The aim of core needle biopsy (CNB) is to provide a diagnosis of a breast abnormality prior to open surgical excision. It is important that the pathologist be aware of the correlation between breast imaging categories and pathology findings, which is gained largely through communication with the radiologist. It is also advised that the submitting radiologist separates cores containing calcifications from those without, and submits them together with the specimen radiograph. For CNB performed for masses and architectural distortions, the nature of the imaging abnormality should be clearly stated on the pathology requisition form.

Processing of CNB does not significantly differ from that of any other specimen. Sectioning protocols vary slightly between laboratories from one hematoxylin and eosin (H&E)–stained section to multiple levels. All protocols should allow preservation of sufficient material in the paraffin block for further levels and/or immunohistochemistry, as needed. If calcifications are not identified in the initial sections, radiography of the paraffin block may be necessary. Calcium phosphate deposits appear blue-purple on H&E, whereas calcium oxalate crystals are translucent, but birefringent under polarized light (1). Rarely, calcifications could be lost during processing, such as: loss of coarse calcifications when cutting the block, detached calcium left in the specimen container, or dissolution of calcium during formalin fixation (1).

The challenges of CNB are similar to those encountered in surgical excisions and are complicated by the availability of only limited material. In uncertain cases, the pathologist should provide enough information to prompt an excision without overdiagnosing the lesion. It is debatable if a pathologist should specifically recommend excision in the pathology report of a CNB.

This discussion focuses on high-risk lesions and lesions that raise management issues.

**Atypical Ductal Hyperplasia (ADH)**

The distinction between ADH and low-grade ductal carcinoma in situ (DCIS) can be difficult on open excisions and is often even more difficult on the limited samples obtained by CNB. Additionally, in many cases ADH is present at the periphery of DCIS (2); therefore, the diagnosis of ADH on a CNB does not rule out the presence of DCIS. Research studies using an automated biopsy gun method and 14 gauge...
needles have shown that excision of ADH on CNB yields carcinoma in 33–87% of patients, suggesting that the diagnosis of ADH on CNB often underestimates carcinoma (3–7). In about 60–75% of these cases, the carcinoma identified at excision was DCIS, and invasive cancer was present in the remainder. Hence, surgical excision follows a diagnosis of ADH on CNB in all cases (8).

Data obtained from studies using mammotome biopsies show a lower rate of upgrade to DCIS, presumably owing to the more extensive tissue sampling and the greater likelihood of complete removal of the lesions by this technique (9–13). With regard to excisions following a diagnosis of ADH on CNB, Darling et al. (12) compared just these cases (one using a 14-gauge automated gun, one a 14-gauge mammotome, and one an 11-gauge mammotome) and showed an underestimation of carcinoma in 44%, 39%, and 19% respectively.

The identification of patients with ADH on CNB who do not need surgical excision is an important area of investigation. Ely et al. (14) found that the likelihood of finding carcinoma on the surgical excision was dependent on the extent of ADH on the CNB. None of the 24 cases in which ADH involved ≤2 foci and was confined to a single terminal duct lobular unit had a worse lesion on excision. In contrast, 87% of cases with ≥4 foci of ADH on CNB had carcinoma on excision. Additional data are needed to confirm these findings. Regardless, for now excision of ADH on CNB is recommended for all patients.

LOBULAR NEOPLASIA (LN)

It is widely debated how to best deal with patients having LN, including atypical lobular hyperplasia and lobular carcinoma in situ, on CNB. LN is a marker of increased risk for breast cancer, and surgical excision of LN on CNB was not performed in the past, a practice still supported by some authors (15). However, recent retrospective data suggest that excision of LN on CNB is associated with a high rate of upgrade (16,17). Elsheikh et al. (18) report that the incidence of carcinoma on excision following the diagnosis of LN on CNB is 18%, but some of the cancers in the series formed a mass lesion on imaging, representing disagreement between the radiologic images and the pathologic findings.

Surgical excision is always recommended if: (a) there is radiologic–pathologic disagreement, suggesting that the lesion targeted by the CNB was not sampled; (b) risk lesion (such as ADH) is present on the CNB; or (c) LN has unusual histologic features (mitoses, necrosis) more commonly seen in DCIS (19).

