biopsy Technique on Detection of Lobular Intraepithelial Neoplasia

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ABSTRACT

Objective: Lobular intraepithelial neoplasia—atypical lobular hyperplasia and lobular carcinoma in situ—is a noninvasive breast lesion occasionally found in core needle biopsy and surgical biopsy specimens. The objective of this study is to identify the increased incidence of lobular carcinoma in situ with current stereotactic biopsy techniques.

Methods: Biopsy results from 1993 to 2004 were reviewed retrospectively. 2,940 stereotactic biopsies were performed using a 14-gauge gun-type needle; 1,807 stereotactic biopsies were performed using an 11-gauge vacuum-assisted needle; and 2,724 ultrasound-guided biopsies were performed using a 14-gauge gun-type needle.

Results: The incidence of lobular intraepithelial neoplasia was 0.4% using the stereotactic 14-gauge technique, 0.4% using the ultrasound-guided 14-gauge technique, and 1.7% using the 11-gauge stereotactic technique. The increased rate of detection of lobular carcinoma in situ with an 11-gauge needle was statistically significant ($p<.0001$).

Conclusion: Lobular intraepithelial neoplasia is believed to be an incidental finding without specific imaging or clinical characteristics. Patients with detected lobular intraepithelial neoplasia have a significantly increased risk for subsequently developing breast cancer. Management recommendations can include no treatment, local excision, chemoprevention, and even bilateral prophylactic mastectomy. Radiologists and referring physicians need to be aware of the wide-ranging treatment recommendations, as lobular intraepithelial neoplasia is being identified more frequently.

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Key Words: Lobular intraepithelial neoplasia, biopsy technique, LCIS

INTRODUCTION

Most breast carcinomas arise in the terminal ducts. There are, however, a smaller number of breast carcinomas that originate in the lobules. Foote and Stewart described a neoplastic process involving the smaller lobular ducts and lobules, which they termed lobular carcinoma in situ (LCIS) in 1941 (1). Atypical lobular hyperplasia (ALH) meets some, but not all, of the criteria for diagnosis of LCIS and does not involve the entire lobule (2). LCIS and ALH are often grouped together under the category of lobular intraepithelial neoplasia (LIN) or lobular neoplasia.

When LCIS was discovered at surgical breast biopsy, Rosen noted that there was a 15% risk of subsequent development of invasive breast cancer (lobular and ductal) in each breast (30% total risk) (2). Because the risk of subsequent breast cancer is bilateral, LIN has traditionally not been thought to represent the same kind of precursor lesion for invasive breast carcinoma that atypical ductal hyperplasia and ductal carcinoma in situ (CIS) are for invasive ductal carcinoma. As a result, therapeutic recommendations for LIN have been varied.

LIN is not associated with any specific clinical or imaging findings. Thus, it is felt to be an incidentally discovered lesion at pathologic examination when biopsy is performed for other reasons. Logically, one would assume that the larger the amount of tissue obtained, the greater the incidence of LIN. Therefore, as radiologists have shifted from smaller ''gun'' type biopsy needles to larger gauge, vacuum-assisted needles, particularly to sample mammographically detected microcalcifications, it makes sense that the incidence of LIN at core needle biopsies would increase.

MATERIALS AND METHODS

We retrospectively analyzed 7,471 image-guided biopsies performed at Ochnser Medical Center from 1993 to 2004. Essentially all of the biopsies were performed for further evaluation of suspicious findings on breast imaging studies (mammography and ultrasound). The average number of specimens was calculated for each of the groups. The choice of guidance technique was based upon lesion location, lesion characteristics, and radiologist preference.

Table 1. Incidence of LIN: 14-gauge vs. 11-gauge.

Needle/Guidance Method	Sample Size	# of Detected LIN	Incidence of LIN
11-gauge Vacuum Stereo	1807	31	1.7%
14-gauge Gun Stereo	2940	11	0.4%
14-gauge Gun US	2724	10	0.4%

LIN = lobular intraepithelial neoplasia
US = ultrasound

RESULTS

At our institution from 1993 to 2004, 2,940 stereotactic biopsies were performed using the 14-gauge gun-type needle; 1,807 stereotactic biopsies performed using an 11-gauge, vacuum-assisted needle; and 2,724 ultrasound-guided biopsies performed using a 14-gauge gun-type needle. This yielded a total of 52 cases of LIN discovered at core biopsy. Of these, 11 were detected in biopsies performed with a 14-gauge gun-type needle with stereotactic guidance; 31 were detected in biopsies performed with an 11-gauge vacuum-assisted needle with stereotactic guidance; and 10 were detected in biopsies performed with a 14-gauge gun-type needle with ultrasound guidance. In our practice, we perform very few vacuum-assisted ultrasound-guided core needle biopsies, and LIN was not identified in the pathologic material from any of those biopsies.

