EDITORIAL

Holly J. Pederson, MD
Director, Medical Breast Services, Cleveland Clinic, Cleveland, OH; Associate Professor, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, OH

Debra Pratt, MD
Departments of General Surgery and Breast Services, Cleveland Clinic, Cleveland, OH; Clinical Assistant Professor, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, OH

Benjamin C. Calhoun, MD, PhD
Director of Breast Pathology, Department of Pathology and Laboratory Medicine, Lineberger Comprehensive Cancer Center, Chapel Hill, NC; Associate Professor, University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, NC

Surgical de-escalation: Are we ready for 'observation' of benign high-risk breast lesions found on core needle biopsy?

One focus of the article by Vegunta and colleagues[1] in this issue of the *Journal* is whether benign proliferative lesions such as atypical hyperplasia diagnosed on core needle biopsy (CNB) require surgical excision. The estimated upgrade rate—that is, finding breast cancer at surgical excision—is variable, and consensus recommendations for an acceptable threshold for excision are emerging.[2] As the sensitivity of breast imaging has improved, more benign lesions are being found,[3–6] and rates of upgrade have been decreasing.

See related article, page 423

Surgical de-escalation is part of a larger movement of de-escalation of multidisciplinary breast cancer treatment. The challenge is to balance oncologic outcomes with surgical morbidity and quality of life. In this case, the de-escalation may be preceding consensus on upgrade thresholds, definitions, standardized clinical workflow, agreement on follow-up, and incorporation of patient preference.

Imaging-guided CNB to assess abnormalities detected on breast imaging has been the standard of care for decades. From 1 to 2 million benign and high-risk CNBs are performed annually in the United States.[7,8] Clear, accepted clinical guidelines are followed for the management of malignant lesions, but management of high-risk lesions differs among institutions. Further, the patient's level of risk and risk tolerance needs to be considered. The question is whether there are currently enough data so that a "recommendation against excision" can be made. One final concern is that surgical de-escalation may actually contribute to disparities.

doi:10.3949/ccjm.90a.23024

BACKGROUND AND DEFINITIONS

The history of the surgical management of breast cancer is a continuum of de-escalation. The early Halsted radical mastectomy, developed in 1894 and used for decades, was a disfiguring surgery removing the breast, all axillary lymph nodes, and the chest wall musculature. Later in the 20th century, it was replaced by the simple mastectomy (sparing the chest wall musculature and axillary lymph nodes) after results of a national trial showed equivalent survival.[9] Toward the end of the 20th century, studies showed breast conservation (partial mastectomy with clear margins) and radiation to be noninferior to mastectomy for early-stage disease.[10–12]

The surgical management of the axilla was the next area of de-escalation, with trials showing equivalent outcomes with sentinel lymph node biopsy and axillary dissection in early-stage breast cancer.[13–16] Simultaneously, de-escalation of radiation therapy for breast conservation was investigated. Shortened courses of radiation (3 weeks compared with 5 weeks), partial breast irradiation, intraoperative radiation therapy, and the option of excluding radiation therapy in select patients (over age 70) have been explored and are finding their places.[12,17–20]

Future areas of de-escalation of surgery include active surveillance for ductal carcinoma in situ.[21–23] Cryoablation is also being investigated.[24] Large ran-

TABLE 1
Curtailing therapy at age 70: Ageism?

Current age	Additional life expectancy, years	Estimated total years
70	17.6	87.6
75	13.7	88.7
80	10.2	90.2
85	7.3	92.3
90	5.1	95.1

Data from reference 25 and 26.

domized controlled trials documenting the safety and efficacy of these approaches have preceded and should precede clinical adoption.[21–23]

Women age 60 and older represent 59% of invasive breast cancer cases, and more than 30% occur in women age 70 and older.[25] Many trials involving de-escalation have resulted in age 70 as a threshold for alternative treatment approaches that are appropriate for most but not all older women. The US Social Security Administration provides an online life-expectancy calculator for citizens to estimate their remaining life span and plan for retirement (**Table 1**).[25,26] An average 70-year-old female has an estimated life expectancy of 17.6 years to an estimated life span of 87.6 years. An average octogenarian has an estimated life expectancy of 10.2 years to 90.2 years, and an average 90-year-old has an estimated life expectancy of 5.1 years to 95.1 years. A healthy 70-year-old may still have a significant risk of recurrence. Both disease-free survival and overall survival should be part of the shared decision-making discussion, particularly in healthy older women.