Immunostaining for E-cadherin helps in determining whether the neoplastic cells have a lobular or ductal phenotype (20), as the loss of membranous reactivity for E-cadherin reliably demonstrates lobular differentiation (21). Nonetheless, more data are needed for definitive conclusion. For now, recommendation is to excise whenever the neoplastic cells are E-cadherin negative but have ambiguous morphology.

PAPILLARY LESIONS

A spectrum of papillary lesions may be encountered in a CNB. These include intraductal papilloma, intraductal papilloma with atypia, intracystic (encapsulated) papillary carcinoma, solid papillary carcinoma, and invasive papillary carcinoma. The current management is to excise all papillary lesions diagnosed on CNB, but this approach has been challenged, and more recent studies suggest that a benign diagnosis on CNB may be followed, if the imaging studies are in agreement with the pathologic findings. In one study of note, none of 18 patients with benign papilloma on CNB had carcinoma in the surgical excision, whereas 29% of patients with papilloma and separate foci of atypia and 92% of patients with “severely atypical papilloma suspicious for carcinoma” had carcinoma in the subsequent excision (22). Another group found that 20% of papillomas diagnosed on CNB showed no atypia in the surgical excision; the remaining patients had no progression of disease on follow-up (23). In contrast, another study yielded a high rate of atypia/malignancy (5 of 28 patients, 17.9%) in the excision specimens of patients with a benign papillary lesion on CNB (24). Liberman et al. (25) first reported no upgrades of benign papillary lesions diagnosed on CNB; however, a consecutive retrospective review of 35 benign, radiologically concordant papillomas diagnosed on imaging guided CNB revealed cancer and high-risk lesions in 14% and 17% of excisions, respectively (26). Likewise, in another study of 36 patients who underwent excision for papilloma on CNB, 8 were found to have adjacent foci of ADH and two had well-differentiated papillary DCIS (27). Even though some suggest that close follow-up is sufficient for a benign diagnosis on CNB, surgical excision is still recommended for all papillary lesions on CNB.
RADIAL SCAR/COMPLEX SCLEROSING LESIONS

Radial scars are composed of a central fibrotic and variably elastotic center from which an epithelial component extends outwards in radial fashion, forming a stellate lesion. Radial scars are infrequent in CNBs, because often patients are referred for surgery given the radiologic differential diagnosis with invasive carcinoma. There are few studies with limited case numbers discussing the findings in excisions of radial scars without atypia on CNB (4,28–31). In one study, two of five patients (40%) with radial scar found on CNB had carcinoma (invasive or DCIS) at excision (4). Another series of nine patients diagnosed with radial scar on CNB reported ADH in 2 (22%) excisions (31). Increased likelihood of finding carcinoma in larger radial scars has also been reported (32); therefore, all patients with radial scar on CNB undergo excision. On the other hand however, more extensive sampling using a 9- or 11-gauge CNB device followed by meticulous radiologic–pathologic correlation and close follow-up could potentially prevent surgery in the majority of radial sclerosing lesion cases without associated atypia on CNB (33). Nonetheless, it is recommended that patients with radial scar diagnosed on CNB undergo excision.

FIBROEPITHELIAL AND SPINDLE CELL LESIONS

The diagnosis by CNB of a fibroadenoma at one end of the spectrum and a malignant phyllodes tumor at the other is usually straightforward. Fibroadenoma diagnosed on CNB can be followed with observation alone, provided that the imaging studies are in agreement with the diagnosis. If the fibroepithelial lesion shows any cellular and/or mitotically active stroma, the differential diagnosis includes a phyllodes tumor. As such, the lesion should be excised for complete evaluation (28,34–36).

Most of the spindle cell lesions encountered on CNB require excision. They include metaplastic spindle cell carcinoma (MSCC), phyllodes tumor, myofibroblastoma, atypical or malignant vascular lesion, fibromatosis, and nodular fasciitis. The most common diagnosis is MSCC, and it is important to remember that negative immunoreactivity for epithelial markers does not rule out MSCC, as positivity can be very heterogeneous and focal (37).

