THE AMERICAN SOCIETY OF Breast Surgeons - Resource Guide -

Resource Guide: Surgical Management of Benign or High-Risk Lesions

Purpose

To outline the management for high-risk lesions identified on image-guided breast biopsy.

The ASBrS is in the process of developing more systematic and comprehensive guidance around the management of these lesions, with an anticipated release in 2025.

Associated ASBrS Guidelines or Quality Measures

- Image-Guided Percutaneous Biopsy of Palpable and Nonpalpable Breast Lesions
- Performance and Practice Guidelines for Stereotactic Breast Procedures
- Concordance Assessment Following Image-Guided Breast Biopsy

Methods

Literature review evaluating the management of various benign and high-risk lesions (including atypical ductal hyperplasia, lobular neoplasia, papillary lesions, radial scar and complex sclerosing lesions, fibroepithelial lesions, mucocele-like lesions, spindle cell lesions, and pseudoangiomatous stromal hyperplasia) identified on image-guided breast biopsies. This is not a complete systematic review but a review of the modern literature on this subject. The ASBrS Research Committee developed a consensus document which the ASBrS Board of Directors reviewed and approved.

ASBrS Recommendations for High-Risk Lesions identified on Percutaneous Breast

Biopsy

The following general considerations of selective versus routine excision can be applied to any high-risk lesion:

- Estimates of the risk of upgrade to malignancy are improved with multi-disciplinary input from breast radiologist, breast surgeon, and breast pathologist.

- Patients with clinical or imaging findings that are discordant with core needle biopsy (CNB) histology (i.e. a benign pathology result that does not account for imaging findings that are suspicious for malignancy) should undergo excision. Consideration can be given to repeat biopsy if the initial biopsy procedure was felt to be inadequate.
- Selective excision for the remaining patients is recommended.
- The final decision to excise depends on shared decision making with the patient and includes the following:
    - careful clinical, imaging, and pathology concordance assessment with multidisciplinary input;
    - patient-specific estimates of the risk of upgrade to malignancy.
    - disclosure of operative and cosmetic risks; and
    - whether the patient can or will comply with follow-up.
- All patients should undergo comprehensive breast cancer risk assessment and be considered for risk reducing medication and high-risk screening as appropriate. The presence of a high-risk lesion is not an indication for genetic testing; however, all patients should be evaluated for personal or family history that would indicate that genetic evaluation is appropriate. Certain high-risk lesions such as lobular neoplasia and atypical ductal hyperplasia are associated with elevated lifetime breast cancer risk which is not mitigated by surgical excision. Management of breast cancer risk is beyond the scope of this resource guide and readers are encouraged to visit the National Comprehensive Cancer Network (NCCN) Guidelines on Detection, Prevention and Risk Reduction for more details.
- A summary of recommended surgical management for each high-risk lesion is presented in the table below. These recommendations assume that the pathology and imaging results are deemed concordant.

Summary of Surgical Management Recommendations for High-Risk Lesions of the Breast

Lesion	Recommendation[a]	Exceptions / Notes
ADH	Surgical excision	Patients who meet low-risk criteria can be considered for observation (see summary of data below)
Classic LCIS / ALH	No excision Observation with clinical and imaging follow-up[b,c]	Excision if other benign lesion with potential for upstaging is present or if not incidental (see summary of data below)
Non-classic LCIS (pleomorphic and florid)	Surgical excision to negative margins[d]	Similar for necrosis and other non-classical lesions
CCL without atypia	No excision Return to screening	

Pure FEA	No excision Observation with clinical and imaging follow-up[b,c]	Excision if extensive calcifications or not adequately sampled
Papilloma without atypia	No excision Observation with clinical and imaging follow-up[b,c]	Consider excision for symptomatic lesions
Papilloma with atypia	Surgical excision	
Complex sclerosing lesions (CSL)	No excision Observation with clinical and imaging follow-up[b,c]	Excision for CSL with atypia For CSL without atypia, consider excision if not adequately sampled or other concerning features
Mucocele-like lesions (MLL)	No excision Observation with clinical and imaging follow-up[b,c]	Surgical excision for MLL with atypia.
Desmoid tumors or fibromatosis	Observation with clinical and imaging follow up every 3-6 months[c] (breast imaging, MRI, CT as clinically indicated)	Excision for symptomatic lesions and those increasing in size (see summary of data below)
PASH	Clinical observation	Consider excision for symptomatic lesions