As one example of de-escalation, the Society of Surgical Oncology Choosing Wisely campaign of 2016, an initiative of the American Board of Internal Medicine Foundation, encouraged the advancement of a national dialogue on avoiding "…sentinel node biopsy in clinically node-negative women ≥ 70 years of age with early stage hormone receptor positive, HER2 negative invasive breast cancer."[27] Patients, however, are hesitant to de-escalate cancer therapy.[28] A survey of newly diagnosed patients showed that 53% accepted aggressive treatments with significant side effects for a 3-month benefit in survival.[29] It has been suggested that an upgrade of 3% or less could be a reasonable threshold for offering surveillance in place of surgery,[30] although it remains to be seen whether women with benign atypical lesions will accept this threshold for risk tolerance. Thresholds for excision based on limited evidence are concerning, and anticipated regret is a real and powerful driver of patient choice.[31]

SELECTING PATIENTS FOR NONOPERATIVE MANAGEMENT: CRITERIA NEEDED

The perception among patients and providers, however, may be that immediate surgical excision avoids underdiagnosis and undertreatment of malignancy. Well-defined, evidence-based criteria for the selection of patients for nonoperative management would help address these concerns.

Active surveillance could first be offered to patients who would have been offered nonoperative management in prospective multi-institutional trials. Two small such trials suggest that an upgrade rate of 3% or lower could be a reasonable threshold for offering surveillance vs surgery.[32,33] The first is a prospective registry of 77 patients with pure lobular neoplasia (atypical lobular hyperplasia or lobular carcinoma in situ) who had an upgrade rate of 1% to 3%. The study also includes a literature summary of upgrade rates ranging from 0% to 27% in small retrospective single-institution studies, thereby demonstrating the need for trials with prospective data.[32]

The second registry involved 116 patients with papillomas without atypia, 66% of whom presented with mammographic mass or distortion, showing a 1.7% upgrade rate (2/116).[33] The 3% threshold is similar to the upgrade rate of less than 2% for Breast Imaging Reporting and Data System Category 3 lesions recommending short-term follow-up with repeat imaging at 6 months as an alternative to biopsy, as the lesion is felt to have a less than 2% chance of being malignant.[34] Individual institutions embarking on processes for determining radiologic-pathologic concordance must agree on patient selection, imaging findings, sampling issues, and expected follow-up. It is also important to remember that the recommendation for observation does not preclude a later recommendation for surgical excision, should findings change.[35]

The stated concerns of proponents of surgical de-escalation involving benign high-risk lesions are those of overdiagnosis and overtreatment (**Table 2**). Overdiagnosis refers to biologically indolent cancers that may not go on to cause the individual harm,[36] as evidenced by the increased rates of ductal carcinoma in situ detection resulting from improved mammographic screening without resultant increases in invasive breast cancer or breast cancer mortality.[37] It is important to note that this could also be viewed

TABLE 2
Definitions surrounding surgical de-escalation

Radiologic-pathologic concordance	The imaging and pathologic findings are considered to be concordant when the pathologic result provides an acceptable explanation for the imaging feature and discordant when they do not
Overdiagnosis	Finding cases of cancer with a screening test (such as a mammography) that will never cause any symptoms
Overtreatment	Interventions that do not benefit the patient or where the risk of harm from the intervention is likely to outweigh any benefit the patient will receive

as early diagnosis, but may lead to falsely improved survival statistics given potential lead-time bias. The US Preventive Services Task Force in 2016 set forth de-escalating screening guidelines that women begin mammograms at the age of 50 and continue every other year until age 74[38] because of concerns regarding overdiagnosis, despite evidence supporting similar mortality reduction with screening mammography in women ages 40 to 49.[39] In May 2023, after recognizing that mammograms starting at age 40 and modeled every other year to save (conservatively) 19% more lives, the US Preventive Services Task Force changed its recommendations to starting at age 40, yet they still recommend screening every other year.[40] The National Comprehensive Cancer Network[41] and the American College of Radiology[42] continue to recommend annual mammograms beginning at age 40.