MUOCCELE-LIKE LESIONS

Mucocele-like lesions consist of cysts filled with mucin and lined by epithelium that may range from benign to ADH or DCIS (38). Rupture of the cysts results in extravasation of mucin into the surrounding stroma (39). It is reasonable to view mucocele-like lesions as part of a spectrum ranging from benign to mucinous carcinoma, with a significant risk of under-diagnosis from the limited material present in a CNB. About 30% of mucocele-like lesions were identified as mucinous carcinoma on surgical excision in one report (40). In another study, no upgrade was found in excision of CNB with extravasated mucin and benign epithelium, and the author suggested that mucinous lesions can be accurately classified on CNB (41). Similarly, a complete correlation of core biopsy and excision results was reported in the largest to date (32 patients) study of mucinous lesions diagnosed on CNB (42). However, as data are limited, excision is recommended whenever an atypical mucocele-like lesion or acellular stromal mucin is identified on CNB. This is carried out so as to rule out in situ or invasive mucinous carcinoma.

COLUMNAR CELL CHANGES WITH ATYPIA/FLAT EPITHELIAL ATYPIA

A spectrum of proliferations can show columnar cell change, ranging from simple hyperplasia [columnar cell hyperplasia (CCH)] through CCH with atypia to intraductal carcinoma (43). Cystic dilatation often accompanies these epithelial proliferations, especially in terminal duct lobular units where the condition seems to arise. They may exhibit varying degrees of cytologic atypia (referred to as “columnar cell changes with atypia” or “flat epithelial atypia”), and if architectural atypia is also present, a diagnosis of ADH or DCIS is given. These lesions are frequently seen in CNBs, and surgical excisions are performed for calcifications. Approximately 25% to 33% of patients with this atypia on CNB have shown a more advanced lesion at excision (44–47), however, these series are retrospective and likely overestimate the rate of upgrade. Nonetheless, excision is performed when any atypical columnar cell lesion is diagnosed on CNB.

In conclusion, when making a diagnosis on a CNB of the breast and in light of the previously documented literature, the pathologist should understandably be
cautious. The report of a CNB specimen should include sufficient information to permit radiologic–pathologic correlation placing the patient into the appropriate therapeutic algorithm.

REFERENCES

1. Tornos C, Silva E, el-Naggar A, Pritzker KP. Calcium oxalate crystals in breast biopsies. The missing microcalcifications. Am J Surg Pathol 1990;14:961–8.

2. Lennington WJ, Jensen RA, Dalton LW, Page DL. Ductal carcinoma in situ of the breast. Heterogeneity of individual lesions. Cancer 1994;73:118–24.

3. Dahlstrom JE, Sutton S, Jain S. Histologic precision of stereotactic core biopsy in diagnosis of malignant and premalignant breast lesions. Histopathology 1996;28:537–41.

4. Jackman RJ, Nowels KW, Rodriguez-Soto J, Marzoni FA Jr, Finkelstein SJ, Shepard MJ. Stereotactic, automated, large-core needle biopsy of nonpalpable breast lesions: false-negative and histologic underestimation rates after long-term follow-up. Radiology 1999;210:799–805.

5. Jackman RJ, Nowels KW, Shepard MJ, Finkelstein SJ, Marzoni FA Jr. Stereotactic large-core needle biopsy of 450 nonpalpable breast lesions with surgical correlation in lesions with cancer or atypical hyperplasia. Radiology 1994;193:91–5.

6. Liberman L, Cohen MA, Dershaw DD, Abramson AF, Hahn LE, Rosen PP. Atypical ductal hyperplasia diagnosed at stereotactic core biopsy of breast lesions: an indication for surgical biopsy. AJR Am J Roentgenol 1995;164:1111–3.

7. Moore MM, Hargett CW III, Hanks JB, et al. Association of breast cancer with the finding of atypical ductal hyperplasia at core breast biopsy. Ann Surg 1997;225:726–31. discussion 31–3. PMCID: 1190878.

8. Bassett L, Winchester DP, Caplan RB, et al. Stereotactic core-needle biopsy of the breast: a report of the Joint Task Force of the American College of Radiology, American College of Surgeons, and College of American Pathologists. CA Cancer J Clin 1997;47:171–90.

9. Adrales G, Turk P, Wallace T, Bird R, Norton HJ, Greene F. Is surgical excision necessary for atypical ductal hyperplasia of the breast diagnosed by Mammotome? Am J Surg 2000;180:313–5.