ADH, atypical ductal hyperplasia; ALH, atypical lobular hyperplasia; CCL, columnar cell lesion; CT, computed tomography; FEA, flat epithelial atypia; LCIS, lobular carcinoma in situ; MRI; magnetic resonance imaging; PASH, pseudoangiomatous stromal hyperplasia

[a]Recommendation are for lesions for which radiologic pathologic concordance has been established

[b]Diagnostic imaging at 6, 12, and 24 months to establish stability is recommended based on American College of Radiology guidelines (see "Indications for excision: discordance and the risk of pathology upgrading")

[c]Strongly consider excision for lesion progression during follow up

[d] Data on appropriate margin width for PLCIS is limited (see "Non classic LCIS")

Summary of Data Reviewed

Indications for excision: discordance and the risk of pathology upgrading

Percutaneous core needle biopsy (CNB) is the preferred, initial, minimally invasive diagnostic procedure for nonpalpable and palpable breast lesions.[1] Concordance assessment determines further management and should be performed after any percutaneous breast biopsy.

Concordance is established when there is agreement between clinical, imaging, and pathologic findings. Radiologic-pathologic concordance assessment requires simultaneous evaluation of the imaging and pathologic results to ensure that the histologic findings are sufficient to explain the radiographic lesion, and ideally involves both radiologist and pathologist. Discordance refers to the situation in which the histologic results from CNB do not provide an acceptable explanation for suspicious imaging findings.[2]

If there is discordance, further histological evaluation is needed. This can be accomplished either by repeat CNB, with consideration of a larger gauge or vacuum-assisted device, or surgical excision.[3-6] Excision should be considered for some CNB findings, despite concordance with imaging, because of their risk of pathology upgrading. A lesion is "upgraded" when it is classified as benign or atypical on CNB, but malignant (ductal carcinoma in situ or invasive carcinoma) on subsequent excision. Lesions may be upgraded to malignancy at surgical biopsy secondary to sampling volume limitations of CNB or inaccurate targeting.[3,7] Although surgical excision is the most definitive method of obtaining more tissue, another option is vacuum assisted excision (VAE), in which a larger sample of tissue is excised percutaneously using a 7-11 gauge vacuum assisted biopsy needle with the goal of removing the radiographic lesion.[8] In the 2024 European guidelines for management of high-risk lesions, VAE is suggested for selected lesions up to 15mm in size as an intermediate approach to avoiding open surgery while still assessing for upgrade.[9] These guidelines state that the use of VAE should take into account country resources, availability of VAE and skills, and follow up, and acknowledge that more data is needed on this technique as it is not widely performed everywhere. VAE is not routinely utilized in the United Sates and specific indications for VAE vs surgical excision is beyond the scope of this document.

Most of the available literature regarding upgrade rates for high-risk lesions is retrospective. A variety of factors influence the likelihood of pathology upgrading, including year of study publication, institution, specialist pathology interpretation, persistence of the target lesion on imaging, lesion palpability, size and type of needle used for sampling, lesion size, pre-procedure BI-RADS score, presence of a mass versus calcifications, and patient baseline breast cancer risk. There is lack of uniformity of opinion regarding the necessity of surgical excision for many of these lesions. The introduction of newer modalities of imaging, improved mammography techniques, and standardization of large gauge percutaneous biopsy devices has likely contributed to the lower upgrade rates reported by more recent studies.

Some histologic lesions associated with a risk of upgrade to malignancy are also markers of increased risk for future breast cancer in either breast, which cannot be mitigated by excision. This equates to roughly a 1% annual risk of breast cancer for patients with atypical hyperplasia and a 1-2% annual risk for patients with lobular carcinoma in situ (LCIS).[10-13] Management of breast cancer risk associated with these lesions is beyond the scope of this statement but should be incorporated into the patient's treatment plan regardless of whether or not excision is undertaken. If the patient qualifies for screening magnetic resonance imaging (MRI) based on calculated lifetime risk, then the absence of enhancement in a high-risk lesion selected for observation rather than excision may be reassuring, as small single institution studies suggest MRI has a >95% negative predictive value for upgrade.[14,15]