Overtreatment refers to the use of therapies with minimal benefit to patients.

GUIDELINE DISAGREEMENT

Accepted guidelines exist for margin width, adjuvant radiation, and sentinel lymph node biopsy in the cancer setting. However, guidelines differ for surgery vs observation for benign high-risk lesions.[43–46] Benign lesions on CNB for which surgical excision was historically recommended include atypical hyperplasia (both ductal and lobular), lobular carcinoma in situ, radial scars, and papillary lesions.[41] Though the 2016 American Society of Breast Surgeons proposed guidelines[47] suggested observation as an option for all but atypical ductal hyperplasia, pleomorphic lobular carcinoma in situ, and papillomas with atypia, the guidelines were not widely adopted. The more conservative National Comprehensive Cancer Network guidelines now recommend that atypical lobular hyperplasia/lobular carcinoma in situ, if radiologically and pathologically concordant and adequately sampled, can be observed for a period of 1 year in select patients (undefined) or excised, at the surgeon's discretion.[41] Screening magnetic resonance imaging (MRI) is not mentioned despite recommendations of the American College of Radiology to offer MRI screening to such patients.[42]

The concept of radiologic-pathologic concordance is difficult to define. Atypical lobular hyperplasia and lobular carcinoma in situ are felt to be incidental findings on performed CNBs as a result of imaging abnormalities. It is unclear how incidental findings can explain imaging abnormalities. There is also no consensus on adequate sampling (core needle size, number of passes, and degree of lesion removal), whether there is pathologic reporting regarding the extent of the abnormality, and whether the mode of detection is relevant. Some authors recommend observation for high-risk lesions in cases involving microcalcifications on a screening mammogram in an asymptomatic woman of average risk. Other authors suggest biopsy of mass lesions and architectural distortion on mammograms. Studies have dissimilar inclusion criteria, and rates of upgrade vary widely.[30] Some studies include masses or non-mass-like enhancement on breast MRI (in high-risk patients by definition). More recent studies have not included cases with these latter findings as true upgrades, partially explaining the trend toward lower upgrade rates in recent literature.

Further, subsequent high-risk screening recommendations are inconsistent, and the uptake of preventive medication is classically poor.[48–50] Many patients are noncompliant with follow-up recommendations (even for Breast Imaging Reporting and Data System-3 imaging studies with short-interval follow-up recommended).[51] Few small prospective studies of observation with limited follow-up have been published and do not seem to be generalizable to different practice settings.[51–55] For instance, Middleton et al[52] published a series of 104 patients with pure lobular

neoplasia followed for a median of 3.4 years: 5 patients were subsequently diagnosed with breast cancer (3 of 5 at an unrelated site). Laws et al[53] noted that in their high-risk clinic where MRI screening is not routinely recommended and following multidisciplinary discussion of all benign high-risk lesions, atypical lobular hyperplasia and classic lobular carcinoma in situ have been safely managed thus far without surgical excision based on 80 patients with pure lobular neoplasia and median follow-up of 27 months.[53]

Another study examined 478 patients with 483 atypical ductal hyperplasia lesions; 309 were observed and 174 underwent excision.[54] With a median follow-up of 5.2 years, 2 cancers were identified at the index site in the surgery group (1.5%) and 3 in those observed (1.2%).[54] A prospective study successfully triaged patients to surgery vs observation following the establishment of predefined firm guidelines and performance of rigorous radiologic-pathologic correlation.[55]

WORSENING DISPARITIES

Finally, it must be considered that women of color and low socioeconomic means do not receive optimal care. It has been demonstrated that Black women are more likely to be screened at nonaccredited facilities, without current equipment (including digital breast tomosynthesis, much less dedicated breast MRI), and with fewer resources for follow-up.[56,57] Disparities in uptake to MRI have been demonstrated according to educational level.[58] Disparities in cancer treatment that have been demonstrated include lower rates of genetic testing in high-risk individuals,[59] delays in diagnosis,[60] and less appropriate surgery, radiation, and chemotherapy.[61,62] Adherence to endocrine therapy in the cancer setting is suboptimal,[63–66] perhaps in part owing to insurance coverage that also impacts MRI screening and uptake of and adherence to risk-reducing medication in following patients with benign high-risk lesions. Owing to these stated concerns, careful observation of benign high-risk lesions in women of low socioeconomic status may be destined for failure due to insurmountable social barriers.