The incidence of LIN was 1.7% for biopsies performed with an 11-gauge vacuum assisted needle and 0.4% for those performed with a 14-gauge needle, with either stereotactic or ultrasound guidance (Table 1). The increased rate of detection of LCIS with an 11-gauge needle was statistically significant ($p<.0001$). In the biopsies that yielded LIN, 14 were performed to evaluate a mass, 1 to evaluate a mass with calcifications, and 37 to evaluate calcifications alone. The average number of samples obtained was 6.8 for biopsies performed with a 14-gauge gun-type needle and 12.4 for biopsies performed with an 11-gauge vacuum-assisted needle.

DISCUSSION

LCIS is a significant risk factor for the subsequent development of breast cancer. Traditionally, it has not been thought to be a precursor to a malignancy. The National Cancer Institute describes LCIS as a ''marker that identifies women at an increased risk for subsequent development of invasive breast cancer'' (3). LCIS has been reported to represent as much as a 12-fold increased risk of subsequent invasive breast carcinoma (3). It is often multicentric within the breast and almost always present in both breasts. In studies by Donegan and Perez-Mesa (4) and Carter and Smith (5) in the 1970s, multicentric LCIS was demonstrated in upwards of 60% of mastectomy specimens (Figs. 1 and 2). For this reason, surgical excision to tumor-free margins may not be a viable treatment option in patients with LCIS normal breast discovered on biopsy. There are no physical examination findings to alert the patient or physician to the presence of LIN, and there are no specific findings on imaging.

LCIS is also more typically found in younger patients than invasive carcinoma and is more commonly seen in denser breasts. Eighty-ninety percent of cases occur in pre-menopausal women with mean age of diagnosis between 44 and 46 years in several series (6). This is significant, as patients who carry a diagnosis of LCIS have an annual incidence upwards of 1% for developing invasive carcinoma of the breast.

The possibility of undersampling is inherent in the performance of needle biopsies. Initially, stereotactic biopsies were performed with 14-gauge automated gun-type needles. The advent of 11-gauge vacuum-assisted needles allowed the acquisition of larger volume samples (Fig. 3) with more reliable retrieval of calcifications (7–9), a lower frequency of pathologic underestimation (10–12), and lower rebiopsy rates (13). Our study clearly demonstrates the increased

Figure 1. Normal histology of breast tissue consists of the lobules. Within the lobules are small acini. Lobules are connected to intralobular ductules and interlobular ducts. Lobules are surrounded by loose connective tissue sensitive to sex hormones.

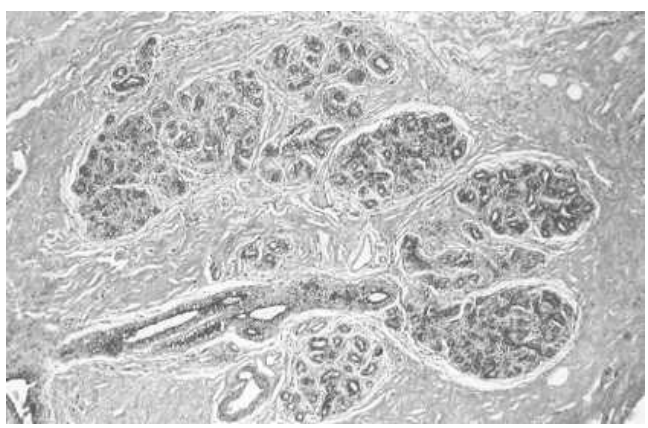


Figure 2. Breast tissue with LCIS. Numerous uniform appearing cells that fill the lobules containing round to oval nuclei that are surrounded by abundant clear cytoplasm.

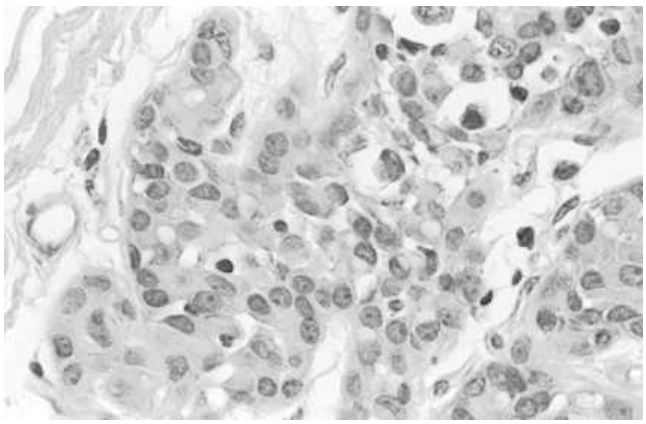
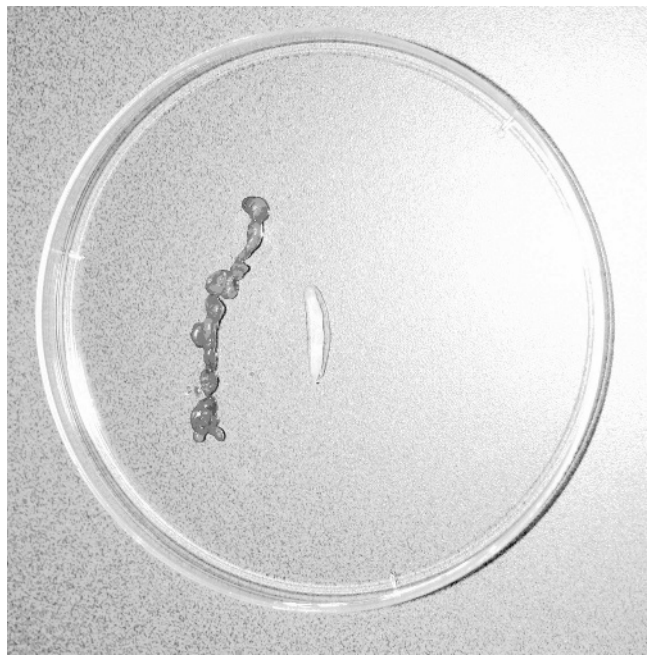