While surgical excision remains the most definitive approach, newer data suggest that close observation and careful follow-up is an acceptable option for selected patients and for lesions with a lower chance

of upgrade. When opting for surveillance instead of surgical excision, patient preference, compliance with follow-up need, reported upgrade rates, and local practices and resources need to be considered on a case-by-case basis.[3,7,16] A standardized process for evaluating and reporting the imaging and pathology findings for high-risk lesions can facilitate this process, as can tracking institutional upgrade rates. Additionally, when surveillance is selected, more frequent imaging follow up should be considered. Diagnostic imaging at 6, 12, and 24 months to establish stability is recommended based on American College of Radiology guidelines.[17]

The following sections provide a brief overview of the literature currently available regarding upgrade to malignancy and indications for surgical excision for the most common high-risk lesions.

Indications for surgical excision for atypical ductal hyperplasia (ADH)

ADH is defined as abnormal epithelial proliferative breast lesions that are not qualitatively or quantitatively abnormal enough to be classified as carcinoma in situ.[18] ADH on CNB may be associated with malignancy, so ADH identified on CNB is often excised. Rates of upgrade to ductal carcinoma in situ (DCIS) or invasive carcinoma are highly variable in the literature, with a pooled upgrade rate in a recent meta-analysis of 29%.[19] The majority of ADH upgrades are to DCIS, not invasive disease.[20] Factors frequently associated with lower rates of upgrade include mammographic calcifications (rather than a mass or architectural distortion), smaller lesion size on imaging, larger sample size (larger gauge needle or more samples), "complete" removal of the calcifications (defined as at least 50%-95% in various studies), smaller volume of ADH in the CNB specimen, and the absence of additional high-risk lesions.[20-24] In a recent single institution review of 318 patients diagnosed with ADH from 2013-2017, the risk of upgrade at surgical excision for patients considered to have low-risk ADH using similar criteria was 2%.[23] In another study which prospectively followed patients with low-risk ADH, 4.4% developed a malignancy at a median follow-up of 5.2 years without surgery, compared with 7.3% of patients who underwent surgical excision of their ADH (P=.2). The only predictor of a subsequent breast cancer diagnosis was a personal history of breast cancer.[21]

Combined, these data suggest that there is a subset of patients diagnosed with ADH that can be safely observed, using the factors cited above, input from the multidisciplinary radiology and pathology teams, and shared decision-making. Surgical excision should be recommended for patients at higher risk of upgrade, who are more risk adverse, and/or for whom follow-up is not feasible.

Indications for surgical excision of lobular neoplasia (LN)

LN encompasses both atypical lobular hyperplasia (ALH) and LCIS. LCIS can be separated into classic (CLCIS) and non-classic variants.

ALH and Classic LCIS

Pathologically, ALH and classic LCIS are characterized by e-cadherin negative, discohesive cells in the terminal ductal lobular unit (TDLU), usually identified incidentally at biopsy for another imaging target. With careful radiographic and pathologic correlation, the upgrade rate is between 0-4%.[25-29] Similar to ADH, LN is associated with an increased risk of future breast cancer; the risk is 1-2% per year.10,11 Currently there is no consensus on whether LN identified on MRI biopsy is associated with a higher upgrade rate.[30,31] Biopsies showing LN but that are discordant with imaging are more frequently upgraded (versus incidental LN) so surgical excision is recommended.[25,28] When LN is associated with other high-risk lesions such ADH and non-classic LCIS , excisional biopsy is recommended due to an upgrade rate of at least 25%.[25,32]

Non-classic LCIS

- Pleomorphic LCIS (PLCIS) is a rare variant of LCIS characterized by large pleomorphic cells with marked nuclear atypia, comedonecrosis, and microcalcifications similar to DCIS. In contrast to CLCIS, PLCIS and its related cancers are more likely to be estrogen receptor negative, HER-2 positive, and higher grade.[33,34] Imaging findings include calcifications, architectural distortion, or a

mass. Retrospective single institution studies have found the upgrade rate for PLCIS identified on CNB to be significantly higher than that for CLCIS, with invasive cancer or DCIS identified in 25-60% of surgical specimens.[32-36] It is recommended that PLCIS be surgically excised with negative margins due to its multifocal nature and high rate of associated invasive disease.[36-39] There is limited data on what constitutes a negative margin for PLCIS; a pooled analysis of 9 studies including 85 patients found recurrences rates of 3.5%, 26.3% and 36.4% for ≥1mm, <1mm, and positive margins, respectively. Therefore, for PLCIS, 2mm margins are recommended similar to the Society of Surgical Oncology/American Society for Radiation Oncology/American Society of Clinical Oncology Consensus Guideline on Margins for ductal carcinoma in situ.[40]