OBSERVATION MAY NOT BE READY FOR WIDESPREAD IMPLEMENTATION

In summary, the potential for upgrade to malignancy at surgical biopsy remains the principal reason for excision of benign high-risk lesions detected on CNB. In the authors' opinion, the recommendation for observation of such lesions may not be ready for widespread implementation. Appropriate surgical de-escalation requires data demonstrating lack of utility of a given intervention combined with an informed shared decision-making discussion with the patient and standardized processes in place to assure quality.

Presently, upgrade rates in the literature are variable and have an unacceptably broad range, criteria for patient selection vary, consensus statements are vague, institutions with multidisciplinary discussions of radiologic-pathologic concordance are the exception, and patients not referred for surgical consultation (particular in lower socioeconomic groups) may have reduced access to and lowered rates of adherence to appropriate imaging and preventive strategies. While many institutions have adopted observation for benign atypical lesions, long-term data on oncologic safety are lacking.

Overdiagnosis and overtreatment are of concern and add to healthcare costs and patient morbidity, but de-escalation in this setting will take time for agreement and standardization, and concern remains regarding appropriate follow-up, particularly in vulnerable populations. Offering surveillance for high-risk lesions identified by CNB is a practice change that may be premature for many institutions.

DISCLOSURES

Dr. Pederson has disclosed consulting for Myriad Genetics and Vira Health. Dr. Calhoun reports serving as advisor or review panel participant for Luminex. The other author reports no relevant financial relationships which, in the context of her contributions, could be perceived as a potential conflict of interest.

REFERENCES

1. **Vegunta S, Mussallem DM, Kaur AS, Pruthi S, Klassen CL.** Atypical hyperplasia of the breast: clinical cases and management strategies. Cleve Clin J Med 2023; 90(7):423–431. doi:10.3949/ccjm.90a.22098
2. **Angarita FA, Brumer R, Castelo M, Esnaola NF, Edge SB, Takabe K.** De-escalating the management of in situ and invasive breast cancer. Cancers (Basel) 2022; 14(19):4545. doi:10.3390/cancers14194545
3. **Bahl M, Lamb LR, Lehman CD.** Pathologic outcomes of architectural distortion on digital 2D versus tomosynthesis mammography. AJR Am J Roentgenol 2017; 209(5):1162–1167. doi:10.2214/AJR.17.17979
4. **Freer PE, Niell B, Rafferty EA.** Preoperative tomosynthesis-guided needle localization of mammographically and sonographically occult breast lesions. Radiology 2015; 275(2):377–383. doi:10.1148/radiol.14140515
5. **Ray KM, Turner E, Sickles EA, Joe BN.** Suspicious findings at digital breast tomosynthesis occult to conventional digital mammography: imaging features and pathology findings. Breast J 2015; 21(5):538–542. doi:10.1111/tbj.12446
6. **Partyka L, Lourenco AP, Mainiero MB.** Detection of mammographically occult architectural distortion on digital breast tomosynthesis screening: initial clinical experience. AJR Am J Roentgenol 2014; 203(1):216–222. doi:10.2214/AJR.13.11047