Figure 3. Comparison of samples using a 11 g vacuum assisted needle (left) and 14 g ''gun-type'' needle (right).



rate of detection of LIN with the use of 11-gauge needles. Our findings are statistically significant ($p<.0001$).

In 2004, the National Surgical Adjuvant Breast and Bowel Project reported their experience with 180 patients who, while participating in a protocol, were found to have LCIS (14). These patients were treated with local excision only. During a 12-year follow-up period, 26 women developed ipsilateral breast tumor recurrence and 14 women developed contralateral breast recurrence. Of the ipsilateral breast recurrences, there were nine invasive cancers, of which eight (89.9%) were invasive lobular carcinomas. Of the contralateral breast recurrences, 10 were invasive cancers, of which six (75%) were invasive lobular carcinomas. In addition, of those patients with ipsilateral breast recurrences, 96% of all carcinomas and 100% of the invasive carcinomas developed at the site of the original LCIS (15). This lends credence to the argument that LCIS is a precursor lesion for invasive cancer. The authors, however, concluded that the recurrence rates are so low (14.4% for ipsilateral breast recurrence and 7.8% for contralateral breast recurrence) that nothing beyond conservative surgical treatment (i.e., local excision) was indicated.

Since LCIS is frequently multifocal and the risk of developing subsequent breast cancer is bilateral, many investigators believe that local surgical excision of the affected area is not indicated (16). Others advocate surgical excision of LIN to exclude sampling error and as a potential treatment option (17). Berg et al. (17) and Foster et al. (18) recommend excisional biopsy for the diagnosis of LCIS or ALH based upon their findings that 7%–17% of these cases are upgraded to DCIS or invasive cancer with excisional biopsy, a rate similar to atypical ductal hyperplasia found at core biopsy (16,19). An even more recent study has indicated that 19% of cases in which LIN was found at core biopsy were found to have a coexistent intraductal or invasive breast carcinoma at excision (20). Certain parameters for surgical excision have been suggested, which include lesions with features that overlap with those of ductal carcinoma in situ, an associated high-risk lesion or pathologic–mammographic discordance (21).

Irrespective of other treatment, all patients diagnosed with LIN need close long-term follow-up, with annual diagnostic mammograms and frequent physical examinations. Estrogen receptor antagonists such as tamoxifen may be another consideration in the routine management of these high-risk patients. In the Breast Cancer Prevention P-1 trial, the risk of developing invasive carcinoma over a follow-up period of 47 months was reduced by 56% in the subset of 826 women with a history of LCIS that used tamoxifen (14). Tamoxifen does have significant side effects, including a small increased risk of endometrial cancer and thrombotic events. Nonetheless, tamoxifen may be a reasonable option for these high-risk patients. Finally, bilateral prophylactic mastectomy could be offered to these patients as a potential option.

CONCLUSION

Our findings support the belief that the greater the amount of tissue obtained at biopsy, the greater the chance of diagnosing ALH or LCIS. The increased rate

of detection of LIN with the use of an 11-gauge needle was statistically significant in our retrospective analysis ($p<.0001$). As expected, the detection rate is less than with surgical excision, where LIN is identified in the specimens in approximately 4%–5% of cases.

Although anxiety-inducing for the patient, there are management options for a patient diagnosed with LIN that can potentially improve patient outcome. The detection of LIN alerts the patient and referring physician to the need for close long-term follow-up, including annual diagnostic mammograms and frequent physical examinations. Additional potential treatment options include estrogen receptor antagonist therapy and even bilateral mastectomy if the patient has additional risk factors. Although no definite guidelines exist, radiologists and referring physicians need to be aware of the management and treatment options available to the patient as we identify LIN more frequently with current stereotactic biopsy techniques.

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