- *Florid LCIS (FLCIS)* was recognized in 2019 by the World Health Organization (WHO) as a distinct LCIS variant, characterized by marked mass-forming distention of the TDLU acini with minimal intervening stroma. It should not be confused with extensive CLCIS which is characterized by involvement of multiple ducts without extensive acinar expansion.[41] Imaging findings are similar to PLCIS. The upgrade rate to invasive cancer or DCIS is 30-40%, so surgical excision with 2mm margins is recommended to exclude upgrade to malignancy similar to PLCIS.[32,33]

In summary, the decision to recommend excisional biopsy versus active surveillance depends on the variant of LN, imaging findings, and the presence of other high-risk lesions. Upgrade rates for LCIS vary significantly based on these factors, so careful attention to the variant type and radiographic-pathologic concordance is essential.

Indications for surgical excision for columnar cell lesions (CCL), including flat epithelial atypia (FEA)

CCLs are often identified with mammographic calcifications and are characterized by enlarged TDLUs lined by columnar epithelial cells with apical snouts. WHO classifies CCLs without atypia as columnar cell change (CCC) and columnar cell hyperplasia (CCH), whereas FEA denotes any columnar cell lesion (CCC or CCH) with cytologic atypia.[41] The upgrade rate of CCL without atypia is low (<2%) and excision is not recommended.[42,43]

In contrast, a 2021 meta-analysis of 2484 cases (from 42 studies between 2004-2020) of isolated FEA identified on CNB found a pooled upgrade rate of 5%. If 90% or more of the calcifications were removed, the rate was 0%. There were no other factors identified that predicted upgrade. In 17% of pure FEA cases in this meta-analysis, ADH was identified in the excision specimen, which could impact patient management.[44] The most recent studies report similar rates of ADH on excision but low malignant upgrade rates of 0-3%.[45-48] Small retrospective single institution studies of observation of FEA suggest that this is a reasonable option in selected patients, especially those in whom the majority of the target was removed on CNB.[49,50]

Indications for excision of papillary lesions

"Papillary lesions," as a term, encompasses a range of pathologies including intraductal papilloma, atypical papillary lesions, papillary DCIS, papillary carcinoma, and encapsulated papillary carcinoma.[41] When no further pathologic characterization is provided, the lesion should be surgically excised.

Intraductal papilloma with atypia or atypical papillary lesions are pathologically upgraded at the time of surgical excision up to 20-30% of the time.[51-53] Therefore, surgical excision for these lesions is recommended.

Intraductal papilloma (IP) without atypia

Management of these lesions has evolved in recent years and varies depending on imaging or clinical presentation. As with other high-risk or benign lesions, careful radiographic and pathologic concordance is recommended.

- *Asymptomatic intraductal papillomas:* These lesions can undergo active imaging surveillance because of the low upgrade rate, based on recent literature. A prospective multicenter registry enrolled 116 asymptomatic patients with intraductal papillomas and BI-RADS $\leq$ 4 and found a 1.7% upgrade to DCIS regardless of lesion size or patient age. No invasive cancers were identified.[54] Several large retrospective studies have reported 1-5% upgrade rates (to DCIS or invasive disease) for asymptomatic intraductal papillomas for which there was excellent clinical, radiologic, and pathologic concordance. Size >1 cm, age >50 years at diagnosis, lesion multiplicity, location (peripheral), and >50% of the lesion remaining after CNB are associated with a higher risk of upgrade, but these associations are not consistent across studies.[51,52,55,56]
- *Symptomatic intraductal papillomas* that present as a palpable mass or with nipple discharge are associated with a slightly higher risk of upgrade to DCIS or invasive cancer. Surgical excision can be considered in this situation both to rule out malignancy and provide symptom relief.[56]