7. **Visscher DW, Frank RD, Carter JM, et al.** Breast cancer risk and progressive histology in serial benign biopsies. J Natl Cancer Inst 2017; 109(10):djx035. doi:10.1093/jnci/djx035
8. **American Cancer Society.** Breast cancer facts & figures: 2019–2020. https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/breast-cancer-facts-and-figures/breast-cancer-facts-and-figures-2019-2020.pdf. Accessed May 24, 2023.
9. **Fisher B, Montague E, Redmond C, et al.** Comparison of radical mastectomy with alternative treatments for primary breast cancer. A first report of results from a prospective randomized clinical trial. Cancer 1977; 39(6 suppl):2827–2839. doi:10.1002/1097-0142(197706)39:6<2827::aid-cncr2820390671>3.0.co;2-i
10. **Favourable and unfavourable effects on long-term survival of radiotherapy for early breast cancer: an overview of the randomised trials.** Early Breast Cancer Trialists' Collaborative Group. Lancet 2000; 355(9217):1757–1770. pmid:10832826
11. **Fisher B, Anderson S, Bryant J, et al.** Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. N Engl J Med 2002; 347(16):1233–1241. doi:10.1056/NEJMoa022152
12. **Clarke M, Collins R, Darby S, et al.** Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and 15-year survival: an overview of the randomised trials. Lancet 2005; 366(9503):2087–2106. doi:10.1016/S0140-6736(05)67887-711
13. **Krag DN, Anderson SJ, Julian TB, et al.** Sentinel-lymph-node resection compared with conventional axillary-lymph-node dissection in clinically node-negative patients with breast cancer: overall survival findings from the NSABP B-32 randomised phase 3 trial. Lancet Oncol 2010; 11(10):927–933. doi:10.1016/S1470-2045(10)70207-2
14. **Giuliano AE, Haigh PI, Brennan MB, et al.** Prospective observational study of sentinel lymphadenectomy without further axillary dissection in patients with sentinel node-negative breast cancer [published correction appears in J Clin Oncol 2000; 18(22):3877]. J Clin Oncol 2000; 18(13):2553–2559. doi:10.1200/JCO.2000.18.13.2553
15. **Veronesi U, Paganelli G, Viale G, et al.** A randomized comparison of sentinel-node biopsy with routine axillary dissection in breast cancer. N Engl J Med 2003; 349(6):546–553. doi:10.1056/NEJMoa012782
16. **Giuliano AE, Ballman KV, McCall L, et al.** Effect of axillary dissection vs no axillary dissection on 10-year overall survival among women with invasive breast cancer and sentinel node metastasis: The ACOSOG Z0011 (Alliance) Randomized Clinical Trial. JAMA 2017; 318(10):918–926. doi:10.1001/jama.2017.11470
17. **Whelan TJ, Pignol JP, Levine MN, et al.** Long-term results of hypofractionated radiation therapy for breast cancer. N Engl J Med 2010; 362(6):513–520. doi:10.1056/NEJMoa0906260
18. **Valente SA, Tendulkar RD, Cherian S, et al.** TARGIT-R (retrospective): 5-year follow-up evaluation of intraoperative radiation therapy (IORT) for breast cancer performed in North America. Ann Surg Oncol 2021; 28(5):2512–2521. doi:10.1245/s10434-020-09432-3
19. **Veronesi U, Orecchia R, Maisonneuve P, et al.** Intraoperative radiotherapy versus external radiotherapy for early breast cancer (ELIOT): a randomised controlled equivalence trial. Lancet Oncol 2013; 14(13):1269–1277. doi:10.1016/S1470-2045(13)70497-2
20. **Shah C, Vicini F, Shaitelman SF, et al.** The American Brachytherapy Society consensus statement for accelerated partial-breast irradiation. Brachytherapy 2018; 17(1):154–170. doi:10.1016/j.brachy.2017.09.004
21. **US National Institutes of Health.** Comparing an operation to monitoring, with or without endocrine therapy (COMET) trial for low risk DCIS (COMET). ClinicalTrials.gov Identifier: NCT02926911. https://clinicaltrials.gov/ct2/show/NCT02926911. Accessed May 24, 2023.
22. **US National Institutes of Health.** Management of low-risk (grade I and II) DCIS (LORD). ClinicalTrials.gov Identifier: NCT02492607. https://clinicaltrials.gov/ct2/show/NCT02492607. Accessed May 24, 2023.
23. **BioMed Central of Springer Nature International Standard Randomised Controlled Trials.** Surgery versus active monitoring for LOw RISk ductal carcinoma in situ. http://isrctn.com/ISRCTN27544579. Accessed May 24, 2023.