10. Brem RF, Behrendt VS, Sanow L, Gatewood OM. Atypical ductal hyperplasia: histologic underestimation of carcinoma in tissue harvested from impalpable breast lesions using 11-gauge stereotactically guided directional vacuum-assisted biopsy. AJR Am J Roentgenol 1999;172:1405–7.

11. Burbank F. Stereotactic breast biopsy of atypical ductal hyperplasia and ductal carcinoma in situ lesions: improved accuracy with directional, vacuum-assisted biopsy. Radiology 1997;202:843–7.

12. Darling ML, Smith DN, Lester SC, et al. Atypical ductal hyperplasia and ductal carcinoma in situ as revealed by large-core needle breast biopsy: results of surgical excision. AJR Am J Roentgenol 2000;175:1341–6.

13. Liberman L, Smolkin JH, Dershaw DD, Morris EA, Abramson AF, Rosen PP. Calcification retrieval at stereotactic, 11-gauge, directional, vacuum-assisted breast biopsy. Radiology 1998;208:251–60.

14. Ely KA, Carter BA, Jensen RA, Simpson JF, Page DL. Core biopsy of the breast with atypical ductal hyperplasia: a probabilistic approach to reporting. Am J Surg Pathol 2001;25:1017–21.

15. Nagi CS, O’Donnell JE, Tismanetsky M, Bleiweiss IJ, Jaffer SM. Lobular neoplasia on core needle biopsy does not require excision. Cancer 2008;112:2152–8.

16. Cangiarella J, Guth A, Axelrod D, et al. Is surgical excision necessary for the management of atypical lobular hyperplasia and lobular carcinoma in situ diagnosed on core needle biopsy?: a report of 38 cases and review of the literature. Arch Pathol Lab Med 2008;132:979–83.

17. Shin SJ, Rosen PP. Excisional biopsy should be performed if lobular carcinoma in situ is seen on needle core biopsy. Arch Pathol Lab Med 2002;126:697–701.

18. Elsheikh TM, Silverman JF. Follow-up surgical excision is indicated when breast core needle biopsies show atypical lobular hyperplasia or lobular carcinoma in situ: a correlative study of 33 patients with review of the literature. Am J Surg Pathol 2005;29:534–43.

19. Liberman L, Sama M, Susan B, et al. Lobular carcinoma in situ at percutaneous breast biopsy: surgical biopsy findings. AJR Am J Roentgenol 1999;173:291–9.

20. Jacobs TW, Plass N, Kouria G, Schnitt SJ. Carcinomas in the breast with indeterminate features: role of E-cadherin staining in categorization. Am J Surg Pathol 2001;25:229–36.

21. Vos CB, Cleton-Jansen AM, Berx G, et al. E-cadherin inactivation in lobular carcinoma in situ of the breast: an early event in tumorigenesis. Br J Cancer 1997;76:1131–3. PMCID: 2228132.

22. Renshaw AA, Derhagopian RP, Tizol-Blanco DM, Gould EW. Papillomas and atypical papillomas in breast core needle biopsy specimens: risk of carcinoma in subsequent excision. Am J Clin Pathol 2004;122:217–21.

23. Ivan D, Selinko V, Sahin AA, Snejie N, Middleton LP. Accuracy of core needle biopsy diagnosis in assessing papillary breast lesions: histologic predictors of malignancy. Mod Pathol 2004;17:165–71.

24. Ioffe OB, Berg WA, Silverberg SG, Simirs A. Analysis of papillary lesions diagnosed on core needle biopsy of the breast. Mod Pathol 2000;13:23A.

25. Liberman L, Bracero N, Vuolo MA, et al. Percutaneous large-core biopsy of papillary breast lesions. AJR Am J Roentgenol 1999;172:311–7.

26. Liberman L, Tornos C, Huzman R, Bartella L, Morris EA, Dershaw DD. Is surgical excision warranted after benign, concordant diagnosis of papilloma at percutaneous breast biopsy? AJR Am J Roentgenol 2006;186:1328–34.

27. Mercado CL, Hamele-Bena D, Oken SM, Singer CI, Cangiarella J. Papillary lesions of the breast at percutaneous core-needle biopsy. Radiology 2006;238:801–8.