Indications for surgical excision of radial scars (complex sclerosing lesions)

Radial scars are characterized histologically by a central sclerotic core from which ducts and lobules radiate circumferentially. Traditionally, the term complex sclerosing lesion (CSL) is reserved for radial scars >1cm in size, but the two are often used interchangeably in modern studies and clinical practice.[57] CSLs may be identified incidentally at the time of CNB or may present as architectural distortion or spiculated masses on breast imaging. Although older studies reported rates of malignancy up to 25% at the time of surgical excision, more modern series describe a much lower upgrade rate.[58-62]

CSLs without atypia

A 2019 meta-analysis of 49 studies that included 3163 CSLs found a 1% upgrade rate in lesions without atypia evaluated with vacuum-assisted biopsy, and a 1-5% upgrade rate in those evaluated with 8-16 gauge CNB.[63] No upgrades were noted for microscopic CSLs found incidentally on evaluation of another target lesion or for radiologic CSLs <5mm. Single institution retrospective studies of short-term observation instead of excision have not identified progression or missed malignancy. Surveillance for pure CSLs with radiologic-pathologic concordance is therefore reasonable depending on the imaging finding, lesion size, and biopsy method. No MRI features have been found to predict the need for excision or likelihood of upgrade as many benign CSL demonstrate enhancement on imaging.[64] Exceedingly low upstage rates are noted for CSL with lack of enhancement on MRI.[65]

CSLs with atypia

The rate of upgrade if atypia is present is as high as 35%[58,66] so routine excision is recommended.

Indications for surgical excision of mucocele-like lesions (MLLs)

MLLs are rare lesions characterized by epithelium-lined cysts filled with mucin that are prone to rupture and extravasate mucin into the surrounding stroma. There are classic and variant forms of MLL, but there is limited information about the clinical significance of the different forms.[67-71] Previously, it was recommended that all MLLs be excised due to the difficulty in distinguishing them from mucinous carcinoma.[72] A MLL typically presents with calcifications on mammography but can also present as a

mass or incidental finding. Due to the rare nature of this lesion, all studies are small single institution retrospective reviews, so careful radiographic-pathologic concordance assessment is recommended.

Mucocele lesions without atypia

Upgrade rate to invasive cancer is rare when there is radiographic-pathologic concordance. Routine surgical excision is not recommended for these patients. Recent studies report a 0-4% risk of upgrade to invasive cancer.[70,73-75]

Mucocele like lesions with atypia

Surgical excision of these lesions is recommended for these lesions. The upgrade rate to breast cancer is as high as 31%.[68,73,76]

Indications for excision of desmoid tumors (aggressive fibromatosis)

Desmoid tumors/fibromatosis are benign, but locally aggressive mesenchymal tumors that occur rarely in the breast. They may be incidental or associated with trauma, prior surgery, Familial Adenomatous Polyposis (FAP), or Gardner syndrome (a variant of FAP). Although wide excision was the standard management, many recurred and surgery can cause significant morbidity, depending on lesion location. Recurrence and progression are more common in young patients, with large tumors, with incomplete resection, and for extra-abdominal locations.

When desmoid tumor or fibromatosis is identified on core biopsy, the current standard is observation given the variable behavior of the tumor. Management may then be directed by the demonstrated behavior of that desmoid tumor. Observation includes imaging every 3-6 months, with mammogram, MRI, or computed tomography (CT) as clinically indicated; most desmoid tumors are best followed with MRI. For patients who are symptomatic or have interval growth of the desmoid tumor/fibromatosis during observation, surgery should be considered with an attempt at an R0 resection if feasible without significant morbidity. Additional adjuvant therapies may be used but are beyond the scope of this guideline.[77-83]

Indications for excision of pseudoangiomatous stromal hyperplasia (PASH)

PASH is characterized by myofibroblast proliferation mimicking a vascular lesion. It can be found incidentally on CNB or may present as a mass or enlargement of the breast.[84,85] When PASH is identified on CNB and pathology is considered concordant with imaging, surgical excision is not necessary.[86-89] However, symptomatic lesions may require excision, and recurrence requiring repeat surgery has been described.[86,90]

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