24. **Fine RE, Gilmore RC, Dietz JR, et al.** Cryoablation without excision for low-risk early-stage breast cancer: 3-year interim analysis of ipsilateral breast tumor recurrence in the ICE3 Trial. Ann Surg Oncol 2021; 28(10):5525–5534. doi:10.1245/s10434-021-10501-4
25. **DeSantis CE, Ma J, Gaudet MM, et al.** Breast cancer statistics, 2019. CA Cancer J Clin 2019; 69(6):438–451. doi:10.3322/caac.21583
26. **Social Security Administration.** Retirement and survivors benefits: life expectancy calculator. https://www.ssa.gov/oact/population/longevity.html. Accessed May 24, 2023.
27. **McKevitt E, Cheifetz R, DeVries K, et al.** Sentinel node biopsy should not be routine in older patients with ER-positive HER2-negative breast cancer who are willing and able to take hormone therapy. Ann Surg Oncol 2021; 28(11):5950–5957. doi:10.1245/s10434-021-09839-6
28. **Wang T, Mott N, Miller J, et al.** Patient perspectives on treatment options for older women with hormone receptor-positive breast cancer: a qualitative study. JAMA Netw Open 2020; 3(9):e2017129. doi:10.1001/jamanetworkopen.2020.17129
29. **Slevin ML, Stubbs L, Plant HJ, et al.** Attitudes to chemotherapy: comparing views of patients with cancer with those of doctors, nurses, and general public. BMJ 1990; 300(6737):1458–1460. doi:10.1136/bmj.300.6737.1458
30. **Harbhajanka A, Gilmore HL, Calhoun BC.** High-risk and selected benign breast lesions diagnosed on core needle biopsy: evidence for and against immediate surgical excision. Mod Pathol 2022; 35(11):1500–1508. doi:10.1038/s41379-022-01092-w
31. **Katz SJ, Lantz PM, Janz NK, et al.** Patient involvement in surgery treatment decisions for breast cancer. J Clin Oncol 2005; 23(24):5526–5533. doi:10.1200/JCO.2005.06.217
32. **Nakhlis F, Gilmore L, Gelman R, et al.** Incidence of adjacent synchronous invasive carcinoma and/or ductal carcinoma in-situ in patients with lobular neoplasia on core biopsy: results from a prospective multi-institutional registry (TBCRC 020). Ann Surg Oncol 2016; 23(3):722–728. doi:10.1245/s10434-015-4922-4
33. **Nakhlis F, Baker GM, Pilewskie M, et al.** The incidence of adjacent synchronous invasive carcinoma and/or ductal carcinoma in situ in patients with intraductal papilloma without atypia on core biopsy: results from a prospective multi-institutional registry (TBCRC 034). Ann Surg Oncol 2021; 28(5):2573–2578. doi:10.1245/s10434-020-09215-w
34. **Berg WA, Berg JM, Sickles EA, et al.** Cancer yield and patterns of follow-up for BI-RADS category 3 after screening mammography recall in the national mammography database. Radiology 2020; 296(1):32–41. doi:10.1148/radiol.2020192641
35. **Marti JL.** ASO author reflections: "high-risk" lesions of the breast: low risk of cancer, high risk of overtreatment. Ann Surg Oncol 2021; 28(9):5156–5157. doi:10.1245/s10434-021-09845-8
36. **Welch HG, Prorok PC, O'Malley AJ, Kramer BS.** Breast-cancer tumor size, overdiagnosis, and mammography screening effectiveness. N Engl J Med 2016; 375(15):1438–1447. doi:10.1056/NEJMoa1600249
37. **Narod SA, Iqbal J, Giannakeas V, Sopik V, Sun P.** Breast cancer mortality after a diagnosis of ductal carcinoma in situ. JAMA Oncol 2015; 1(7):888–896. doi:10.1001/jamaoncol.2015.2510
38. **Siu AL; US Preventive Services Task Force.** Screening for breast cancer: US Preventive Services Task Force recommendation statement [published correction appears in Ann Intern Med 2016; 164(6):448]. Ann Intern Med 2016; 164(4):279–296. doi:10.7326/M15-2886
39. **Giannakeas V, Narod SA.** The incidence of fatal breast cancer measures the increased effectiveness of therapy in women participating in mammography screening. Cancer 2019; 125(12):2130. doi:10.1002/cncr.32008
40. **US Preventive Services Task Force.** Task Force issues draft recommendation statement on screening for breast cancer. May 9, 2023. https://www.uspreventiveservicestaskforce.org/uspstf/sites/default/files/file/supporting_documents/breast-cancer-screening-draft-rec-bulletin.pdf. Accessed May 25, 2023.
41. **Bevers TB, Helvie M, Bonaccio E, et al.** Breast cancer screening and diagnosis, Version 3.2018, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw 2018; 16(11):1362–1389. doi:10.6004/jnccn.2018.0083