28. Dershaw DD, Morris EA, Liberman L, Abramson AF. Non-diagnostic stereotactic core breast biopsy: results of rebiopsy. Radiology 1996;198:323–5.

29. Lee CH, Eggin TK, Philippots L, Mainiero MB, Tocino I. Cost-effectiveness of stereotactic core needle biopsy: analysis by means of mammographic findings. Radiology 1997;202:849–54.

30. Lee CH, Philippots LE, Hovarth LJ, Tocino I. Follow-up of breast lesions diagnosed as benign with stereotactic core-needle biopsy: frequency of mammographic change and false-negative rate. Radiology 1999;212:189–94.

31. Philippots LE, Shaheen NA, Jain KS, Carter D, Lee CH. Uncommon high-risk lesions of the breast diagnosed at stereotactic core-needle biopsy: clinical importance. Radiology 2000;216:831–7.

32. Sloane JP, Mayers MM. Carcinoma and atypical hyperplasia in radial scars and complex sclerosing lesions: importance of lesion size and patient age. Histopathology 1993;23:225–31.

33. Resekova E, Edelweiss M, Albarracin CT, Yang WT. Management of radial sclerosing lesions of the breast diagnosed using percutaneous vacuum-assisted core needle biopsy: recommendations
for excision based on seven years’ of experience at a single institution. Breast Cancer Res Treat 2008. DOI: 10.1007/s10549-008-0119-x.

34. Ioffe OB, Berg WA, Silverberg SG, Kumar D. Mammographic-histopathologic correlation of large-core needle biopsies of the breast. Mod Pathol 1998;11:721–7.

35. Komenaka IK, El-Tamer M, Pile-Spellman E, Hibshoosh H. Core needle biopsy as a diagnostic tool to differentiate phyllodes tumor from fibroadenoma. Arch Surg 2003;138:987–90.

36. Meyer JE, Smith DN, Lester SC, et al. Large-needle core biopsy: nonmalignant breast abnormalities evaluated with surgical excision or repeat core biopsy. Radiology 1998;206:717–20.

37. Schnitt SJ, Collins LC. Spindle cell lesions. In: Epstein JI, ed. Biopsy Interpretation of the Breast. Philadelphia: Lippincott Williams & Wilkins, 2008:323–43.

38. Ro JY, Sneige N, Sahin AA, Silva EG, del Junco GW, Ayala AG. Mucocele-like tumor of the breast associated with atypical ductal hyperplasia or mucinous carcinoma. A clinicopathologic study of seven cases. Arch Pathol Lab Med 1991;115:137–40.

39. Rosen PP. Mucocele-like tumors of the breast. Am J Surg Pathol 1986;10:464–9.

40. Carder PJ, Murphy CE, Liston JC. Surgical excision is warranted following a core biopsy diagnosis of mucocele-like lesion of the breast. Histopathology 2004;45:148–54.

41. Renshaw AA. Can mucinous lesions of the breast be reliably diagnosed by core needle biopsy? Am J Clin Pathol 2002;118:82–4.

42. Wang J, Simsir A, Mercado C, Cangiarella J. Can core biopsy reliably diagnose mucinous lesions of the breast? Am J Clin Pathol 2007;127:124–7.

43. Schnitt SJ. The diagnosis and management of pre-invasive breast disease: flat epithelial atypia – classification, pathologic features and clinical significance. Breast Cancer Res 2003;5:263–8. PMCID: 314429.

44. Brogi E, Tan LK. Findings at excisional biopsy (EBX) performed after identification of columnar cell change (CCC) of ductal epithelium in breast core biopsy (CBX). Mod Pathol 2002;15:29A–30A.

45. Harigopal MYD, Hoda SA, DeLellis RA, Vazquez MF. Columnar cell alteration diagnosed on mammotome core biopsy for indeterminate microcalcifications: results of subsequent mammograms and surgical excision. Mod Pathol 2002;15:36A.

46. Kunju LP, Kleer CG. Significance of flat epithelial atypia on mammotome core needle biopsy: should it be excised? Hum Pathol 2007;38:35–41.

47. Nasser S, Fan MJ. Does atypical columnar cell hyperplasia on breast core biopsy warrants follow-up excision? Mod Pathol 2003;16:62A.