42. **Monticciolo DL, Newell MS, Moy L, Niell B, Monsees B, Sickles EA.** Breast cancer screening in women at higher-than-average risk: recommendations from the ACR. J Am Coll Radiol 2018; 15(3 pt A):408–414. doi:10.1016/j.jacr.2017.11.034
43. **Glenn ME, Throckmorton AD, Thomison JB 3rd, Bienkowski RS.** Papillomas of the breast 15 mm or smaller: 4-year experience in a community-based dedicated breast imaging clinic. Ann Surg Oncol 2015; 22(4):1133–1139. doi:10.1245/s10434-014-4128-1
44. **Georgian-Smith D, Lawton TJ.** Variations in physician recommendations for surgery after diagnosis of a high-risk lesion on breast core needle biopsy. AJR Am J Roentgenol 2012; 198(2):256–263. doi:10.2214/AJR.11.7717
45. **Kappel C, Seely J, Watters J, Arnaout A, Cordeiro E.** A survey of Canadian breast health professionals' recommendations for high-risk benign breast disease. Can J Surg 2019; 62(5):358–360. doi:10.1503/cjs.009018
46. **Nizri E, Schneebaum S, Klausner JM, Menes TS.** Current management practice of breast borderline lesions—need for further research and guidelines. Am J Surg 2012; 203(6):721–725. doi:10.1016/j.amjsurg.2011.06.052
47. **American Society of Breast Surgeons.** Consensus guideline on concordance assessment of image-guided breast biopsies and management of borderline or high-risk lesions. https://www.breastsurgeons.org/docs/statements/Consensus-Guideline-on-Concordance-Assessment-of-Image-Guided-Breast-Biopsies.pdf. Accessed May 24, 2023.
48. **Gao Y, Albert M, Young Lin LL, et al.** What happens after a diagnosis of high-risk breast lesion at stereotactic vacuum-assisted biopsy? An observational study of postdiagnosis management and imaging adherence. Radiology 2018; 287(2):423–431. doi:10.1148/radiol.2017171665
49. **Ropka ME, Keim J, Philbrick JT.** Patient decisions about breast cancer chemoprevention: a systematic review and meta-analysis. J Clin Oncol 2010; 28(18):3090–3095. doi:10.1200/JCO.2009.27.8077
50. **Smith SG, Sestak I, Forster A, et al.** Factors affecting uptake and adherence to breast cancer chemoprevention: a systematic review and meta-analysis. Ann Oncol 2016; 27(4):575–590. doi:10.1093/annonc/mdv590
51. **Chung CS, Giess CS, Gombos EC, et al.** Patient compliance and diagnostic yield of 18-month unilateral follow-up in surveillance of probably benign mammographic lesions. AJR Am J Roentgenol 2014; 202(4):922–927. doi:10.2214/AJR.13.11137
52. **Middleton LP, Sneige N, Coyne R, et al.** Most lobular carcinoma in situ and atypical lobular hyperplasia diagnosed on core needle biopsy can be managed clinically with radiologic follow-up in a multidisciplinary setting. Cancer Med 2014; 3(3):492–499. doi:10.1002/cam4.223
53. **Laws A, Katlin F, Nakhlis F, Chikarmane SA, Schnitt SJ, King TA.** Atypical lobular hyperplasia and classic lobular carcinoma in situ can be safely managed without surgical excision. Ann Surg Oncol 2022; 29(3):1660–1667. doi:10.1245/s10434-021-10827-z
54. **Kilgore LJ, Yi M, Bevers T, et al.** Risk of breast cancer in selected women with atypical ductal hyperplasia who do not undergo surgical excision. Ann Surg 2022; 276(6):e932–e936. doi:10.1097/SLA.0000000000004849
55. **Li X, Ma Z, Styblo TM, Arciero CA, Wang H, Cohen MA.** Management of high-risk breast lesions diagnosed on core biopsies and experiences from prospective high-risk breast lesion conferences at an academic institution. Breast Cancer Res Treat 2021; 185(3):573–581. doi:10.1007/s10549-020-05977-9
56. **Betancourt JR, Tan-McGrory A, Flores E, López D.** Racial and ethnic disparities in radiology: a call to action. J Am Coll Radiol 2019; 16(4 pt B):547–553. doi:10.1016/j.jacr.2018.12.024
57. **Lee CI, Zhu W, Onega T, et al.** Comparative access to and use of digital breast tomosynthesis screening by women's race/ethnicity and socioeconomic status. JAMA Netw Open 2021; 4(2):e2037546. doi:10.1001/jamanetworkopen.2020.37546
58. **Haas JS, Hill DA, Wellman RD, et al.** Disparities in the use of screening magnetic resonance imaging of the breast in community practice by race, ethnicity, and socioeconomic status. Cancer 2016; 122(4):611–617. doi:10.1002/cncr.29805
59. **Reid S, Cadiz S, Pal T.** Disparities in genetic testing and care among black women with hereditary breast cancer. Curr Breast Cancer Rep 2020; 12(3):125–131. doi:10.1007/s12609-020-00364-1
60. **Lawson MB, Bissell MCS, Miglioretti DL, et al.** Multilevel factors associated with time to biopsy after abnormal screening mammography results by race and ethnicity. JAMA Oncol 2022; 8(8):1115–1126. doi:10.1001/jamaoncol.2022.1990
61. **Freedman RA, He Y, Winer EP, Keating NL.** Racial/ethnic differences in receipt of timely adjuvant therapy for older women with breast cancer: are delays influenced by the hospitals where patients obtain surgical care? Health Serv Res 2013; 48(5):1669–1683. doi:10.1111/1475-6773.12063
62. **Zhang L, King J, Wu XC, et al.** Racial/ethnic differences in the utilization of chemotherapy among stage I–III breast cancer patients, stratified by subtype: findings from ten National Program of Cancer registries states. Cancer Epidemiol 2019; 58:1–7. doi:10.1016/j.canep.2018.10.015
63. **Partridge AH, Wang PS, Winer EP, Avorn J.** Nonadherence to adjuvant tamoxifen therapy in women with primary breast cancer. J Clin Oncol 2003; 21(4):602–606. doi:10.1200/JCO.2003.07.071
64. **Wu XC, Lund MJ, Kimmick GG, et al.** Influence of race, insurance, socioeconomic status, and hospital type on receipt of guideline-concordant adjuvant systemic therapy for locoregional breast cancers. J Clin Oncol 2012; 30(2):142–150. doi:10.1200/JCO.2011.36.8399
65. **Huiart L, Ferdynus C, Giorgi R.** A meta-regression analysis of the available data on adherence to adjuvant hormonal therapy in breast cancer: summarizing the data for clinicians. Breast Cancer Res Treat 2013; 138(1):325–328. doi:10.1007/s10549-013-2422-4
66. **Warner ET, Tamimi RM, Hughes ME, et al.** Racial and ethnic differences in breast cancer survival: mediating effect of tumor characteristics and sociodemographic and treatment factors. J Clin Oncol 2015; 33(20):2254–2261. doi:10.1200/JCO.2014.57.1349

Address: *Holly Pederson, MD, Department of Breast Services, A80, Cleveland Clinic, 9500 Euclid Avenue, Cleveland, OH 44195; pedersh@ccf.org*